Definitions
Enteral nutrition is the process of nourishing a patient with a liquid diet of defined composition, usually given through a nasogastric, nasointestinal, gastrostomy, or jejunostomy tube. Parenteral nutrition is the administration of nutrients directly into the bloodstream through a central venous catheter or by peripheral infusion. When the only source of nutrient intake is via the parenteral route, it is called total parenteral nutrition (TPN). The term nutritional support refers to the use of enteral or parenteral nutrition rather than to an oral diet, with or without supplements.

Etiology of Malnutrition
In circumstances in which food is available, malnutrition has three main causes: (1) insufficient intake of food, as a result of conditions such as anorexia, coma, dysphagia, gastric lesions, and psychological factors; (2) heightened metabolic requirements, as may occur in burns, trauma, sepsis, and neoplasia; and (3) intestinal failure, which comprises all conditions that prevent the proper intake, digestion, or absorption of a normal oral diet. Malnutrition from reduced food intake or gastrointestinal failure is most amenable to treatment or prevention with nutritional support. Although nutritional support may overcome some of the effects of trauma, burns, sepsis, or cancer, nutritional support alone may be unable to prevent the development of critical malnutrition in such cases.

Effects of Malnutrition
Even in the absence of disease, malnutrition adversely influences function and survival. A study of Irish hunger strikers found a 30% mortality in strikers who lost 35% to 40% of their body weight. Similarly, in patients with cancer, weight loss of about 30% preceded death. In 12 human volunteers, semistarvation (with a 15% to 20% weight loss over 24 weeks) led to a 60% decrease in function on the basis of a fitness score. Even after 20 weeks of refeeding, the fitness score and handgrip strength in these individuals did not return to normal. Other studies have shown that lack of food intake results in substantial loss of muscle function in addition to loss of body mass. Surgical patients who had weight loss greater than 10% and clinical evidence of dysfunction of two or more organ systems (including skeletal and respiratory muscles) preoperatively had significantly more postoperative complications than did normal patients or those with weight loss but no physiologic dysfunction.

The presence of various diseases compounds the effects of malnutrition. In ill patients, malnutrition results in nutritionally associated complications such as poor wound healing, increased infections, delayed rehabilitation, and increased mortality.

Evidence Regarding Nutritional Support
Well-nourished patients are unlikely to benefit from nutritional support. However, in patients with initial malnutrition and poor function who have continued inability to eat or to absorb ingested food, randomized controlled trials have demonstrated that nutritional support favorably influences outcome by reducing nutritionally associated complications.

Parenteral Nutrition
Three large meta-analyses of parenteral nutrition have given inconsistent results. In a comparison of parenteral nutrition with standard care in 26 trials, Heyland and colleagues found that parenteral nutrition did not influence overall mortality but did reduce complications in malnourished patients. Benefit from TPN was observed in studies performed before 1988, in studies deemed to be of less statistical quality, and in patients who did not receive lipid. These researchers found only six trials of parenteral nutrition in critical illness; in these trials, complications and mortality were significantly higher than in trials done in surgical patients. Another meta-analysis showed that in malnourished patients, standard care, compared with parenteral nutrition, was associated with increased mortality and a trend toward increased infectious complications; in well-nourished patients, infections were more frequent with parenteral nutrition than with standard care or enteral nutrition. These authors speculated that the increased infectious complications in patients on parenteral nutrition were attributable to hyperglycemia. Not all the studies included in this meta-analysis mentioned blood glucose, but of the seven that did, six found both hyperglycemia and increased infectious complications.

Koretz and colleagues have done a technical review and made recommendations to the American Gastroenterological Association about parenteral nutrition. They found that overall, mortality with parenteral nutrition was no lower than mortality with standard care. In contrast to the meta-analysis by Heyland and colleagues, this analysis showed that total complications and length of stay were lower only in studies in which lipid was a component of TPN. Infectious complications were increased with TPN, especially in cancer patients. Benefit from parenteral nutrition was seen only in patients with upper GI cancer, who had significantly fewer complications when given perioperative parenteral nutrition.

Enteral Nutrition
Enteral nutrition has not been compared with standard care in the same systematic way as has parenteral nutrition. However, comparisons of enteral nutrition with parenteral nutrition have consistently shown fewer infectious complications with enteral nutrition than with parenteral nutrition. Data from a large controlled trial in intensive care unit patients showed that keeping blood glucose levels below 127 mg/dl (7 mmol/L) significantly reduced mortality from sepsis-related multisystem organ failure. Hyperglycemia probably was more frequent with parenteral nutrition because patients randomized to parenteral nutrition received more calories than those on enteral nutrition.
Determining the Need for Nutritional Support

Unfortunately, for many clinical situations there are no data from randomized, controlled trials to help clinicians determine how to identify patients who are likely to progress to critical weight loss and to determine when to start nutritional support in patients who are at risk. In the absence of reliable data, clinicians have to make decisions about nutritional support at the bedside. Obviously, a previously healthy person who does not eat for 1 or 2 days does not need nutritional support. On the other hand, if inadequate nutritional intake persists for weeks, weight loss will continue; the loss will accelerate if there is added trauma or sepsis; and when loss of body weight exceeds 30%, there is an increased likelihood of death.

