VI. Parenteral Nutrition (PN)

Parenteral nutrition is indicated for patients who are temporarily or permanently unable to meet nutritional requirements through enteral routes.

A. Nutrient Solutions for Parenteral Nutrition

1. The base solution is composed of amino acids, dextrose and lipid emulsion to which vitamins, minerals and electrolytes are added. The goal of parenteral nutrition is to provide adequate nutrients to support protein synthesis and metabolic homeostasis.

a. Nitrogen

Nitrogen is supplied in parenteral nutrition solutions as a mixture of essential and nonessential crystalline L-amino acids. Ordering of specialized solutions requires consultation with the Nutrition Support Service. The standard amino acid solution provides 4 kcal/g of protein and 6.25 g protein/g of nitrogen. At KUH a 15% amino acid concentration is typically used to compound PN unless a specialized solution is specified.

**15% Clinisol® (Amino Acid Injection)-sulfite free**

Each 100 mL of 15% Clinisol® contains:

- Amino Acids ........................................ 15.0 g
- Total Nitrogen .................................... 2.37 g

**Essential Amino Acids**

- Lysine ............................................. 1.18 g
- Leucine ............................................. 1.04 g
- Phenylalanine ..................................... 1.04 g
- Valine .............................................. 960 mg
- Histidine ........................................... 894 mg
- Isoleucine ......................................... 749 mg
- Methionine ......................................... 749 mg
- Threonine ........................................... 749 mg
- Tryptophan ......................................... 250 mg
Nonessential Amino Acids
Alanine ............................................... 2.17 g
Arginine .............................................. 1.47 g
Glycine ............................................... 1.04 g
Proline ............................................... 894 mg
Glutamic Acid ................................... 749 mg
Serine ............................................... 592 mg
Aspartic Acid .................................... 434 mg
Tyrosine ............................................. 39 mg

TrophAmine® 10% (Amino Acid Injections)

Each 100 mL of Trophamine® 10% contains:

Essential Amino Acids............... 10%
Isoleucine USP................................. 0.82 g
Leucine USP .................................... 1.4 g
Lysine ........................................... 0.82 g
(Methionine USP......................... 0.34 g
Phenylalanine USP ...................... 0.48 g
Threonine USP.............................. 0.42 g
Tryptophan USP............................. 0.20 g
Valine USP ..................................... 0.78 g
Cysteine ..........................................<0.016 g
Histidine USP .................................... 0.48 g
Tyrosine .............................................. 0.24 g
(added as Tyrosine USP ........ 0.044 g
and N-Acetyl-L-Tyrosine .......... 0.24 g)

Nonessential Amino Acids
Alanine USP....................................... 0.54 g
Arginine USP...................................... 1.2 g
Proline USP...................................... 0.68 g
Serine USP ....................................... 0.38 g
Glycine USP ...................................... 0.36 g
L-Aspartic Acid................................. 0.32 g
L-Glutamic Acid .............................. 0.50 g
Taurine ............................................. 0.025 g
Sodium Metabisulfite NF .......... <0.050 g
Water for Injection USP ......... qs

Total Amino Acids (grams/liter) ....... 100
Total Nitrogen (grams/liter) ........... 15.5
Protein Equivalent (grams/liter) ....... 97
Electrolytes (mEq/liter)
Sodium ....................................................... 5
Acetate ..................................................... 97
(provided as acetic acid and lysine acetate)
Chloride .................................................... <3

Anion profiles per liter
Acetate ..........................................127 mEq
(from Lysine Acetate and glacial acetic acid)

b. **Dextrose**

The majority of calories in the base parenteral nutrition solution is provided by hydrated dextrose yielding 3.4 cal/g. The dextrose concentration of the commercially available formula used to compound PN is 70%. The final concentration of peripheral parenteral solutions (PPN) is no greater than 10% dextrose. Solutions providing a final dextrose concentration of >10% must be infused via a central venous catheter. Dextrose infusions should be limited to 3-4 mg/kg/min (20-25 cal/kg/day) of dextrose calories to prevent complications associated with excessive glucose intake such as hepatic dysfunction, fatty liver and hyperglycemia.

