

17 - 346 Enteral and Parenteral Nutrition

346 Enteral and Parenteral Nutrition

TABLE 345-2 Common Body Composition Studies, Laboratories, and Other Studies Used in Nutrition Assessment

TEST NOTES

Functional tests (Recommended)

Clinical Frailty Scale A tool that measures frailty, which is defined as a state of increased vulnerability to adverse health outcomes due to reduced physiologic reserves. It uses various self-reported factors (e.g., physical mobility, cognitive function, and the ability to perform daily activities) to classify frailty into nine classifications, ranging from very fit (level 1) to severely frail (level 9). Patients who score ≥ 5 are considered frail.

Sit-to-Stand Test Assesses lower limb strength, balance control, and functional mobility by measuring the time required for a person to transfer from a seated to a standing position and back to sitting five times.

Handgrip strength A measure of muscular strength generated by one's forearm muscles to screen for upper body strength. Low grip strength is associated with poorer clinical outcomes. Patients with low grip strength may benefit most from personalized nutritional support.

SARC-F A screening tool that determines the risk of sarcopenia, which is defined as a progressive and generalized loss of skeletal muscle mass and strength. It uses self-reported deficiencies in strength, walking, rising from a chair, climbing stairs, and experiencing falls to provide a score from 0 to 10, and a score ≥ 4 is considered at risk of sarcopenia.

6-Meter Walk Test Assesses walking speed (meter/sec) over a 6-m distance to determine functional mobility, gait, and vestibular function.

Acknowledgments The authors are grateful to Dr. Gordon L. Jensen for contributions to this chapter in previous editions of Harrison's.

■ ■ **FURTHER READING** Cederholm T, Bosaeus I: Malnutrition in adults. *N Engl J Med* 391:155, 2024. Gonzalez CC et al: Calf circumference: Cutoff values from NHANES 1999-2006. *Am J Clin Nutr* 113:1679, 2021. Guerra RS et al: Usefulness of six diagnostic and screening measures for undernutrition in predicting length of hospital stay: A comparative analysis. *J Acad Nutr Diet* 115:927, 2015. Jensen GL et al: GLIM criteria for the diagnosis of malnutrition: A consensus report from the global clinical nutrition community. *J Parenter Enteral Nutr* 43:32, 2019. Lew CCL et al: Association between malnutrition and clinical outcomes in the intensive care unit: A systematic review. *J Parenter Enteral Nutr* 41:744, 2017. Schuetz P et al: Individualized nutritional support in medical inpatients at nutritional risk: A randomized clinical trial. *Lancet* 393:2312, 2019. Uhl S et al: Interventions for malnutrition in hospitalized adults. *J Hosp Med* 17:556, 2022. White JV et al: Consensus statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition. Characteristics recommended for the identification and documentation of adult malnutrition (under-nutrition). *J Parenter Enteral Nutr* 36:275, 2012. Wong A et al: An umbrella review and meta-analysis of interventions, excluding enteral and parenteral nutrition, initiated in

the hospital for adults with or at risk of malnutrition. *Am J Clin Nutr* 118:672, 2023. L. John Hoffer, Bruce R. Bistrian

Enteral and Parenteral

Nutrition There are three kinds of specialized nutritional support (SNS): (1) optimized voluntary nutritional support, which is indicated when a patient's barriers to adequate nutrition can be overcome by special attention to the details of how their food is constituted, prepared, and served and its consumption optimized; (2) instrumental enteral nutrition (EN), in which a liquid nutrient formula is delivered through a tube placed in the stomach or small intestine; and (3) parenteral nutrition (PN), in which

(Continued) a nutritionally complete mixture of crystalline amino acids, glucose, lipid emulsions, minerals, electrolytes, and micronutrients is infused directly into the bloodstream. When does a hospitalized adult patient need SNS, and when it's indicated, how should it be provided? This chapter summarizes the physiologic principles that guide the correct use of SNS and offers practical information about the diagnosis and management of nutritional disorders in adult hospitalized patients. The management of in-hospital nutritional disorders follows three steps: (1) screening and diagnosis; (2) determination of the severity and urgency of treating a diagnosed nutritional disorder in its overall clinical context; and (3) selection of the kind of SNS to provide, its composition, and the details of providing it. To follow these steps properly, physicians require a general understanding of nutritional physiology, nutrient requirements, the pathophysiology and diagnosis of the nutritional disorders, and familiarity with the indications, advantages, risks, and administration of the different kinds of SNS. Because most physicians lack formal clinical nutrition training, they should, in general, collaborate with clinical dietitians and specialized pharmacists in this process.