The risk of malnutrition can be assessed with a clinical tool called the Subjective Global Assessment (SGA). The SGA, which can be used by physicians, dietitians, or nurses after brief training, is based on a focused history and physical examination that includes the degree and progression of any weight loss, dietary intake, ability to take and absorb food (state of the GI tract), the degree of stress from comorbidity, and functional loss, dietary intake, ability to take and absorb food (state of the GI tract), the degree of stress from comorbidity, and functional loss. This information is used to classify the patient into one of three groups: A (normally nourished and unlikely to progress to a malnourished state), B (normally nourished but likely to progress to a malnourished state), or C (malnourished and progressing to increasing malnutrition).

The SGA not only provides an assessment of the patient’s current nutritional status but also predicts the possible nutritional outcome if nutritional support is not instituted. More important, it allows the clinician to weigh the role of disease severity versus limited nutrient intake as the cause of malnutrition.

Two controlled studies of the SGA have shown that the likelihood of nutritionally associated complications progressively increased from grades A to C. Patients who are classified as SGA C are very likely to develop nutritionally associated complications and therefore should benefit from nutritional support. These studies also found that the SGA grade correlated with other objective measures of nutritional status but was more likely to predict nutritionally associated complications than several of the objective measures taken individually. SGA has been shown to be a valid predictor of nutritionally associated complications in general surgical patients, patients on dialysis, and liver transplant patients. In two large studies, SGA independently identified increased mortality and morbidity from malnutrition, even when the data were adjusted for other factors influencing survival and complications.

Nutritional Support in Specific Clinical Conditions

Insufficient Oral Intake Despite a Normal Gut

Well-nourished Patients

In general, most patients with serious illness have reduced food intake, partly from the illness itself and partly as a result of iatrogenic factors. Most hospital inpatients eat insufficient food or are prevented from eating. Several studies have indicated that a significant number of hospital patients have signs of malnutrition. Patients likely to have an inadequate intake of food are those with critical illness (e.g., trauma, burns, severe sepsis, respiratory failure); coma and neurologic diseases; or major psychiatric illnesses. Although many hospital patients fit these categories, there are no controlled trials to provide guidelines that can be confidently used to guide nutritional support in such patients and to confirm that nutritional support can reduce the occurrence of nutritionally associated complications. Clinically, it is a common practice to start nutritional support if the period of reduced intake exceeds 7 to 10 days or weight loss exceeds 10%. Unfortunately, this practice has no supporting data except consensus and expert opinion.

Early enteral feeding has been recommended on the basis of a randomized trial in trauma patients who were to undergo a laparotomy and had an abdominal trauma index greater than 15. This subset constituted 20% of all trauma patients admitted during the period of study. These patients, who were well nourished on admission, were randomized to a group who received early (12 to 18 hours after surgery) institution of enteral feeding through a jejunostomy tube inserted at surgery or to a control group in whom TPN was started 5 days after surgery if the patient was not yet on a regular oral diet. There was no difference in overall complications between the groups, but septic complications were significantly lower in the early-fed group (4%, versus 26% in the TPN group). Such data are subject to the criticism that there was no control group receiving standard care. However, there are other reasons to support early feeding. In a randomized trial of postoperative supplemental sip...
feeding of a liquid formulation, grip strength significantly improved and the occurrence of serious infections was reduced. In a trial of 501 hospitalized elderly patients randomized to oral supplements or a ward diet, Larsson and colleagues showed that irrespective of their initial nutritional status, the supplemented patients had lower mortality, better mobility, and a shorter hospital stay. The difference between ward diet and supplementation was even more pronounced in a secondary analysis of patients with weight loss.

**Recommendations**  The available data suggest that well-nourished patients who are admitted with major trauma should receive enteral nutrition. Elderly patients should receive supplemental feeding or enteral nutrition if they are incapable of eating adequately. However, all hospitalized patients should have their SGA assessed so that possible future outcome without nutritional support can be documented and considered. For example, if a previously healthy patient has a severe head injury and is likely to remain comatose (and therefore unable to eat) for an indefinite period, it is easy to predict that malnutrition will occur in the absence of nutritional support. Such a patient should be started on enteral nutrition. Similarly, major burns, the hypermetabolic state, anorexia, and ileus all result in rapid weight loss unless nutritional support is given. Each case needs to be assessed individually, however. Repeated evaluation of the SGA allows the clinician to determine any impediment to the intake of food, the presence of GI dysfunction, and progressive functional loss and weight loss, which signal the need to start nutritional support.

The purely scientific approach would be to avoid nutritional support in all situations for which proof of benefit from randomized, controlled studies is lacking; however, in patients without adequate oral intake, this approach could in some cases result in starvation and death. The pragmatic approach is to evaluate the patient, using the SGA, and start nutritional support if the clinical evidence shows that otherwise the patient is likely to progress to critical malnutrition.

**Malnourished Patients**

There are no controlled trials to show that nutritional support will reduce complications in all patients classified as SGA C. However, there are several indirect lines of evidence suggesting that nutritional support in such patients will reduce complications and improve outcome.