c. **Lipid Emulsions**

Parenteral nutrition solutions at KUH use only 20% lipid emulsions. Lipid compositions vary between 10% and 20% emulsions. The lipid content of propofol is identical to that of Intralipid® 10% fat emulsion. Generally, the highest concentration of emulsifier per number of lipid droplets (phospholipid to TG ratio) exists in the 10% lipid emulsion formulation. The potential for an increase in circulating plasma TG’s must be considered whenever an intravenous fat emulsion (IVFE) is given, particularly in the case of the use of 10% emulsions. Although both 10% and 20% IVFEs lead to an increase within plasma of both free cholesterol and phospholipids, a greater increase is usually observed with use of the 10% emulsion. The presence of the higher concentration of phospholipids in 10% IVFE’s may result in phospholipid in complex with free cholesterol that forms particles in the presence of albumin and apolipoproteins. These phospholipid-cholesterol particles may ultimately compete with TG-rich particles for lipoprotein lipase. This competition for lipase activity may therefore lead to less TG hydrolysis with the concomitant result of an increase in circulating TG’s. Consequently, provision of a 20% IVFE will reduce the risk of worsening the hypertriglyceridermia associated with elevated
phospholipid to triglyceride ratio found with some 10% lipid emulsions.

Propofol

Propofol is an intravenous anesthetic sedative agent commonly used in ICU patients because it is easily titratable to desirable clinical effect and offers rapid termination of action. Propofol administration must be considered in determining energy delivery to ICU patients. The most frequently cited adverse effects documented with propofol administration have been associated with the lipid portion of the sedative. High infusion rates of lipid administration (high cumulative dose) have been linked to decreased lipid clearance. There may be an increased risk of hypertriglyceridemia due to the quantity of lipids provided to this patient via propofol administration. Triglyceride (TG) concentrations have been shown to be significantly correlated with the total dosage of propofol administered to ICU patients (McLoad 1997). Hyperlipidemia has been reported in 3-10% of ICU patients receiving propofol (propofol package insert). Maximal fat elimination rates have been reported to be 3.8 g lipid/kg per 24 h (Lindh,1987). However, fat elimination rates are dependent upon the concentration and biological activity of the patient's lipoprotein lipase and may be influenced by chronic and acute conditions. Factors which may influence fat clearance may include the presence of obesity, renal status, diabetes mellitus and critical illness.
TABLE 6.1
LIPID EMULSION CHARACTERISTICS

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>10%</th>
<th>20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmolarity</td>
<td>260 mOsm/L</td>
<td>260 mOsm/L</td>
</tr>
<tr>
<td>Calories</td>
<td>1.1 cal/ml</td>
<td>2.0 cal/ml</td>
</tr>
<tr>
<td>Particle size</td>
<td>1 micron</td>
<td>1 micron</td>
</tr>
</tbody>
</table>

d. Electrolytes

Average daily electrolyte requirements reflect the sum of repletion needs, daily requirements and losses (see Section IV.C for requirements). Electrolytes must be individually added to a parenteral nutrition order based on the mEq per day calculations.

e. Vitamins/Trace Minerals

The recommended daily intravenous requirements of all vitamins are met by the addition of a multivitamin solution to the parenteral solution. Trace elements are provided by a multiple trace element mixture and are added daily to PN.