CHAPTER 346 Enteral and Parenteral Nutrition ■ ■ NUTRITIONAL PHYSIOLOGY (See Chaps. 343–345.)

Energy The total daily energy expenditure of a healthy sedentary adult is ~36 kcal/kg. Resting energy expenditure accounts for ~75% of this total. Resting energy expenditure can be measured by indirect calorimetry or estimated using a variety of predictive equations that input weight, height, age, sex, and sometimes, disease-related factors. Fever and some diseases increase resting energy expenditure; prolonged semi-starvation triggers an adaptive reduction in resting and total energy expenditure. Total energy expenditure determines how much dietary energy must be consumed to maintain an existing store of body fat and protein. The amount of energy a patient actually requires may be less than their total energy expenditure, as in obesity therapy or during temporary periods of exogenous energy intolerance, or greater than total energy expenditure during recovery from starvation disease.

Protein and Amino Acids Dietary protein provides the 23 essential and nonessential amino acids required for protein synthesis. Protein must be consumed throughout life, because endogenous protein turnover entails a minimum obligatory rate of amino acid catabolism. Amino acid catabolism is regulated, appropriately increasing and decreasing in response to variations in protein intake, but it cannot fall below a certain minimum rate—the “protein minimum”—that determines an individual's minimum dietary protein requirement. The average daily minimum protein requirement for a healthy adult consuming an otherwise adequate diet is 0.65 g/kg; the “safe” or “recommended” intake is 0.80 g/kg. Average protein consumption in wealthy societies is approximately twice the average minimum requirement. Energy balance affects the minimum protein requirement. Positive energy balance, when achieved by greater carbohydrate consumption,

can improve body protein retention. Negative energy balance, such as during therapeutic weight reduction, reduces the efficiency of protein turnover and increases the dietary protein requirement. Some diseases (or their treatments) increase the protein requirement, by (1) increasing amino acid loss from the body (as in malabsorption and protein loss via wound exudates, fistulas, or inflammatory diarrhea), removing amino acids from the circulation (renal replacement therapy), or (2) increased muscle protein catabolism, which occurs as an adverse effect of high-dose glucocorticoid therapy and, most commonly, as part of the metabolic response to the systemic inflammation that accompanies major injury, serious infections, and intense immune system activation. A highly protein-catabolic patient may excrete 15 g N (nitrogen)/d or more in their urine in the absence of dietary protein provision: this is more than three times faster than occurs with simple fasting. Since 1 g N lost from the body reflects the loss of 6.25 g formed protein, 15 g N loss/d implies the loss of $15 \times 6.25 = 94$ g protein per day. Since the body's hydrated metabolically active tissue mass (also called body cell mass) is ~20% protein, one may calculate that 94 g protein loss/d indicates a loss from the body of ~470 g (1 lb) of active tissue mass per day. Sufficiently generous protein provision can mitigate this kind of active tissue loss. The extent to which protein-catabolic disease increases the protein requirement is debated, but a common recommendation for critically ill patients is 1.2–2.0 g protein/kg of normal body weight per day—close to the habitual protein intake of healthy people in wealthy societies.