A multicenter, randomized, controlled trial undertaken by the Veterans Affairs Total Parenteral Nutrition Cooperative Study Group stratified patients into three nutritional groups. In the group of severely malnourished patients, the rate of major noninfectious complications was significantly lower in patients randomized to TPN than in control subjects (5.3% versus 42.9%). Overall rates of complications and infectious complications in TPN-treated patients in this trial were not different from those in control patients, however.

Other studies have shown that nutritional supplementation can significantly reduce rehabilitation time in patients with hip fractures who had severe weight loss [see Figure 1] and that elderly patients with hip fractures, especially those with weight loss, benefit the most from supplemental feeding.

**Recommendations**  Elderly patients, especially those with weight loss, should receive nutritional supplements in the hospital. Despite the lack of data from well-designed controlled trials, patients who are classified as SGA C should be given nutritional support.

**Surgery**

In a meta-analysis of perioperative parenteral nutrition, Det-sky and colleagues combined the results of 14 randomized or quasi-randomized trials and showed that absolute morbidity was reduced by 5.2% and the relative risk reduction was 20.7%. These differences were not statistically significant, however ($P = 0.21$). Of the 14 studies, only one showed a significant reduction in complication and fatality rates with TPN. These authors concluded that perioperative TPN did not influence outcome. On the other hand, only three of the 14 trials were limited to malnourished patients (who were the most likely to benefit from TPN), so the negative result may simply reflect the fact that the trials were weighted by patients who were unlikely to benefit from nutritional support. In contrast, Twomey concluded that the pooled estimate in malnourished surgical patients shows a 7.1% reduction in morbidity with TPN. In the VA trial, secondary analysis showed that the severely malnourished patients had a reduction in overall morbidity from 47% to 26% with perioperative TPN.

Fan and colleagues conducted a controlled trial of perioperative nutritional support in 124 patients undergoing major hepatic resection for hepatocellular carcinoma. The patients were randomized to parenteral nutrition plus oral diet or to diet only. Patients in the treatment arm received 1.5 g/kg of amino acids, of which 35% were branched-chain amino acids (BCAA), with 30 kcal/kg of a glucose-lipid mixture for energy. Medium-chain triglycerides (MCT) constituted 50% of the lipid infused. The parenteral formulation was given for 14 days. At least 20% of the patients had a preoperative weight loss of greater than 10% and therefore were likely to be malnourished, but 80% did not have weight loss. Overall morbidity, morbidity from sepsis, and diuretic use for ascites all were lower in patients who received nutritional support.

Although the benefits of parenteral nutrition in the perioperative state are controversial, randomized trials of postoperative enteral feeding have shown improved outcome. In hip fracture patients, supplemental feeding of a liquid formula diet reduced recovery time. In general surgical patients, the rate of infectious complications with early enteral feeding was lower than that with nil per os (NPO).

**Recommendations**  Postoperatively, patients who have undergone major surgery should receive supplemental liquid formula feeding. The data do not support the routine use of parenteral nutrition for perioperative nutritional support, but parenteral nutrition clearly reduces complications in patients undergoing hepatic resection. It is not clear whether standard parenteral formulations will reduce complications in patients undergoing hepatic resection or whether it is necessary to give BCAA or MCT. Patients with hip fracture and weight loss will benefit from enteral feeding. Despite the lack of proven benefit, other severely malnourished patients (i.e., those classified as SGA C) should receive perioperative nutritional support.

**Serious Compromise of Bowel Function**

In patients with massive small bowel resection (i.e., less than 60 cm remaining), chronic bowel obstruction, extensive bowel disease, severe radiation enteritis, or end jejunostomy in which
oral feeding results in uncontrolled fluid and electrolyte losses, parenteral nutrition is needed because oral feeding is very unlikely to provide sufficient nourishment. An economic analysis of such patients showed that provision of parenteral nutrition at home was associated with improved quality of life and was cost-effective. The outlook was especially good for those with chronic intestinal failure from benign disease. 

Recommendations

Initially, all patients with a short bowel (see above) need parenteral nutrition. Later, about 30% (especially those with an intact or partially intact colon) can be treated with oral diet and supplements. Enteral nutrition is not necessary in these patients; controlled studies have shown that enteral nutrition was no better than an oral diet in patients with a short bowel and end jejunostomy. Patients with a massive resection can absorb 50% to 60% of an oral diet. By using oral rehydration solution, supplements, and a high-calorie oral diet, about 30% of such patients can reduce or stop home parenteral nutrition. The remaining patients will require supplemental fluid and electrolytes or parenteral nutrition to maintain a normal weight and electrolyte-fluid status.

Bowel Rest

Parenteral Nutrition

Bowel rest is widely used in pancreatitis, intestinal fistulas, and inflammatory bowel disease. The bowel is rested by keeping the patient NPO. Malnutrition is avoided by instituting parenteral nutrition.

