

CLINICAL THERAPEUTICS

Parenteral Nutrition in the Critically Ill Patient

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This Journal feature begins with a case vignette that includes a therapeutic recommendation. A discussion of the clinical problem and the mechanism of benefit of this form of therapy follows. Major clinical studies, the clinical use of this therapy, and potential adverse effects are reviewed. Relevant formal guidelines, if they exist, are presented. The article ends with the author's clinical recommendations.

A 67-year-old woman with type 2 diabetes mellitus undergoes extensive resection of the small bowel and right colon with a jejunostomy and colostomy because of mesenteric ischemia. In the surgical intensive care unit, severe systemic inflammatory response syndrome with possible sepsis develops. The patient is treated with volume resuscitation, vasopressor support, mechanical ventilation, broad-spectrum antibiotics, and intravenous insulin infusion.

Low-dose tube feedings are initiated postoperatively through a nasogastric tube. However, these feedings are discontinued after the development of escalating vasopressor requirements, worsening abdominal distention, and increased gastric residual volume, along with an episode of emesis. The hospital nutritional-support service is consulted for feeding recommendations. A discussion with the patient's family reveals that during the previous 6 months, she lost approximately 15% of her usual body weight and decreased her food intake because of abdominal pain associated with eating. Her preoperative body weight was 51 kg (112 lb), or 90% of her ideal body weight. The physical examination reveals mild wasting of skeletal muscle and fat. Blood tests show hypomagnesemia, hypophosphatemia, and normal hepatic and renal function. Central venous parenteral nutrition is recommended.

THE CLINICAL PROBLEM

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Malnutrition, including the depletion of essential micronutrients and erosion of lean body mass, is very common in patients who are critically ill, with 20 to 40% of such patients showing evidence of protein-energy malnutrition.¹⁻⁸ The incidence of malnutrition worsens over time in patients who require prolonged hospitalization.^{2,9-11}

Protein-energy malnutrition before and during hospitalization is associated with increased morbidity and mortality in hospitalized patients.^{2,10-18} Adequate nutrient intake is critical for optimal cell and organ function and wound repair.^{19,20} Protein-energy malnutrition is associated with skeletal-muscle weakness, an increased rate of hospital-acquired infection, impaired wound healing, and prolonged convalescence in patients who are admitted to an intensive care unit (ICU).^{1-4,11,16,17-19,21} However, the relationship between malnutrition and adverse clinical outcomes is complex, because malnutrition may contribute to complications that worsen nutritional status, and patients who are more difficult to feed are more critically ill and at higher risk for death and complications. Thus, the true cost of malnutrition cannot be estimated with accuracy in critically ill patients.

PATHOPHYSIOLOGY AND EFFECT OF THERAPY

The pathophysiology of malnutrition in patients in the ICU is multifactorial. Critical illness is associated with catabolic hormonal and cytokine responses. These include increased blood levels of counterregulatory hormones (e.g., cortisol, catecholamines, and glucagon), increased blood and tissue levels of proinflammatory cytokines (e.g., interleukin-1, interleukin-6, interleukin-8, and tumor necrosis factor α), and peripheral-tissue resistance to endogenous anabolic hormones (e.g., insulin and insulin-like growth factor 1).^{2,12,20,22,23} This hormonal milieu increases glycogenolysis and gluconeogenesis, causes a net breakdown of skeletal muscle, and enhances lipolysis, which together provide endogenous glucose, amino acids, and free fatty acids that are required for cellular and organ function and wound healing.^{2,12,22} Unfortunately, although plasma substrate levels may be increased, their availability for use by peripheral tissues may be blunted (because of factors such as insulin resistance and inhibition of lipoprotein lipase), and plasma levels of certain substrates (e.g., glutamine) may be insufficient to meet metabolic demands.^{22,23}

Critically ill patients often have a history of decreased spontaneous food intake before ICU admission, because of anorexia, gastrointestinal symptoms, depression, anxiety, and other medical and surgical factors. In addition, their food intake may have been restricted for diagnostic or therapeutic procedures.^{2,16} Such patients commonly have episodes of abnormal nutrient loss from diarrhea, vomiting, polyuria, wounds, drainage tubes, renal-replacement therapy, and other causes.² Bed rest, decreased physical activity, and neuromuscular blockade during mechanical ventilation cause skeletal-muscle wasting and inhibit protein anabolic responses.²⁴ Drugs that are frequently administered to patients in the ICU may themselves increase skeletal-muscle breakdown (corticosteroids), decrease splanchnic blood flow (pressor agents), or increase urinary loss of electrolytes, minerals, and water-soluble vitamins (diuretics). Infection, operative trauma, and other stresses may increase energy expenditure and protein and micronutrient needs.^{2,12,16,23,25-28}