Parenteral Multivitamin Products for Adults
(Infuvite Adult®)

<table>
<thead>
<tr>
<th>Vitamins</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fat-Soluble Vitamins</strong></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>3300 IU</td>
</tr>
<tr>
<td>D</td>
<td>200 IU</td>
</tr>
<tr>
<td>E</td>
<td>10 IU</td>
</tr>
<tr>
<td>K</td>
<td>150 mcg</td>
</tr>
<tr>
<td><strong>Water-Soluble Vitamins</strong></td>
<td></td>
</tr>
<tr>
<td>Thiamin (B1)</td>
<td>6 mg</td>
</tr>
<tr>
<td>Riboflavin (B2)</td>
<td>3.6 mg</td>
</tr>
<tr>
<td>B6</td>
<td>6 mg</td>
</tr>
<tr>
<td>B12</td>
<td>5 mcg</td>
</tr>
<tr>
<td>Niacin</td>
<td>40 mg</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>600 mcg</td>
</tr>
<tr>
<td>Pantothenic Acid</td>
<td>15 mg</td>
</tr>
<tr>
<td>Biotin</td>
<td>60 mcg</td>
</tr>
<tr>
<td>C</td>
<td>200 mg</td>
</tr>
</tbody>
</table>
Daily Parenteral Trace Element Supplementation
for Adults (Multitrace-5®)

<table>
<thead>
<tr>
<th>Trace Element</th>
<th>Recent Recommendations (ASPEN, 2004)</th>
<th>Multi-Trace-5®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc</td>
<td>2.5 – 5 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>Copper</td>
<td>0.3 – 0.5 mg</td>
<td>1 mg</td>
</tr>
<tr>
<td>Chromium</td>
<td>10 – 15 mcg</td>
<td>10 mcg</td>
</tr>
<tr>
<td>Manganese</td>
<td>60 – 100 mcg</td>
<td>0.5 mg</td>
</tr>
<tr>
<td>Selenium</td>
<td>20 – 60 mcg</td>
<td>60 mcg</td>
</tr>
</tbody>
</table>

f. Fluid Requirements

In general, daily volume requirements for adults can be calculated by allowing 1000 cc for the first 10 kg of body weight, 500 cc for the second 10 kg of body weight and 20 cc for each kg thereafter. For example, a 70 kg man would receive 1000 cc for the first 10 kg, 500 cc for the second 10 kg and 20 cc x 50 remaining kg = 1000 cc or a total daily fluid requirement of 2500 cc/day. (An alternate method is 20cc/Kg + 1100cc = 24 hr maintenance.) Fluid requirements are important when ordering PN as you can specify a final volume and infusion rate needed for a patient and the pharmacy can calculate appropriate dilutions for the preparation. Fluid requirements may vary from the above maintenance calculations for certain disease states and situations.

B. Route of Administration

1. Parenteral nutrition administered via the peripheral venous route is known as peripheral parenteral nutrition (PPN). Indications for PPN include short term use, low energy requirements and contraindications to central access. PPN requires healthy veins for cannulation. Patients with fragile veins (elderly, history of steroid use, etc.) are not good candidates for PPN unless midline access can be attained. Macronutrients are reduced in PPN due to the contributions of dextrose and amino acids to the osmolarity of the solution. Osmolarity greater than 900mOsm/L is not recommended for any patient receiving PPN at the University of Kansas Hospital. Because of these limitations it is very difficult to safely provide adequate support via PPN for a patient with severe metabolic stress or nutritional depletion.

2. Central parenteral nutrition (PN) is indicated in patients expected to be NPO or have significantly decreased enteral intake for greater than seven days. There are, however, significant risks
associated with central line placement and maintenance including pneumothorax, occlusion and thrombosis and increased incidence of CVC associated bloodstream infections.

C. Writing PN Orders

1. Orders for PN are written as a 24 hour supply in a single bag. All orders must be received in the pharmacy by 1300. All adult PN orders require initial consultation with the Nutrition Support Service.

2. PN orders may be individualized to each patient or standard PN may be ordered. Standard PN orders are not used long term because, generally speaking, they do not meet the individual nutritional needs of the patient.

3. Solutions and all changes to PN orders, including rate changes, must be ordered using the Adult Parenteral Nutrition Order form.

D. Electrolyte Concentrations for PN formulas

Electrolytes provided in PN solutions must maintain neutrality, therefore all cations (positive charge) must be matched with an equal number of anions (negative charge).

1. Sodium\(^c\)  Normally expressed in fractions of NSS or normal saline solution. NSS equals 154 (rounded to 150) mEq of sodium per liter so if your patient requires 1/2 NS, that is equivalent to 75 mEq/L.