Parenteral nutrition is used in pancreatitis because eating often induces pain in such cases. The only controlled trial of parenteral nutrition versus oral diet in patients with mild pancreatitis showed that TPN did not influence recovery. In two trials comparing parenteral nutrition with enteral nutrition in patients with mild or acute pancreatitis, the trial of patients with mild pancreatitis found no difference in septic complications, whereas the trial of patients with severe pancreatitis found less sepsis with enteral nutrition. However, in the latter trial, twice the number of patients on parenteral nutrition were hyperglycemic, a factor known to increase septic complications. Again, these trials do not prove that enteral nutrition is better than standard care.

Parenteral nutrition is useful in patients with intestinal fistulas, in whom eating increases output and fasting reduces output by 30% to 50%. However, there are no controlled trials comparing the effect of bowel rest plus parenteral nutrition with that of oral intake in the healing of fistulas.

In inflammatory bowel disease, bowel rest reduces abdominal discomfort and diarrhea. Controlled trials have not shown that bowel rest aids recovery in these patients, however.

Recommendations Because pancreatitis, intestinal fistulas, and inflammatory bowel disease may prevent the ingestion or absorption of oral nutrients and result in malnutrition, the use of bowel rest and parenteral nutrition is a reasonable strategy in some of these cases, despite the lack of evidence that bowel rest alters the course of the disease. Specifically, enteral or parenteral nutrition should be given to prevent or treat malnutrition when a patient cannot take in or absorb nutrients for 7 to 10 days, when a patient loses nutrients because of a fistula for 7 to 10 days, or when a patient is clearly malnourished (SGA C). The route of administration selected should be capable of delivering the ideal nutrient intake successfully. For example, enteral nutrition is unlikely to be successful in a patient with a high jejunal fistula who is putting out large volumes of intestinal contents.

Enteral Nutrition in Crohn Disease

Controlled trials in Crohn disease have shown that enteral nutrition reduces the activity of the disease and, in children, promotes growth. However, a recent meta-analysis of eight randomized, controlled trials of 413 patients with Crohn disease showed that enteral nutrition was not as effective as corticosteroids in inducing a remission (odds ratio of enteral nutrition/corticosteroids, 0.35; confidence interval, 0.23–0.53). In addition, there was no difference between elemental and polymeric diets in inducing clinical remission. Regrettably, there are no placebo-controlled trials to show whether enteral nutrition is an effective modality for treatment of active Crohn disease.

Recommendations Enteral nutrition is not a replacement for routine drug treatment of active Crohn disease, but under certain circumstances it has definite benefits. Enteral nutrition is especially useful in promoting growth and reducing disease activity in children with growth failure. In such children, enteral nutrition can be given on a long-term basis at home, along with other treatment to promote growth.

In line with other recommendations for nutritional support, patients with active Crohn disease who are SGA C should be treated with enteral nutrition and other modalities as required. However, if they are SGA C and are unable to tolerate enteral nutrition, parenteral nutrition should be used until they can tolerate adequate nutrition by the oral route. Nutritional support is also necessary when serial SGA determinations show evidence of poor intake and the patient has severe GI symptoms and continued functional impairment that could lead to critical malnutrition. The route used depends on the capacity of the GI tract to absorb nutrients.

Cancer Malnutrition

Malnutrition in metastatic cancer has been used as an indication for parenteral nutrition. Controlled trials have failed to substantiate that nutritional support is beneficial in patients with metastatic cancer, however, and in fact have suggested that parenteral nutrition may have adverse effects. On the other hand, parenteral nutrition has been shown to favorably influence graft survival in patients receiving a bone marrow transplant.

Recommendations In cancer patients, nutritional support with enteral or parenteral nutrition is appropriate for preventing or treating malnutrition that is not caused by the tumor per se. For example, patients whose colon cancer has been eradicated but who suffer from short bowel because of extensive radiation enteritis should respond to parenteral nutrition. Criteria for nutritional support in cancer patients are as follows: (1) there is no evidence of tumor or its progression; (2) the patient has a GI complication, such as radiation enteritis or resection; and (3) as a result of this GI complication, critical malnutrition has occurred or will predictably occur (i.e., the patient is SGA C, or serial evaluation of SGA indicates progression toward SGA C).
The most difficult ethical question concerns the use of parenteral nutrition for patients in whom tumor progression causes intestinal obstruction or cachexia. Parenteral nutrition is being increasingly used for this indication [see Home Parenteral Nutrition, below].

RENA L FAILURE

Because patients with renal disease cannot excrete nitrogen normally, parenteral nutrition in which the source of nitrogen is limited to essential amino acids (EAA) has been used to reduce urea production. A meta-analysis has concluded that parenteral nutrition with EAA does not improve survival to discharge when the trials were adjusted for quality, there was no effect of EAA.39

Recommendations

Patients with renal failure who cannot meet their nutritional requirements by the oral route should be given nutritional support and have fluid, electrolytes, and nitrogenous metabolites removed by dialysis or continuous arteriovenous hemofiltration. Fluid intake is minimized by using enteral nutrition with a calorie density of 2 kcal/ml or parenteral nutrition containing 35% dextrose or 20% lipid as the source of energy. Sodium intake should be restricted to 40 to 70 mmol/day, and other electrolytes should be added if their plasma levels fall. Acidosis should be controlled by appropriate dialysis. Trace elements and vitamin supplements need not be curtailed.