Most critically ill patients who require specialized nutrition (85 to 90%) can be fed enterally

through gastric or intestinal tubes and then transitioned to an oral diet with supplements.^{1,2,16,19,29} However, in approximately 10 to 15% of such patients, enteral nutrition is contraindicated.^{1,2,16} Complete intravenous parenteral nutrition provides fluid, dextrose, amino acids, lipid emulsion, electrolytes, vitamins, and minerals (Table 1). Insulin and selected drugs may also be added. Therapeutic effects of parenteral nutrition accrue through the combined provision of energy (primarily as the dextrose and lipid components), essential and nonessential amino acids, essential fatty acids, vitamins, minerals, and electrolytes.² These elements support vital cellular and organ functions, immunity, tissue repair, protein synthesis, and capacity of skeletal, cardiac, and respiratory muscles.^{1,12,15,27,28}

CLINICAL EVIDENCE

Few well-designed, randomized, controlled trials of the efficacy of parenteral nutrition in critical illness have been conducted.^{1,29-31} Most trials have been limited by a small number of patients, varying definitions of critical illness, inappropriate blinding strategies, or the lack of an intention-to-treat design.³⁰ Also, the dextrose and calorie doses that are used in parenteral solutions in most of the earlier trials would now be considered excessive.^{32,33} The role of hyperglycemia in morbidity and mortality among patients in the ICU is complex, but most investigators agree that a blood glucose value exceeding 180 mg per deciliter (10 mmol per liter) may be associated with increased rates of death and complications.^{34,35}

Despite these limitations, studies suggest that patients with moderate-to-severe protein-energy malnutrition may benefit from parenteral nutrition if enteral nutrition is not possible.^{5,36} However, extensive data also support the use of enteral nutrition, as compared with parenteral nutrition, in patients in the ICU who have a functional gastrointestinal tract and who are able to receive adequate enteral nutrition.^{1,2,4,5,11,14,16,19,33,37-40}

A meta-analysis of well-designed intention-to-treat trials comparing enteral nutrition with parenteral nutrition in critically ill patients (with each study enrolling fewer than 200 patients) showed a significant reduction in mortality among patients receiving parenteral nutrition (odds ratio, 0.51; 95% confidence interval [CI],

Table 1. Composition of a Typical Adult Formulation of Central Venous Parenteral Nutrition.*

Component	Content
Total volume (liters/day)	1–2
Dextrose (%)	10–25
Amino acids (%)†	3–8
Lipids (%)‡	2.5–5.0
Electrolytes (mmol/liter)	
Sodium	40–150
Potassium	30–50
Phosphorus	10–30
Magnesium	5–10
Calcium	1.5–2.5
Trace elements§	
Vitamins¶	

* Electrolytes in parenteral nutrition are adjusted as indicated according to renal function, gastrointestinal losses, and other indicators to maintain serially measured serum levels within the normal range. In the presence of elevated blood levels, lower doses (or elimination) of specific electrolytes, as compared with the typical ranges that are listed, may be indicated until blood levels normalize. Higher dextrose levels typically increase requirements for potassium, magnesium, and phosphorus. The percentage of sodium and potassium salts as chloride is increased to correct metabolic alkalosis, and the percentage of salts as acetate is increased to correct metabolic acidosis. Regular insulin is added to parenteral nutrition as needed to achieve blood glucose goals, and separate intravenous insulin infusions are commonly required in patients with hyperglycemia.

† Parenteral nutrition provides all nine essential amino acids and eight nonessential amino acids. Some guidelines recommend the routine addition of glutamine as a conditionally essential amino acid in critically ill adults. The dose of amino acids is adjusted as a function of the respective degrees of renal and hepatic dysfunction.

‡ In the United States, only soybean oil–based fat emulsions are available. Intravenous lipid is provided as a 20% emulsion when given as a separate infusion over a period of 10 to 12 hours per day; when pharmacy parenteral-nutrition compounding machines are used, 20% or 30% lipid emulsions may be mixed with dextrose, amino acids, and micronutrients in the same infusion bag. In European and other countries, intravenous fish oil, mixtures of olive and soybean oils, medium-chain triglyceride–soybean oil mixtures, and combinations of these oils are approved for use in parenteral nutrition.

§ Trace elements that are added on a daily basis to parenteral nutrition are typically mixtures of chromium, copper, manganese, selenium, and zinc. Minerals can also be supplemented individually.