Protein-Energy Interactions Both energy deficiency and systemic inflammation increase the dietary protein requirement; how do these factors interact? The loss of body protein caused by energy deficiency can be prevented or minimized by increased protein consumption. Systemic inflammation reduces the benefit of increased protein provision under hypocaloric conditions but does not eliminate it. Some evidence suggests that a minimum energy dose, such as 50% of total energy expenditure, may help preserve the active tissue store during severe systemic inflammation. It is clear, however, that energy doses

“ 70% of total energy expenditure do not have any greater protein-sparing effect, and the additional amounts of glucose and fluid volume required to deliver them can have adverse effects that include hyperglycemia, dyslipidemia, and extracellular volume expansion. **PART 10 Disorders of the Gastrointestinal System** **Permissive Underfeeding and Hypocaloric Nutrition** These terms have different meanings, and they should not be conflated. Permissive underfeeding refers to the deliberate underprovision of all nutrients including protein, whereas hypocaloric nutrition refers to reduced energy provision combined with increased protein to compensate for the known protein-wasting effect of negative energy balance. **Micronutrients** Minimum amounts of the nine water-soluble vitamins (the B vitamins and vitamin C), four fat-soluble vitamins (A, D, E, and K), eight minerals (calcium, phosphorus, potassium, sodium, chloride, magnesium, zinc, and iron), essential fatty acids, and several essential trace elements are required to avoid deficiency diseases. Overt deficiencies of potassium, sodium, magnesium, and phosphorus are so common in hospitalized patients that it is standard practice to monitor for and correct them. Some drugs cause renal potassium, magnesium, or zinc losses that require increased

provision. Gastrointestinal losses from nasogastric drainage tubes or intestinal losses from fistulas or diarrhea incur losses of potassium, sodium, calcium, magnesium, and zinc. Less investigated, but common, are subclinical deficiencies of zinc, vitamin C, vitamin D, and possibly other micronutrients. Physicians often assume that consumption of a regular hospital diet protects patients from micronutrient deficiencies. This assumption is unwarranted when the patient's nutritional status is deficient upon admission and remains so during their hospital stay. Systemic inflammation can complicate the clinical laboratory evaluation of micronutrient status. It increases the requirements for certain micronutrients, partially redistributing them from the extracellular compartment into tissue stores, as occurs with iron, selenium, zinc, and perhaps other nutrients. This effect reduces the reliability of many

standard laboratory tests of micronutrient status. The evaluation of a patient's micronutrient status should begin with a determination of their previous and current intake and health status, including the identification of potential routes of excessive micronutrient loss. In acute-care clinical settings, the intensity of systemic inflammation should be determined using clinical criteria and by measuring serum concentrations of albumin or C-reactive protein, an acute-phase protein whose wide dynamic range and short half-life make it particularly useful in this situation, ■

■ **MACRONUTRIENT MALNUTRITION SYNDROMES** The decision to embark on SNS must be justified by a well-formulated nutritional diagnosis and a clearly defined therapeutic goal. This chapter focuses on the diagnosis, treatment, and prevention of in-hospital adult starvation-related malnutrition (SRM) and two related conditions: chronic disease-related malnutrition (CDM) and acute disease-related malnutrition (ADM). As explained in Chap. 345, SRM is the disease brought about by prolonged semi-starvation. Synonyms for this disease are "starvation-induced protein-energy malnutrition" and "starvation disease." CDM can be understood as SRM (simple starvation disease) that is combined and compounded by moderately severe systemic inflammation. SRM and CDM are anatomically similar but etiologically and metabolically different, as elaborated upon below. ADM refers to an injury-induced metabolic condition that creates a high risk of severe body protein deficiency, rather than to an already existing anatomic starvation disease. **Starvation-Related Malnutrition** The pathologic features that make SRM a disease, and distinguish it from the semi-starvation that precedes it, emerge when the patient's active tissue mass has been depleted enough to impair specific physiologic functions. The body normally adapts to sustained inadequate energy provision by reducing energy expenditure and net protein catabolism, partly through hormone- and nervous system-regulated alterations in cellular metabolism, but mostly from loss of muscle, which is the major generator of energy expenditure. (Visceral organ mass and function have a higher priority for protection during starvation.) These adaptations permit prolonged survival, although at a cost that includes muscle loss (including cardiac and respiratory muscle), skin thinning, lethargy, a tendency to hypothermia, and functional disability. The cardinal anatomic features of SRM—generalized muscle loss and subcutaneous adipose tissue depletion—are easy to detect by simple physical examination. SRM always manifests as weight loss, but weight loss alone may not reveal its full severity. Semistarvation increases the extracellular fluid (ECF) volume, sometimes seriously enough to cause edema. Starvation-associated edema may occur even in the absence of its known common causes (it is termed "starvation edema"). In adults with initially