HEPATIC FAILURE AND ALCOHOLIC LIVER DISEASE

The discovery that hepatic encephalopathy is associated with reduced BCAAs and increased aromatic amino acids in plasma has led to the use of parenteral nutrition formulas enriched in BCAAs and reduced in aromatic amino acids. Meta-analysis of trials comparing BCAA-enriched mixtures with standard therapy has shown significant improvement in encephalopathy and, possibly, in short-term mortality.40 On the other hand, there is no evidence that standard amino acid mixtures or enteral nutrition providing 0.8 to 1 g/kg/day of protein or amino acids has precipitated encephalopathy. In fact, 75 g/day of supplementary amino acids with 400 kcal/day of dextrose improved liver function and was tolerated by patients with severe alcoholic hepatitis.41

Recommendations

Patients with hepatic failure who are unable to be on a normal diet need enteral or parenteral nutrition. The protein intake should be about 0.8 to 1 g/kg/day of a high-quality protein or balanced amino acids. Carbohydrates and fat should be given in equal proportions because these patients are carbohydrate intolerant but utilize fat well, and fat infusions increase the levels of BCAA in plasma.42 Because these patients are sodium and water overloaded, they should receive a total of about 1,500 ml of water daily, and their sodium intake should be restricted to 20 mmol/day. Supplemental potassium, vitamins (A, D, and B complex), and zinc should be given.

Practice of Nutritional Support

GENERAL PRINCIPLES OF NUTRITIONAL CARE

At hospital admission, all patients should be interviewed by a dietician and have their SGA calculated to determine whether they can be maintained on a normal or modified oral diet (with supplements) in sufficient quantities or whether nutritional support is indicated and, if so, how urgently. In patients requiring nutritional support, the physician and the dietician should define nutrient intake, route of administration, and goals. The most important objective is maintenance of uninterrupted nutrient intake, to avoid weeks of starvation followed by the urgent institution of parenteral nutrition to an iatrogenically malnourished patient.

Oral Nutrition

In patients who can eat, close attention to maintenance of oral dietary intake—and use of supplements, where required—should be the standard of care. Enteral nutrition should be considered if it becomes clear that this approach does not permit sufficient intake to meet requirements.

Enteral Nutrition

Enteral nutrition is applicable to all patients, but it should be used with caution in patients with (1) clinically significant gastroesophageal reflux; (2) intestinal obstruction; (3) GI fistula or recent surgical anastomosis, unless the tube can be inserted distal to the area in question or threaded at operation past the area; and (4) cardiovascular instability with shock. Gastric retention is a relative contraindication. In patients who accumulate secretions in the stomach and then aspirate, it may be possible to pass a feeding tube into the small intestine and aspirate the stomach with a second tube. However, in such cases the relative discomfort of two tubes versus parenteral nutrition should be considered. A recent survey showed that patients preferred parenteral nutrition over enteral nutrition.42

Short-term enteral access Nasogastric or nasoenteric placement of a feeding tube provides short-term enteral access. The tube should be small bore (9 to 12 French) and 105 to 110 cm long [see Table 1]. These tubes are usually made of Silastic or...
polyurethane. The latter become very slippery when wet, thus aiding insertion. I prefer intestinal placement of the tube, because controlled trials have shown better achievement of nutrient intake and, possibly, reduced risk of aspiration when the tube is placed beyond the ligament of Treitz.

Long-term feeding The definition of long-term feeding is arbitrary. Children with Crohn disease have been fed for months by teaching them to pass a nasogastric tube each night, receive a nocturnal feeding, and then remove the tube in the morning before going to school. However, in many instances nasal tubes become uncomfortable, and a gastrostomy tube can be placed endoscopically by a gastroenterologist or an interventional radiologist. This method has been shown to be safer and more cost-effective than a surgically placed gastrostomy. There are two methods of percutaneous endoscopic gastrostomy (PEG): the pull (Ponsky-Gauderer) method and the push (Russell) method.

Feeding into the small bowel can be performed after the insertion of a percutaneous endoscopic jejuno-stomy (PEJ). After the tract of the PEG tube is established, a PEJ tube with two arms can replace the tube. One arm remains in the stomach and can be used to drain this organ; the other arm is advanced under endoscopic guidance through the pylorus into the small intestine. In this way, the stomach can be decompressed, and simultaneously, the patient can be fed into the small bowel.

To eliminate the inconvenience of the bulky feeding tube, patients with long-term gastrostomies can be fitted with a so-called button device, which lies flush with the abdominal wall. Between feedings, a valve in the device closes off access to the stomach; during feedings, the feeding tube is inserted past the valve, permitting access to the stomach.

Parenteral Nutrition

The intravenous route is used as a supplement to oral or enteral nutrition or is used as the sole source of nutrition (TPN) when it becomes clear that the patient is not receiving sufficient nutrients by the other routes. Regular evaluation of SGA should be performed during TPN to ensure that the patient’s nutrient requirements are being met.