2. Potassium\(^c\)  Normal maintenance is 60 - 120 mEq per day. However, initial replacement doses can be quite high in nutritionally depleted patients. Additionally, certain drugs can have a profound effect on potassium excretion rates.

3. Chloride\(^a\)  Can be matched with either sodium or potassium. It is associated with decreased pH and acidosis.

4. Acetate\(^a\)  Can be matched with either sodium or potassium. It is converted to bicarbonate and is associated with increased pH and alkalosis. The acetate salt should be used only if necessary, as the amino acid solutions used in the manufacture of PN formulations contain acetic acid as a buffer as well as acetate salts as a metabolic buffer to the amino acids (approx. 1 mEq/gm of amino acids).
5. **Phosphate** Can be matched with either sodium or potassium. It is associated with energy storage and release. Dosing and monitoring during initiation of nutrition support is critical in the prevention of refeeding syndrome. Initial dose should be a minimum of 14mM per 24 hrs.

6. **Magnesium** Is involved in many reactions as a catalyst, especially important here in glucose metabolism. Routine dosing (as the sulfate salt) is approximately 8 - 24 mEq (8 mEq = 1gm MgSO₄) daily, although patients may require more upon initiation of nutrition support. Certain drugs such as cyclosporine, furosemide, and amphotericin may cause substantial urinary loses of magnesium.

7. **Calcium** Normal requirements are 9 - 22 mEq daily. Low albumin levels may give falsely low serum calcium levels. In these cases, ionized calcium levels may be checked. Calcium may also be dosed in gms of a salt form. KUH utilizes the gluconate salt in PN compounding (4.5 mEq = 1gm) as the chloride form causes significant compatibility problems.

E. **Vitamins/Trace Elements**

Normally dosed as the RDA for the 13 vitamins in the available commercial preparation (see sect. VI). Additional replacement doses of some vitamins may be added to PN solutions based on diagnosed deficiency states or expected additional needs due to increased metabolic responses.

Trace elements are dosed on current recommendations in the literature and currently available commercial products. KUH currently uses MTE-5® concentrate (see sect. VI.e). These metals are also available as individual preparations and may be added to PN solutions as additional needs are recognized.

F. **Medications**

1. **Insulin**

   Roughly half of parenteral nutrition patients will not tolerate the glucose load supplied by the PN. Insulin can be added to the PN to assist with glucose metabolism if necessary. The initial dose of insulin may be calculated as 0.1 units per gram of dextrose infused, however, some patients may require substantially higher doses. Only regular insulin can be added to PN solutions.
2. **H2 blockers**

Protection of the gastric mucosa may require use of Histamine2 receptor blockers to decrease gastric pH. Famotidine is used in PN at this institution. It is compatible in PN solutions and effective when given as a 24 hour infusion.

G. **Infusion Rates**

**Cycled PN**

Cycled PN may be indicated for patients that require long term PN and those that may be receiving it at home. The goal of cycling is to infuse the calories and protein the patient requires in a shorter period of time, usually 12-14 hours. Candidates for a cycling schedule include those patients who have attained glycemic control on a 24-hour continuous infusion, as well as a demonstrated tolerance for rapid infusion of 1.5 to 3.0 liters over a shorter period of time.

For some patients, a 16-18 hour infusion time may be a more realistic schedule to assist in glycemic and fluid management. In addition, cycling of PN generally is not recommended for critically ill patients.

Cycling can be achieved over a period of a few days by reducing the infusion time by 4-hour increments, ie. 24 to 20 to 16 to 12 hours. As the patient is cycled the blood sugar should be monitored during the cycle to assess the need for the addition of insulin. Typically, capillary blood glucose level measurement should be obtained 1 hour into the infusion, mid cycle and 1 hour after the infusion is completed. If blood glucose is high mid cycle (> 180 mg/l) the patient may be treated with a sliding scale insulin and then the addition of regular insulin added to the next bag of PN. Fluid status should be monitored and demonstration of the patient’s tolerance for the cyclic PN schedule ascertained prior to discharge. Cycled formulations require a one-hour taper both at the beginning and end of the cycle and are usually figured by reducing the primary infusion rate by half.