¶ Vitamins that are added on a daily basis to parenteral nutrition are mixtures of vitamins A, B₁ (thiamine), B₂ (riboflavin), B₃ (niacinamide), B₆ (pyridoxine), B₁₂, C, D, and E; biotin; folate; and pantothenic acid. Vitamin K is added on an individual basis (e.g., in patients with cirrhosis). Specific vitamins can also be supplemented individually.

with enteral nutrition, as compared with parenteral nutrition (odds ratio, 0.64; 95% CI, 0.47 to 0.87; $P=0.004$) but no significant difference in mortality (odds ratio, 1.08; 95% CI, 0.70 to 1.65; $P=0.70$).³⁷

Given the changes in the methods of ICU nutritional support during the past several years, including tighter blood glucose control and the use of lower caloric loads and alternative substrates, there is a need for further trials that are based on current practice.

CLINICAL USE

Serial assessment of nutritional status should be a routine component of ICU care (Table 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). The objective is to detect preexisting malnutrition or the risk of nutritional depletion. Nutritional assessment involves clinical judgment that is based on data derived from the patient's history (especially the dietary and weight history), medical records, physical examination, and biochemical testing (Table 1 in the Supplementary Appendix and Table 2). In critically ill patients, circulating levels of proteins, such as albumin and prealbumin, are often decreased because of inflammation, infection, or fluid overload and are therefore not useful as biomarkers of protein nutrition.^{1,2}

The appropriate use of parenteral nutrition in the ICU continues to be a subject of debate.^{29,36–45} As compared with parenteral nutrition, enteral nutrition is less expensive, may better maintain intestinal mucosal structure and gut absorptive and barrier functions (as clearly shown in animal studies), and is associated with fewer infectious and mechanical and metabolic complications.^{2,11,46} However, the use of enteral feeding in patients with gastrointestinal intolerance is associated with underfeeding and consequent malnutrition.^{10,25} Given the range of opinion on the efficacy of parenteral nutrition, the use of this therapy varies widely among ICUs, among regions of the United States, and among countries worldwide.^{9,10,16,25,26} The administration of parenteral nutrition in children, which requires special considerations beyond the scope of this article, is covered in pediatric guidelines for hospital-based nutritional support.^{2,47,48}

Generally recognized, but largely not evidence-based, indications for parenteral nutrition in critically ill patients include massive small-bowel

0.27 to 0.97; $P=0.04$).³¹ This effect was influenced by whether enteral nutrition was started early (within 24 hours after ICU admission or injury), in which case no significant benefit of parenteral nutrition was seen. The risk of infection was significantly increased with parenteral nutrition. A systematic review of 13 randomized clinical trials involving critically ill adults showed a significant reduction in infectious complications

Table 2. Clinical Manifestations of Nutrient Deficiencies.*

Sign or Symptom	Potentially Depleted Nutrient
Muscle and fat wasting, weakness	Calories, protein, or both
Peripheral edema	Thiamine (heart failure), protein (low oncotic pressure)
Glossitis (discolored, smooth, or painful tongue)	Folate, vitamin B ₁₂ , niacin, riboflavin, thiamine, iron
Cheliosis, angular stomatitis	Riboflavin, niacin, folate, vitamin B ₁₂
Loss of vibratory or position sense, fatigue	Vitamin B ₁₂
Dermatitis (sun-exposed skin), diarrhea, dementia	Niacin (pellagra)
Symmetric motor or sensory dysfunction, ataxia, nystagmus, heart failure, mental status changes or confusion	Thiamine (beriberi)
Bleeding gums, petechiae, ecchymosis	Vitamin C, vitamin K
Poor wound healing	Calories, protein, calories and protein, vitamin C, vitamin A, zinc, other micronutrients
Bone pain	Vitamin D (osteomalacia)
Follicular hyperkeratosis, night blindness, Bitot's spots	Vitamin A
Flaky, whitish dermatitis	Essential fatty acids (linoleic, linolenic)
Sparse hair, easily pluckable hair, or both	Zinc, protein
Pale skin, nail spooning (koilonychia)	Iron
Loss of taste; reddish dermatitis around nose, mouth, and groin; hair loss	Zinc
Peripheral neuropathies, gait abnormalities, weakness, fatigue	Copper
Muscle pain, heart failure (cardiomyopathy)	Selenium
Paresthesias, carpal pedal spasm	Calcium, magnesium, phosphorus, or potassium

* Alternatively, the signs and symptoms may have a variety of non-nutritional causes. Typically, severe deficiency of specific nutrients has occurred before physical manifestations of deficiency, with initial depletion of tissue concentrations of the nutrient, followed by decreased blood concentrations.