Short-term parenteral feeding Short-term infusions are best given through a peripherally inserted central catheter (PICC). These catheters are inserted into an arm or forearm vein and advanced into the superior vena cava. PICCs are comfortable and avoid the risks of subclavian puncture or the difficulties of maintaining sterility of the exit sites of jugular catheters. In addition, full TPN with hypertonic mixtures can be given through these catheters without risk of thrombosis. Despite the designation “short term,” these catheters can be used for months.

Long-term parenteral feeding Patients with intestinal failure often require parenteral feeding for years. To permit long-term parenteral feeding, an interventional radiologist advances a specially designed catheter through a subcutaneous tunnel via the jugular vein to the superior vena cava. The tip of this catheter should lie just above the right atrium, to avoid thrombotic complications. Near the exit site, within the subcutaneous tunnel, the catheter is surrounded by a Dacron cuff. Fibroblasts will grow into the cuff, sealing and anchoring the skin exit site.

Nutrient Requirements

Protein

Protein requirements are met by giving whole proteins, peptides, or amino acids in enteral nutrition and by infusing an amino acid mixture in parenteral nutrition. The goal is to promote nitrogen retention and protein synthesis. Although limiting glucose and lipid (energy) intake will maximize nitrogen retention, dietary protein has an anabolic effect independent of energy intake, and will reduce nitrogen losses when infused alone. Thus, the amount of amino acids given appears to be a very important determinant of nitrogen balance.

About 1 to 1.5 g/kg of ideal body weight of protein or amino acids will be sufficient for most patients with normal renal function. Additional amounts should be added for losses from prior depletion or current hypercatabolism. In patients with hepatic failure, protein intake should be restricted to 0.8 to 1.0 g/kg a day.

Glutamine

Glutamine is an amino acid released by muscle and used by immune cells and enteral cells for energy. In malnutrition and after trauma, muscle glutamine and muscle protein synthesis are reduced. The infusion of glutamine normalizes muscle glutamine and restores protein synthesis. Clinically, bone marrow transplant patients were noted to have fewer episodes of sepsis and a shorter hospital stay if they received a glutamine-supplemented amino acid solution. Because glutamine does not have a long shelf-life in solution, dipeptides containing glutamine have been used as a substitute. Infusion of solutions containing such dipeptides has been found to increase muscle glutamine and improve protein synthesis.

Immunonutrition

Enteral formulations enriched in arginine, omega-3 fatty acids, and glutamine nucleotides are considered to enhance the immune response; treatment with these formulations is referred to as immunonutrition. These formulations vary in composition, but they are distinguished by high (12 to 15 g/L) or low (4 to 6 g/L) arginine content, presence or absence of glutamine and nucleotides, and different concentrations of omega-3 fatty acids. A recent summit on immune-enhancing enteral therapy concluded, on the basis of published literature, that immunonutrition should be given to malnourished patients undergoing elective GI surgery and to trauma patients with an injury severity score of 18 or greater or an abdominal trauma index of 20 or greater. Immunonutrition was also recommended, despite lack of evidence, in patients undergoing head and neck surgery or aortic reconstruction, as well as in patients with severe head injury or burns, and in ventilator-dependent nonseptic patients. It was not recommended for patients with splanchic hypoperfusion or bowel obstruction distal to the access site or after major upper GI hemorrhage.

A systematic review of immunonutrition by Heyland and colleagues showed that it reduced septic complications but did not reduce mortality. Their analysis of 22 randomized, controlled trials covering 2,419 critically ill or surgical patients indicated that only high-arginine formulations reduced infectious complications and length of stay. These authors concluded that in patients undergoing elective surgery, immunonutrition may reduce complications and reduce length of stay. Pending further studies, however, immunonutrition was not recommend-
ed in patients with critical illness. Because many trauma and septic patients may be critically ill, these authors’ recommendations are at variance with those of the immunonutrition summit (see above). The finding that benefit is seen only with the formulation containing higher amounts of arginine raises the question whether arginine per se or the higher nitrogen intake is responsible for the benefit.

Energy (Glucose and Lipids)

In healthy persons, basal energy expenditure (BEE), or basal metabolic rate (BMR), in kilocalories a day can be predicted with the Harris-Benedict equation:

BEE in males = 66.5 + (13.8 \times \text{weight in kg}) + (5.0 \times \text{height in cm}) – (6.8 \times \text{age in yr})

BEE in females = 655.1 + (9.6 \times \text{weight in kg}) + (1.8 \times \text{height in cm}) – (4.7 \times \text{age in yr})

A calculator for determining BEE according to the Harris-Benedict equation can be found on the Internet, at www-users.med.cornell.edu/~spon/picu/calc/beecalc.htm.

For patients substantially on bed rest, about 30% should be added to the BEE to meet their metabolic requirements. In practice, this calculates as a daily expenditure of about 31 kcal/kg. An expert group has suggested a daily intake of 25 kcal/kg in ICU patients. Therefore, 25 to 30 kcal/kg/day will meet the needs of most patients, except those with burns. Malnutrition reduces the expected BEE by as much as 35%; injury, sepsis, and, especially, burns increase requirements.