normal body composition, starvation-induced weight loss linearly tracks the loss of active tissue mass; this occurs because the weight loss caused by the depletion of adipose tissue is counterbalanced by increased ECF volume. A 25% reduction in body weight (and active tissue mass) significantly compromises physiologic function; a 50% reduction places otherwise uncompromised young adults on the cusp of thermodynamic survival; older people with comorbidities are at even greater risk. People with SRM are frail, feel unwell, lack strength and emotional range, and are at risk of hypothermia. The main cause of SRM worldwide is involuntary food deprivation. Its causes in hospitalized patients are many: inadvertent or physician-ordered food deprivation; psychological depression or distress; anorexia nervosa; poorly controlled pain or nausea; badly presented unappealing food; communication barriers; physical or sensory disability; dysphagia and other mechanical difficulties ingesting food; partial obstruction of the esophagus, stomach, or intestines; thrush; intestinal angina; and most commonly, combinations of these causes. Chronic Disease-Related Malnutrition and Cachexia These terms refer to SRM combined with and complicated by chronic systemic inflammation. CDM is common among patients suffering from chronic infection; inflammatory autoimmune disease; chronic severe

hepatic, renal, cardiac, or pulmonary disease; and neoplastic diseases that induce a systemic inflammatory response or cause tissue injury. CDM induces anorexia—a strong disinclination to eat even when there is no physical barrier to it—and is worsened by it. Its features include muscle loss, weakness, fatigue, and impaired adaption to starvation, all of which contribute to a vicious cycle of worsening starvation disease. Fortunately, the nutritional deficit on the input side of this equation (anorexia-driven inadequate food consumption) is usually the strongest driver of the patient's CDM, making it amenable to a wellorganized nutritional intervention while an effective treatment plan for the primary disease is identified and implemented. Cachexia is an older term now used with varying meanings. It generally refers to a metabolic syndrome of moderate systemic inflammation, unrelenting generalized muscle loss, and their associated symptoms, including anorexia, fatigue, frailty, and mood disturbance. For the purpose of this chapter, it may be considered as roughly synonymous with CDM. Acute Disease-Related Malnutrition Other terms for ADM are “injury-induced malnutrition” and “protein-catabolic critical illness.” The metabolic-inflammatory response to severe tissue injury and sepsis mobilizes muscle amino acids and leads to rapid and severe generalized muscle loss and increased resting energy expenditure under conditions in which voluntary food intake is usually impossible. SRM or CDM may be absent at the onset of a patient's critical illness, but muscle loss will rapidly develop unless the inciting medical or surgical disease is rapidly and effectively treated and SNS provided. Death from simple starvation of nonobese adults typically occurs within ~8 weeks, whereas death from untreated starvation in patients with sustained ADM will occur much sooner. ■ ■NUTRITIONAL DIAGNOSIS The cardinal anatomic features of starvation disease (either SRM or CDM) are generalized muscle loss and diminished body fat. Routine physical examination will immediately reveal these features, but, perhaps surprisingly, what ought to be an easy diagnosis is often overlooked. This section explains the details and pitfalls of diagnosing SRM and CDM. Muscle Mass Muscle tissue normally accounts for ~80% of an adult's active tissue mass. It is easy to detect loss of muscle mass, and its severity is determinable almost at a glance. But generalized muscle loss has many causes: (1) old age-related muscle loss (sarcopenia); (2) disuse muscle atrophy; (3) high-dose glucocorticoid therapy and certain endocrine diseases (uncontrolled diabetes mellitus, adrenocortical insufficiency, hyperthyroidism, androgen deficiency, hypopituitarism); and (4) primary muscle or neuromuscular diseases. The guiding principle is that SRM and CDM are very common treatable causes of muscle