resection with or without colonic resection and proximal high-output fistulae or perforated small bowel. Other conditions in which enteral nutrition may be contraindicated or not tolerated include severe diarrhea or emesis, substantial abdominal distention, partial or complete bowel obstruction, severe gastrointestinal bleeding, and severe hemodynamic instability.^{1,2} The likely persistence of any of these conditions for more than 3 to 7 days is commonly accepted as an indication for parenteral nutrition.^{1,2,16}

Generally accepted contraindications for parenteral nutrition (also largely not evidence-based) include adequate gastrointestinal tract function with access for enteral feeding, evidence that parenteral nutrition is unlikely to be required for more than 5 to 7 days, intolerance of the intravenous fluid load required for parenteral nutrition, severe hyperglycemia, severe electrolyte abnormalities on the planned day of initiation of parenteral nutrition, and any circumstance that

may substantially increase the risk of intravenous-catheter placement.^{1,2,4,16}

Parenteral nutrition can be given either by peripheral or central vein. However, because of the risk of phlebitis, peripheral-vein parenteral nutrition cannot be highly concentrated and therefore must be given in a large volume to meet nutrient requirements. Fluid restriction because of renal, hepatic, or cardiac dysfunction often precludes the use of large fluid volumes; thus, peripheral-vein parenteral nutrition is generally not indicated in ICU patients. Central venous catheters allow concentrated nutrient delivery and are typically more appropriate for such patients.

Proper insertion and maintenance of the intravenous catheter are essential for the safety and success of parenteral nutrition.^{2,49} Many hospitals have a dedicated vascular-access service for the purpose of inserting catheters specifically for parenteral nutrition. In general, a catheter that

is inserted for parenteral nutrition should not be used for any other purpose, such as phlebotomy or the administration of medications.^{2,49} Particular care must be taken to maintain the catheter and the percutaneous entry site with appropriate sterile access and dressing techniques.

Parenteral-nutrition formulations are prepared in a sterile environment by pharmacists with specific training in preparing such formulations. Computerized formulation guidance is increasingly used to ensure proper composition. Because of the risk of biochemical degradation and bacterial contamination, fresh solutions are prepared every 24 hours and are kept refrigerated and protected from light. The parenteral-nutrition solution is allowed to warm to room temperature before administration. The solution is administered by infusion pump to control the rate of delivery. In-line filters are used to remove particulate matter.

Energy (calorie) needs in adult patients in the ICU often vary considerably because of day-to-day changes in clinical conditions.^{9,50,51} Optimal caloric requirements in critically ill patients are unknown owing to the lack of data from rigorous randomized clinical trials.^{1,30} Resting energy expenditure can be measured with the use of indirect calorimetry or more conveniently estimated with the use of standard predictive equations. The most common is the Harris-Benedict equation, which incorporates the patient's age, sex, weight, and height (Table 3).^{2,51} Current clinical practice guidelines suggest that an adequate energy goal for most ICU patients is approximately equivalent to the measured or estimated resting energy expenditure multiplied by 1.0 to 1.2.^{2,16} An alternative method is to use 20 to 25 kcal per kilogram of body weight as the total caloric target range for most adults in the ICU.^{16,19}

The principal macronutrient components of central venous parenteral nutrition include amino acids, lipids, and dextrose (Table 1). The common recommendation for the amino acid dose ranges from 1.2 to 1.5 g per kilogram per day for most patients with normal renal and hepatic function, although some guidelines recommend higher doses (2.0 to 2.5 g per kilogram per day) under specific conditions (Table 3).^{1,2,16,27} The recommended maximal dose of lipid emulsion infusion is approximately 1.0 to 1.3 g per kilogram per day.² Typically, lipid emulsions are given as

separate infusions, although with the use of specialized pharmacy compounding machines, all the components of parenteral nutrition may be mixed in the same infusion bag.

In central venous parenteral nutrition, a reasonable initial guideline is to provide 60 to 70% of non-amino acid calories as dextrose and 30 to 40% of non-amino acid calories as fat emulsion (Table 3).^{2,16} I find it useful to provide approximately half the estimated dextrose goal on the first day of therapy and to advance the dextrose dose to the target amount over the next 2 to 3 days if the formula is well tolerated.

Recent studies indicate that relatively tight blood glucose control in ICU settings is associated with an improved clinical outcome.^{1,32,34,35} However, there is debate about the optimal upper and lower limits of blood glucose.^{34,35} Data from the Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial (ClinicalTrials.gov number, NCT00220987) suggest that maintaining a blood glucose level of less than 180 mg per deciliter may be an appropriate goal for ICU patients, although uncertainty persists with regard to surgical ICU patients.^{34,35} Mild degrees of hyperglycemia can be treated by decreasing the dextrose content or by adding regular insulin to the parenteral-nutrition mixture to maintain blood glucose within the desired range. Separate intravenous insulin infusions provide flexibility and should be used to treat marked hyperglycemia in the ICU.