Energy requirements during TPN can be met by infusing glucose or lipid emulsions. These nonprotein energy sources enhance nitrogen retention. The most striking increase in nitrogen balance has been found to occur when energy was increased from 0 kcal/kg to 30 kcal/kg of ideal body weight. Increases above that provided only slight improvement. In obese persons, a high-protein formulation with only about 14 kcal/kg/day meets nitrogen requirements and is associated with satisfactory wound healing.

Figure 2  Controlling hyperglycemia in intensive care unit patients receiving nutritional support.

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GASTROENTEROLOGY:XIII  Enteral and Parenteral Nutrition
Because glucose spares nitrogen in fasting persons, it has been advocated as the main source of energy for parenteral nutrition. However, recent studies have shown that in malnourished patients and septic patients, lipids can promote nitrogen retention and increase total body nitrogen to the same extent as glucose, provided amino acids are given.\(^50\) Fats constitute about 30% of total energy in most enteral formulas. Furthermore, glucose-lipid mixtures facilitate the control of severe hyperglycemia from the glucose component.

Infusion of glucose at rates that exceed energy requirements elevates \(O_2\) consumption, \(CO_2\) production, resting energy expenditure, and urinary norepinephrine excretion. However, the magnitude of increased \(CO_2\) production is small if total calories infused conform to levels recommended for the patient’s clinical situation.\(^51\)

The exact amount of lipid to include in the parenteral nutrition regimen is controversial. In a randomized, controlled trial of 512 bone marrow transplant patients receiving TPN, sepsis was no more frequent in patients who received 30% of energy as lipid than in those who received only sufficient lipids to meet essential fatty acid (EFA) needs (6% to 8% of energy intake).\(^52\) In addition, EFA deficiency developed in some of the latter patients, and in some, this small amount of lipid was insufficient to meet energy requirements without induction of hyperglycemia from the glucose component. These authors recommend giving 25% to 30% of energy as long-chain triglycerides (LCTs). In contrast, a study in 57 trauma patients found that TPN with added lipid increased sepsis and hospital stay.\(^53\) It was not clear whether the adverse effect was from the lipid per se or the increased energy intake while on lipid.

Because of their glucose content, both enteral nutrition and TPN enhance the risk of sepsis if the blood glucose level is allowed to rise above 127 mg/dl (7 mmol/L).\(^54\) Therefore, insulin should be infused in patients receiving nutritional support to keep them as close to normoglycemia as possible [see Figure 2].

Whereas the major concern with glucose-based formulations is hyperglycemia, the key concern with lipid emulsions is hypertriglyceridemia, which may induce pancreatitis. Lipid particles also reduce gas diffusion in the lungs and inhibit the reticuloendothelial system. Provided that lipid emulsions are infused continuously at a rate that does not exceed 110 mg/kg/hr, hypertriglyceridemia does not occur. When these principles are followed, 30% to 50% of nonprotein calories can be given as fat, especially in glucose-intolerant patients.

Electrolytes, Trace Elements, and Vitamins

In patients receiving nutritional support, levels of electrolytes and trace elements should be adjusted to fit the clinical circumstances [see Table 2]. Carbohydrate feeding induces sodium retention, resulting in refeeding edema. In malnourished patients, great care should be taken to prevent salt and water overload.

Body potassium is disproportionately reduced relative to nitrogen in malnourished patients. Positive nitrogen balance does not occur unless potassium, phosphorus, and magnesium are given.\(^56\) During enteral and parenteral nutrition, serum phosphorus may drop precipitously and cause dangerous neurologic symptoms.\(^57\)

Micronutrients comprise vitamins and trace elements. The former are complex organic compounds; the latter are inorganic elements. Trace elements important to nutritional support include zinc, copper, chromium, and selenium. Diarrhea increases zinc requirements markedly and copper requirements modestly [see Table 2]. Oral chromium requirements have not been precisely determined, but deficiency occurs in patients receiving TPN; in one of my patients, the daily chromium needs were increased to 10 to 20 \(\mu\)g. Patients receiving parenteral nutrition may develop selenium deficiency, with muscle pains and cardiomyopathy. Increased losses of selenium can occur from the GI tract and from wounds. The recommended dose of selenium for stable patients is 40 \(\mu\)g/day. Patients depleted of selenium may require as much a 120 \(\mu\)g/day to regain normal levels.

The current recommendations for vitamins [see Table 3] specify the amounts required to maintain normal plasma or blood levels in patients on long-term home parenteral nutrition. There are no clearly defined recommendations for critically sick or septic patients.