H. **Administration of Solutions**

1. Due to the nature of the PN solutions infused and the potential for contamination or chemical incompatibilities, it is imperative that the central line be solely reserved for infusion of the PN. If a multilumen catheter is used, one port should be dedicated solely for the administration of the PN.

2. The following procedures are not permitted:
a. Piggybacking medications other than IV lipid emulsions with the PN (except in special critical care situations with approval of the pharmacy)

b. Administration of blood or blood products or albumin in the PN line

c. Introduction of stopcocks into the PN line

d. CVP readings

e. Drawing blood from the PN line is not recommended (this can result in contaminated blood draws and grossly misleading lab data, as well as an increased risk for CVC associated bloodstream infection).

3. If the parenteral nutrition solution is not available for any reason, a 10% dextrose solution should be hung and run at the same rate until PN becomes available. This will prevent symptomatic hypoglycemia.

I. Monitoring

Appropriate monitoring of patients receiving parenteral nutrition is critical to minimize complications and ensure cost effective therapy. Table 6.2 is a schedule of laboratory and clinical monitoring parameters for patients receiving parenteral nutrition support.

Note that laboratory results with much higher than normal values, most notably potassium, serum glucose and triglycerides, are frequently obtained from blood specimens that have been contaminated by PN solution. Poor technique during blood draws from PN lines can result in serum potassium levels as high or greater than 6.0 and glucose values in 300-500 mg/dl range. When encountering very high serum potassium and glucose levels, compare concurrent FSBS results; note any acute elevations in serum lab values as compared to the previous blood draw, and any changes in patient's clinical status or treatments that could account for the increased levels. If contamination of the blood specimen by PN solution is suspected, request a repeat laboratory test to verify, holding PN infusion until results obtained. Taking these steps helps to alleviate any unnecessary and/or potentially harmful treatments for hyperkalemia and/or hyperglycemia and interruption to the patient's PN, possibly for several hours.
TABLE 6.2
FREQUENCY OF CLINICAL MEASUREMENTS

<table>
<thead>
<tr>
<th></th>
<th>INITIAL ASSESSMENT</th>
<th>FOLLOW-UP ASSESSMENT</th>
<th>STABLE PERIOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Clinical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body Weight I &amp; Os</td>
<td>x</td>
<td>M-W-F Daily</td>
<td>M-W-F Daily</td>
</tr>
<tr>
<td>2. Blood:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accuchecks</td>
<td>x</td>
<td>Q 6 hours</td>
<td>Q 6 hours</td>
</tr>
<tr>
<td>BCP</td>
<td>x</td>
<td>5 x weekly</td>
<td>5 x weekly</td>
</tr>
<tr>
<td>CMP</td>
<td>x</td>
<td>2 x weekly</td>
<td>2 x weekly</td>
</tr>
<tr>
<td>Pre-albumin</td>
<td>x</td>
<td>2 x weekly</td>
<td>2 x weekly</td>
</tr>
<tr>
<td>Magnesium</td>
<td>x</td>
<td>2 x weekly</td>
<td>2 x weekly</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>x</td>
<td>2 x weekly</td>
<td>2 x weekly</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>x</td>
<td>2 x weekly</td>
<td>2 x weekly</td>
</tr>
</tbody>
</table>

J. Complications of PN

The complications of parenteral nutrition can be mechanical or metabolic. The following describe potential alterations in normal metabolism that may occur with the use of PN.

1. Glucose related abnormalities

Patients receiving PN are at significant risk for hyperglycemia. PN for patients at risk (history of diabetes mellitus) may be initiated with a decreased concentration of dextrose until the impact of the parenteral nutrition infusion can be evaluated and blood sugars stabilize.