Specific requirements for intravenous trace elements and vitamins have not been well defined in subgroups of critically ill patients.^{6,7} Therefore, standardized intravenous preparations of combined vitamins and minerals are commonly used (Table 1).²

Monitoring of central venous parenteral nutrition in the ICU requires routine assessment of multiple factors (Table 1 in the Supplementary Appendix).^{2,49} Blood glucose should be monitored several times daily to ensure adequate metabolic control, and blood electrolytes (including potassium, sodium, chloride, magnesium, and phosphorus) and renal function should generally be assessed daily. Blood triglyceride levels may be monitored at baseline and then generally weekly, particularly in patients with known lipid disorders, pancreatitis, or liver or renal disease, to assess clearance of intravenous fat.^{2,16} Hepatic func-

Table 3. Suggested Parenteral-Nutrition Requirements for Critically Ill Adult Patients.*

Variable	Dose†
Energy	Resting energy expenditure in kcal/day \times 1.0 to 1.2, or 20 to 25 kcal/kg/day‡
Dextrose	Initial parenteral nutrition order with 60 to 70% of non-amino acid calories as dextrose§
Lipid emulsion	Initial parenteral nutrition order with 30 to 40% of non-amino acid calories as lipid§
Essential and nonessential amino acids (g/kg/day)	
Normal renal and hepatic function	1.2–1.5¶
Hepatic failure (cholestasis)	0.6–1.2 (based on estimated function)
Encephalopathy	0.6 (may be temporarily discontinued)
Acute renal failure in patients not on renal-replacement therapy	0.6–1.0 (based on renal function)
Renal failure in patients on renal-replacement therapy	1.2–1.5

* Caloric needs can be estimated by indirect calorimetry; they can be inaccurate in mechanically ventilated patients receiving high levels of inspired oxygen or because of air leaks or other technical issues. In obese subjects, an adjusted body weight should be used in the calculation of energy and protein needs according to the following equation: Adjusted body weight = ideal body weight (from standard tables or equations) + (current weight – ideal body weight) \times 0.25.

† The energy density is 3.4 kcal per gram for dextrose, 10 kcal per gram for lipid emulsion, and 4 kcal per gram for amino acids.

‡ The Harris–Benedict equation can be used to estimate resting energy expenditure in kcal per 24 hours and for men is as follows: $66.5 + (13.8 \times \text{body weight in kg}) + (5.0 \times \text{height in cm}) - (6.8 \times \text{age in yr})$. The equation for women is: $655 + (9.6 \times \text{body weight in kg}) + (1.8 \times \text{height in cm}) - (4.7 \times \text{age in yr})$. The equation may over- or underestimate resting energy expenditure in certain critically ill patients, particularly when clinical conditions are changing and when body weight fluctuates because of changes in fluid status.

§ Caloric needs can also be estimated as 20 to 25 kcal per kilogram per day (using dry weight or ideal body weight). Some studies suggest that 15 to 20 kcal per kilogram per day or lower may be appropriate.

¶ The clinical practice guidelines of some professional societies recommend protein or amino acid doses up to 2.0 g per kilogram per day in certain subgroups.

|| The clinical practice guidelines of some professional societies recommend protein or amino acid doses up to 2.0 or 2.5 g per kilogram day in patients receiving renal-replacement therapy.