Table 2  Daily Electrolyte and Trace Element Requirements for Adults on Total Parenteral Nutrition

<table>
<thead>
<tr>
<th>Element</th>
<th>Normal</th>
<th>Increased GI Losses</th>
<th>Renal Failure</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mmol)</td>
<td>80–120</td>
<td>Meet losses</td>
<td>20–40</td>
<td>Reduce in heart failure</td>
</tr>
<tr>
<td>Potassium (mmol)</td>
<td>40–80</td>
<td>80–120</td>
<td>0–20</td>
<td>Correct hypokalemia before starting nutrition</td>
</tr>
<tr>
<td>Magnesium (mmol)</td>
<td>5–10</td>
<td>10–20</td>
<td>0–5</td>
<td>Correct hypomagnesemia before starting nutrition</td>
</tr>
<tr>
<td>Phosphorus (mmol)</td>
<td>10–15</td>
<td>10–15</td>
<td>0–5</td>
<td>Risk of dangerously low serum levels when feeding patients with severe malnutrition</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>TPN: 3–4</td>
<td>TPN: 12–25</td>
<td>No change</td>
<td>—</td>
</tr>
<tr>
<td>Copper (mg)</td>
<td>TPN: 0.25–0.3</td>
<td>Enteral: 0.5–0.7</td>
<td>No change</td>
<td>Reduce to 0.1 in hepatic failure</td>
</tr>
</tbody>
</table>

### Home Parenteral Nutrition

Patients with intestinal failure from a short bowel, chronic bowel obstruction, radiation enteritis, or untreatable malabsorption can be nourished by parenteral nutrition given at home. Arteriovenous shunts were initially used for long-term venous access in these patients, but success was limited because of clotting or disruption of the shunt. Long-term success has been achieved with a tunneled silicone rubber catheter or an implanted reservoir. Premixed nutrients are infused overnight. The catheter is then disconnected and a heparin lock applied, leaving the patient free to attend to daily activities. We have used home parenteral nutrition for more than 20 years in

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two patients with total jejunoileal resection; one continues to receive it after 30 years. Survival of patients with short bowel from treatment for Crohn disease or pseudo-obstruction is excellent. Home parenteral nutrition increases quality-adjusted years of life in these patients and is cost-effective. On the other hand, mean survival in AIDS patients or those with metastatic cancer who receive home parenteral nutrition is about 3 months. There is no evidence that home parenteral nutrition prolongs their survival or enhances their quality of life. Trials are urgently required to justify the use of home parenteral nutrition in terminal cancer and AIDS.

Complications of Long-term Home Parenteral Nutrition

At the start of nutritional support, patients are vulnerable to complications related to venous and enteral access and to metabolic complications. Careful and frequent monitoring and adjusting of nutrient intake will prevent these complications. Over the longer term, patients receiving TPN are vulnerable to three organ-specific complications: hepatic disease, bone disease, and gallstones.

Hepatic disease The most serious form of hepatic disease related to TPN is chronic cholestasis with fibrosis. This condition is most common in patients with a very short bowel. The exact cause is unknown, but absorption of endotoxin or alteration in bile salts by bacterial dehydroxylation are possible factors. Successful treatment with metronidazole and with ursodeoxycholic acid has been reported. In some patients, carnitine infusions have corrected cholestasis.

Bone disease Bone loss during long-term TPN is a complex issue. In a prospective longitudinal study, patients were noted to have a high bone turnover before the institution of home parenteral nutrition, but during TPN this changed to osteomalacia and slow bone turnover. This process has been attributed to aluminum toxicity but occurs in its absence and seems to respond to withdrawal of vitamin D from the TPN formula. In a prospective 4-year study of patients on home parenteral nutrition, withdrawal of vitamin D increased spinal bone mass. On the other hand, patients on home parenteral nutrition can lose bone mass as a result of factors such as active inflammatory bowel disease, corticosteroid therapy, and inactivity. Some clinicians are treating reduced bone mineral density in these patients with intravenous bisphosphonates such as pamidronate and clodronate (the latter is not available in the United States). Although there are no controlled trials of bisphosphonates in patients receiving home parenteral nutrition, there are anecdotal reports of improvement of bone mass with this therapy.

Gallstones The short bowel state results in bile salt deficiency and increased biliary cholesterol secretion. In addition, sludge composed of bilirubin and calcium forms in the gallbladder. Consequently, the incidence of gallstones is high in these patients. These stones are mixed cholesterol and pigment.

The author has no commercial relationships with manufacturers of products or providers of services services for this subsection.

References

16. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. JPEN J Parenter Enteral Nutr 26(suppl):1SA, 2002

Table 3  Recommendations for Vitamins in Adults on Total Parenteral Nutrition

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Recommended Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>3,300 IU</td>
</tr>
<tr>
<td>D₂</td>
<td>200 IU</td>
</tr>
<tr>
<td>E</td>
<td>10 IU</td>
</tr>
<tr>
<td>K₁</td>
<td>150 mg</td>
</tr>
<tr>
<td>Ascorbate</td>
<td>200 mg</td>
</tr>
<tr>
<td>Thiamin</td>
<td>6 mg</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>3.6 mg</td>
</tr>
<tr>
<td>Pyridoxine</td>
<td>6 mg</td>
</tr>
<tr>
<td>Niacin</td>
<td>40 mg</td>
</tr>
<tr>
<td>Pantothenate</td>
<td>15 mg</td>
</tr>
<tr>
<td>Biotin</td>
<td>60 µg</td>
</tr>
<tr>
<td>Folate</td>
<td>600 µg</td>
</tr>
<tr>
<td>Cobalamin</td>
<td>5 µg</td>
</tr>
</tbody>
</table>

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