loss. Whenever generalized muscle loss is identified, its potential causes should be considered and the treatable ones addressed. Old age is irreversible, but adequate protein and energy provision, combined with physical rehabilitation, can be lifesaving. Generalized muscle loss of any cause is especially dangerous in ADM, because the combination of ADM and preexisting muscle loss places patients at the cliff edge of lethal depletion of their active tissue store. A diminished muscle mass is less able to release adequate amounts of amino acids into the circulation for protein synthesis at sites of tissue injury and healing and to the central protein pool to regulate the immunoinflammatory response. Subcutaneous Adipose Tissue Severe adipose tissue depletion almost always indicates starvation disease, but it is not required to make the diagnosis. The current obesity epidemic has created a population of obese patients with SRM or CDM in whom muscle loss has outpaced fat loss. A conscientious physical examination will easily identify the patient's diminished muscle mass beneath their residual subcutaneous fat. ECF Volume The ECF compartment normally represents ~20% of body weight. SRM moderately increases ECF volume. CDM is associated with additional edema-promoting conditions, especially the

hypoalbuminemia associated with systemic inflammation. The effect of increased ECF volume to increase body weight and distort physical appearance should be borne in mind, for it may conceal the severity of muscle loss.

Body Mass Index Body mass index (BMI) is defined as body weight (kg) divided by the square of height (m²). The normal reference range is 20–25 kg/m². BMI <19–20 usually indicates nonpathologically reduced muscle and fat mass. BMI <15 indicates severe starvation disease, and BMI <13 is usually thermodynamically incompatible with life, especially in older patients with comorbidities. Some guidelines and clinical trial enrollment criteria have defined what they term as “malnutrition”—meant as starvation disease—as a BMI <16 or 17. But it is wrong to rely on BMI as the sole basis for diagnosing starvation disease. A BMI <17 certainly implies starvation disease, for the body composition required for such a BMI can only develop by jettisoning a large fraction of the body's active tissue and adipose tissue store. But a BMI >17 does not rule out starvation disease. Many patients with starvation disease have a normal or above-normal BMI, despite important muscle loss, because of residual obesity or an expanded ECF volume. Visual BMI With some practice, clinicians can learn to accurately predict the BMI of nonobese, nonedematous patients by systematically examining their muscle groups. This skill enables them to evaluate the severity of starvation disease even in obese or edematous patients—for whom measured BMI is unreliable—simply by evaluating their muscle groups while consciously discounting their subcutaneous fat and edema. Visual BMI can be used to estimate a patient's “normalized dry body weight”—what their body weight would be without obesity, edema, or ascites. For example, the normalized dry body weight of a 1.75-m adult with a visual BMI of 17 is $1.75^2 \times 17 = 52$ kg.

CHAPTER 346 Laboratory and Technical Assessment Clinical laboratory measurements have three main purposes in the evaluation and management of starvation disease. Enteral and Parenteral Nutrition MUSCLE MASS Bedside ultrasound is proving to be a valuable technique for quantifying muscle mass at specific body sites. However, it need not and should not replace the immediate information provided by the eyes, hands, and mind of an astute clinician. SYSTEMIC INFLAMMATION The absence or presence of systemic inflammation is what fundamentally distinguishes SRM from CDM. The most useful laboratory indicators of systemic inflammation are a reduced serum albumin concentration and increased serum C-reactive protein concentration. Systemic inflammation increases the permeability of capillary walls to large molecules, and the resulting osmotic shift