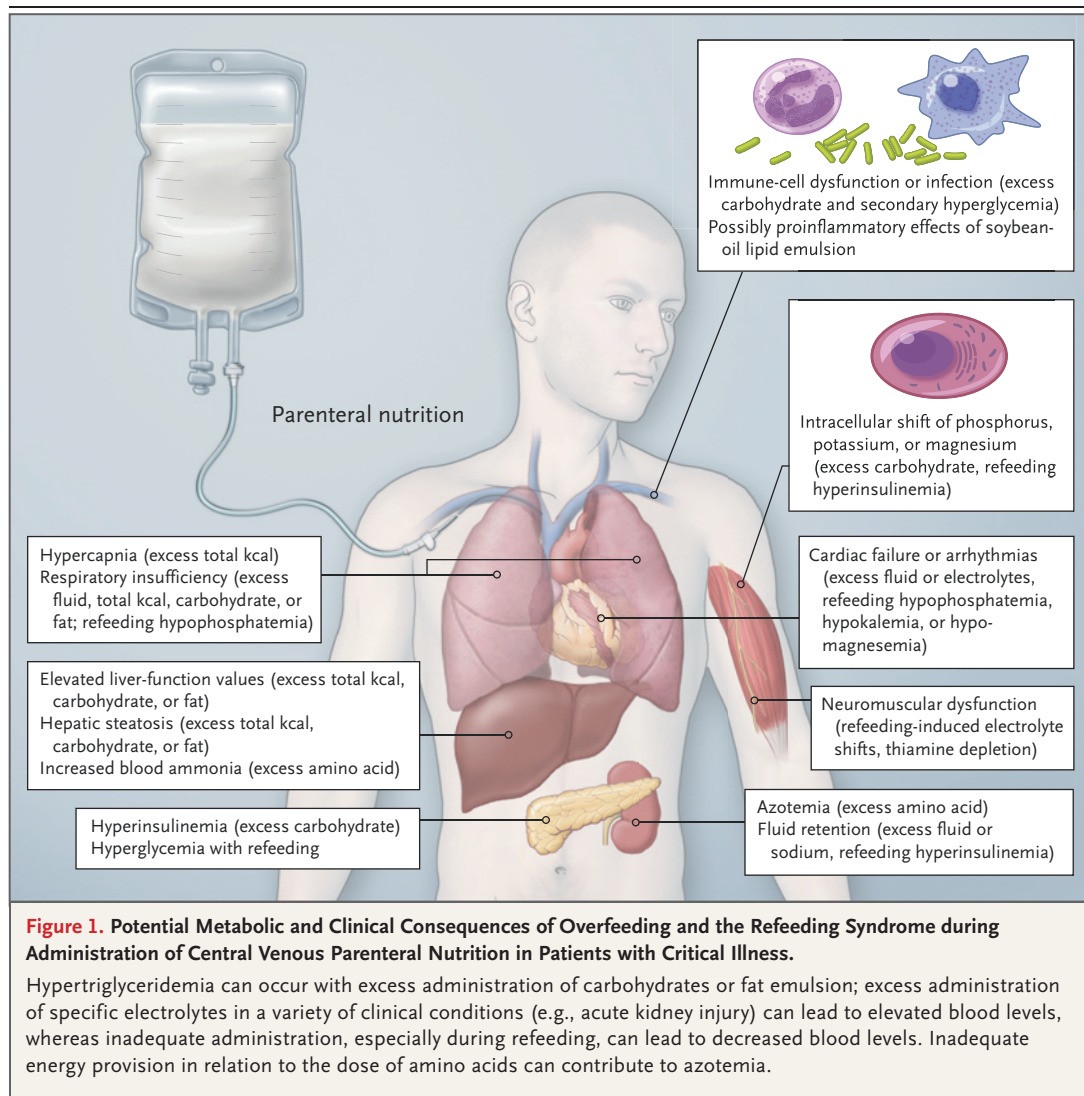
tion should probably be measured at least a few times weekly.⁵² The pH of arterial blood gases should be monitored in patients who are undergoing mechanical ventilation.^{2,49} I find it useful to periodically measure blood levels of zinc, copper, selenium, vitamin C, thiamine, vitamin B₆, vitamin B₁₂, and 25-hydroxyvitamin D in some patients. Consultation with an experienced, multidisciplinary nutritional-support team for recommendations regarding the parenteral-nutrition prescription and for monitoring may reduce complications and costs and may decrease inappropriate use of these specialized feeding methods.^{2,53,54}

The estimated daily cost of standard central venous parenteral nutrition is approximately \$60 to \$90, depending on additives (e.g., supplemental micronutrients). Personnel costs for monitoring by nutritional-support health professionals and for preparation of parenteral nutrition by

pharmacists is approximately \$20 per day, with additional minor costs for intravenous tubing, nursing time, and so forth.

ADVERSE EFFECTS

Central-vein parenteral nutrition is associated with mechanical, metabolic, and infectious complications.² Such complications are much more common when parenteral nutrition is not properly administered and when current standards of practice are not applied. Complications such as pneumothorax, bleeding, and thrombus formation can occur owing to the insertion of the central venous catheter, which is typically performed as a component of usual critical care. Catheter-related and non-catheter-related infections are not uncommon and are associated with hyperglycemia,^{16,32,41} the use of internal jugular-vein



or femoral-vein central venous catheters, and the use of nondedicated infusion ports for parenteral nutrition.⁴⁹

Overfeeding (the administration of excess dextrose, fat, or calories) and the refeeding syndrome (rapid feeding of patients with preexisting malnutrition) can induce a variety of metabolic complications during parenteral nutrition (Fig. 1).^{2,55-57} Accelerated carbohydrate metabolism increases the body's use of thiamine and can precipitate symptoms and signs of thiamine deficiency.⁵⁶ Insulin has an antinatriuretic effect,⁵⁸ which, when coupled with increased sodium and fluid intake during refeeding, can cause a rapid expansion of the volume of extracellular fluid in some patients.^{55,56} Decreased levels of blood elec-

trolytes can induce cardiac arrhythmias. In rare cases, these responses result in heart failure, particularly in patients with preexisting cardiac dysfunction.^{55,56} Other metabolic effects can include hypercapnia, hepatic steatosis, neuromuscular dysfunction, and immunologic defects (Fig. 1).