Hypoglycemia may be the result of a sudden decrease in infusion rate or discontinuation of PN. Occasionally, patients who receive PN at high infusion rates may over secrete insulin and develop a symptomatic hypoglycemia. More common is a change in stress level that causes a decrease in glucose tolerance.

Insulin Requirements

Predisposing conditions such as diabetes mellitus or glucocorticoid administration may contribute to hyperglycemia. Hyperglycemia can usually be controlled initially by use of sliding scale insulin and then subsequently by adding the patient’s insulin requirements to the PN solution. Occasionally a very stressed patient will be insulin resistant. Such patients requiring large insulin doses should be monitored in a critical care setting to keep serum glucose in a safe range. Under these conditions, a separate intravenous infusion of insulin may be administered by pump, titrating the dose as required without interfering with the PN.
solution. Once the patient has stabilized, the insulin can be added to the PN solution.

2. Lipid related abnormalities

a. Essential Fatty Acid Deficiency (EFAD)

Essential fatty acid deficiency was documented in animals by Burr and Burr in 1929. It was not until the development of PN four decades later that EFAD begin to be demonstrated in humans. During this time period in the early 1970s and 1980s, biochemical and clinical manifestations of EFAD (both linoleic and α-linolenic fatty acids) begin to occur in patients requiring PN for extended periods of time (2-4 weeks). The predominant clinical changes associated with linoleic acid deficiency are characterized by a dry, scaly skin rash. However, other clinical symptoms have been noted including increased susceptibility to infection, impaired wound healing and immune dysfunction. Biochemical changes that occur in response to linoleic acid deficiency are manifested by a fall in both linoleic and arachidonic acids (Tetraenoic acid) and a rise in Mead acid (Triene acid, 20:3n-9). Mead acid is only produced in humans in the absence of EFAs. A triene-tetraene ratio of >0.2 (Holman Index) has been used to identify the presence of EFAD. The time required to exhibit an EFAD in adults is variable, based upon underlying disease and nutritional status. EFAD may occur rapidly in continuous fat-free PN administration due to elevated insulin levels that prevent adipose tissue lipolysis. Usually, EFAD may be seen in patients after 4 weeks of fat-free PN, although clinical signs may be detected earlier, i.e., between 10 and 20 days. Hypocaloric fat-free PN or a cyclic feeding schedule of fat-free PN may extend the period of time before EFAD is exhibited. When PN is cycled or hypocaloric PN is provided, it is thought that EFA’s are mobilized and enter the circulation as a result of increased lipolysis of endogenous fat stores in response to a reduction in serum insulin concentration. Hypocaloric feeding additionally prevents the risk of hepatic dysfunction that may occur if the caloric deficit (caused by the removal of lipids) is corrected by increasing the dextrose or protein calories to maintain energy requirements. When lipids are contraindicated, short-term, hypocaloric fat-free PN has shown to be safe and appropriate for the critically ill patient.

b. Lipid Infusion

Immediate or early adverse reactions (rare) that most commonly occur with the initial administration of
intravenous lipid emulsions include: dyspnea, cyanosis, allergic reactions, nausea, vomiting, headache, flushing, fever, sweating and chest pain. Delayed adverse reactions include thrombocytopenia, leukopenia (rare), transient increases in liver function tests and accumulation of lipid in the reticuloendothelial system (seen with too rapid infusion rate).

2. Liver dysfunction

The relationship between the administration of parenteral nutrition and liver dysfunction is poorly understood. PN related liver dysfunction in adults is primarily diagnosed by elevations in liver enzymes and less frequently, bilirubin. The diagnosis of liver dysfunction in short term parenteral nutrition is difficult and is often confounded by hepatic complications associated with underlying disease processes and/or concurrent medications. Excessive calories (either from lipids or dextrose) have been linked to hepatic steatosis. Dextrose infusions greater than 4g/kg/day have been associated with PN associated liver dysfunction. Recommendations to prevent liver abnormalities include: reduce risk of overfeeding (reducing energy to 1.3 X BEE or less), changing from continuous PN to a cyclic PN schedule and treating small bowel overgrowth if present.