AREAS OF UNCERTAINTY

The optimal timing for the initiation of parenteral nutrition and the efficacy of various energy doses in critical care remain major areas of uncertainty.^{1,2,59-62} Few prospective data are available on the clinical effects of minimal or no feeding over a period of more than 7 days.⁴³ In patients who cannot tolerate adequate amounts

of enteral feeding, it is also unclear whether the initiation of supplemental parenteral nutrition is clinically beneficial in achieving goals for caloric and protein or amino acid intake.^{1,2,16,21,43} In addition, the clinical efficacy of conventional soybean oil-based lipid emulsions, as compared with alternatives (e.g., fish oil, olive oil plus soybean oil, medium-chain triglycerides plus soybean oil, and combinations of these oils), remains uncertain.⁶³⁻⁶⁷

Available data suggest that the body's requirement for glutamine may exceed its endogenous production in certain ICU patients.^{4,12,16,22} Several clinical trials have shown that glutamine-supplemented parenteral nutrition has protein anabolic effects, enhances indexes of immune function, and decreases the rate of hospital-acquired infections.^{12,22,68-70} However, clinical practice guidelines differ on the question of whether glutamine, if available, should be routinely added to parenteral nutrition in the ICU.^{1,4,16}

The optimal target for blood glucose control in ICU patients remains an area of uncertainty and has not been specifically investigated in patients receiving parenteral nutrition. Trials are also needed among subgroups of ICU patients to define biochemically and clinically optimal doses of specific vitamins and minerals.^{1,2,6,7,16,71,72}

GUIDELINES

Comprehensive clinical practice guidelines by expert professional societies in Canada, Europe, and the United States are available.^{1,2,4,16,19,47-49} Guidelines that were published earlier this year suggest that when enteral feeding is not possible, parenteral nutrition should be initiated within 7 days (according to one guideline¹) or within 3 days (ac-

cording to another guideline¹⁶). Among such patients who have protein-energy malnutrition at the time of admission to the ICU, the American clinical practice guidelines suggest that parenteral nutrition should be initiated without delay.¹

RECOMMENDATIONS

The patient in the vignette has a preadmission history of poor food intake, substantial weight loss, and evidence of skeletal-muscle and fat wasting. She is at risk for further nutrient depletion owing to catabolic effects of major surgery and inflammation, glycosuria, and gastrointestinal nutrient losses. It is unlikely that her nutrient needs will be fully met through enteral nutrition alone, in light of the extensive small-bowel resection.

I would therefore recommend the use of central venous parenteral nutrition. The patient is at risk for the refeeding syndrome, so the initial volume of parenteral nutrition should be 1 liter, and the administration of dextrose should be modest (e.g., 100 g per day) in an otherwise complete formulation. I would add additional magnesium and phosphorus in light of her blood levels, as well as supplemental thiamine. When the patient's upper bowel is functional and her condition is hemodynamically improved and stable, I would initiate enteral nutrition as tolerated. I would recommend management of the patient's nutritional issues by an experienced nutritional-support team.

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Supplementary Appendix

This appendix has been provided by the author to give readers additional information about his work.

Supplement to: Ziegler TR. Parenteral nutrition in the critically ill patient. N Engl J Med 2009;361:1088-97.

Supplemental online Table 1: Comprehensive nutritional assessment in critically ill adult patients*

- Review past medical and surgical history and current illness
 - Degree of catabolic stress (e.g. fever, infections, sepsis, surgeries, lung failure)
 - Organ function (e.g. liver, kidneys, lung, heart/vascular, GI)
 - Use of medications that may decrease nutrient absorption (e.g. phenytoin, elixer-based medications), alter nutrient metabolism/utilization (e.g. coumadin, isoniazid, methotrexate, phenytoin), increase nutrient excretion (e.g. diuretics), or cause hyperglycemia (e.g. corticosteroids).
 - Recent intravenous fluid and electrolyte therapy
 - Medical and surgical procedures that are likely in the near-term
 - Hemodynamic status and requirements for pressor agents
- Obtain body weight history
 - Current body weight [dry weight if available (e.g. preoperative, recent clinic visit)] and usual body weight when healthy or clinically stable; calculate percent body weight loss from usual body weight over the past several weeks and months
 - Calculate current weight as % of ideal body weight ¹
 - Determine body mass index (BMI = weight (kg)/height (m)²; BMI < 18.5 is considered underweight)
- Determine dietary intake pattern in relation to nutrient needs
 - General food and beverage intake pattern, percent of usual dietary intake consumed in recent weeks and months (e.g. % of usual), unusual or excessive consumption of specific foods or beverages, including alcoholic beverage consumption

- Previous use and type of enteral tube feedings and/or parenteral nutritional support
- Previous use of liquid or solid nutritional supplements, multivitamin-mineral preparations, specific vitamins or minerals
- Consult registered dietitian for more detailed nutrient intake assessment
- Perform detailed physical examination (see Table 2 in text)
 - Skeletal muscle wasting (cannot be assessed accurately in overweight or obese patients)
 - Loss of body fat stores
 - Presence and qualities of wounds
 - Skin/hair/tongue/conjunctival lesions suggestive of micronutrient deficiency
 - Evidence of organ dysfunction (GI, liver, renal, cardiopulmonary)
 - Fluid status (e.g. normal, dehydrated, fluid overload, capillary leak); fluid requirements are typically $\approx 30\text{-}40$ mL/kg body weight
- Evaluate gastrointestinal tract function
 - Swallowing or chewing difficulties, nausea, emesis, abdominal pain, enteral nutrition tolerance
 - Intestinal ileus, motility disorders, partial or complete obstruction
 - Diarrhea history (frequency, amount, other characteristics)
 - Acute or chronic gastrointestinal bleeding
 - Presence of fistulae; history of recent abdominal surgery
 - Drainage tube requirements and losses (e.g. gastric, biliary, intestinal, peritoneal)
- Determine functional status
 - Ability to perform daily activities, ambulatory capacity, bedrest, chemical paralysis

- History or physical examination evidence of muscle weakness and fatigue
- Confusion, dementia and other disorders affecting mental capacity that may impair spontaneous oral food intake
- Serial evaluation of selected biochemical tests²
 - Standard blood tests for organ function indices
 - Electrolytes, including calcium, potassium, sodium, magnesium, and phosphorus
 - pH (in ICU patients on mechanical ventilation)
 - Blood triglycerides (in patients receiving intravenous lipid emulsion)
 - Blood concentrations of selected vitamins and minerals if suggested by medical or dietary history, physical exam, or underlying illness (e.g. blood zinc, selenium, copper, thiamine, vitamin B6, vitamin B12, folate, 25-hydroxyvitamin D)
- Estimate caloric (kcal), protein and micronutrient needs (see Table 3 in text)
- Evaluate enteral and parenteral access for nutrient delivery
 - Ability to take oral diet and/or liquid supplements
 - Central venous or PICC line access; peripheral line access
 - Nasogastric, nasoenteric or percutaneous feeding tube availability or feasibility]
- Consultation with a multidisciplinary nutrition support team (ideally comprised of physicians, dietitians, nurses and pharmacists)

BMI = weight (kg)/height (m)², BMI < 18.5 is considered underweight; GI=gastrointestinal;

ICU=intensive care unit; PICC= peripherally-inserted central venous catheter.

¹ Ideal body weight can be estimated in adult men as 48 kg (106 pounds) per 5 feet of height + 2.7 kg (6 pounds) for each inch of height above 5 feet, and in adult women as 45 kg (100 pounds) per 5 feet of height + 2.3 kg (5 pounds) for each inch of height above 5 feet.

² Blood concentrations of albumin and prealbumin in hospitalized patients, especially in the ICU setting, are markedly decreased by non-nutritional factors (inflammation, infection, capillary leak, decreased hepatic synthesis, and/or increased clearance from blood) and may also be increased (volume depletion) or decreased (volume overload) in blood based on fluid status. Because of the long circulating half-life of albumin (18-21 days), levels in blood remain low despite adequate feeding and are slow to respond to nutritional repletion, irrespective of the other confounding factors noted above. Serial blood prealbumin or albumin levels may be useful as a general index of protein status in clinically stable, euvolemic patients in the outpatient setting to monitor response to nutritional therapy.

* Integration of the factors above allows determination as to whether patients are likely to be adequately nourished, to have mild, moderate or severe protein-energy malnutrition, and/or to have depletion or deficiency of specific vitamins, minerals or electrolytes. Patients with an involuntary body weight loss of 5-10% or more of their usual body weight in the previous few weeks or months (including overweight and obese patients), those weighing less than 90% of their ideal body weight, or those who have a body mass index (BMI) less than 18.5 kg/m² should be carefully evaluated, as these individuals are likely to be malnourished.