increases ECF volume. As intravascular albumin redistributes in this larger volume, its serum concentration decreases. Variably increased albumin catabolism and reduced liver albumin synthesis also contribute. Dietary protein deficiency and muscle loss perpetuate inflammation-induced hypoalbuminemia, because the amino acids required for hepatic albumin synthesis come from the diet and endogenous muscle protein. Hypoalbuminemia and a reduced serum prealbumin concentration are often considered as indicators of “malnutrition.” This is incorrect. These serum proteins are negative acute-phase reactants that indicate the presence of systemic inflammation. Systemic inflammation induces anorexia and increases muscle catabolism, effects that increase the risk of CDM, but the disease itself may or not exist at the time, and it may never develop. Serum acute-phase reactants will remain abnormal as long as systemic inflammation persists. Appropriate nutrition can mildly improve serum albumin concentration, but it will not fully normalize until after the systemic inflammation subsides. Even then, full normalization may require several weeks because of albumin’s serum half-life of at least 2 weeks.

PROTEIN-CATABOLIC INTENSITY The defining feature of protein-catabolic disease is generalized muscle loss. Situations of greatly increased protein loss can be identified by measuring body N loss. Most N leaves the body in the urine (almost all of it in urea, ammonia, and creatinine). Total N is not usually measured in hospital

laboratories, but urinary urea N (which normally accounts for ~85% of urinary N) can be measured and is routinely available. A recent, validated formula estimates daily total N loss as follows: $N \text{ loss (g)} = g \text{ N in urinary urea} / 0.85 + 2$.

Net muscle protein catabolism follows approximately first-order kinetics; this means that the rate of N loss from muscle is proportional to the amount of N available to be lost. Protein-catabolic muscle-depleted patients will lose less body N per day than equally catabolic patients with a preserved muscle store, but they are at greater risk of succumbing to their disease because they are closer to lethal depletion. Rate of N loss always has to be interpreted in the context of existing muscle mass.

Instrumental Nutritional Assessment Many nutritional assessment instruments claim to identify “malnutrition” by enumerating and summing a list of risk factors, laboratory results, and physical findings. These tools are often hindered by ambiguity about their definition of malnutrition and by failure to distinguish between screening and diagnosis. Correct clinical diagnosis is the identification of a known pathologic entity—SRM or CDM, for example—by considering the patient’s medical history, pertinent findings on physical examination, and laboratory or imaging reports. Diagnosis also involves an estimation of the probability that the diagnosis is correct and a judgment of its severity. By contrast, screening is the application of a simple test that identifies people at sufficiently high risk of a certain disease to warrant definitive procedures to establish the diagnosis or rule it out or that identifies people at sufficiently high risk of developing it to warrant specific preventive interventions. Screening tools and risk predictors are extremely useful, but they should not be confused with clinical diagnosis.

PART 10 Disorders of the Gastrointestinal System

■ **SPECIALIZED NUTRITIONAL SUPPORT** Optimized Voluntary Nutritional Support When feasible, this is the approach of choice because it engages and empowers the patient, encourages mobilization and reconditioning, is consistent with the objectives of patient-centered medicine, and is risk-free. Its disadvantage is that it is time-consuming and labor-intensive, and it demands astute attention to the specific needs of individual patients.

Enteral Nutrition This is nutrition provided through a feeding tube placed through the nose into the stomach or beyond it into the duodenum, by insertion of a tube through the abdominal wall into the stomach or beyond it into

the jejunum, or by a surgical approach to access the stomach or small intestine. EN is usually the treatment of choice when optimized voluntary nutritional support is impossible or has failed. It is relatively simple, safe, and inexpensive, and it maintains the digestive, absorptive, and immunologic barrier functions of the gastrointestinal tract. EN is appropriate when optimized voluntary nutrition is not feasible or has failed and the patient's gastrointestinal tract is functioning and can be accessed.

EN Products The most common forms of EN are commercially manufactured formulas.

STANDARD POLYMERIC FORMULAS These are the most widely used EN products. They are available in a wide variety of formats designed to meet the nutritional requirements of a normal, healthy person. Carbohydrates provide most of the energy. The proteins are intact and of high biologic value (casein, whey, or soy) and require adequate pancreatic and intestinal enzyme function for digestion and absorption. They are isotonic or nearly so and provide 1000–2000 kcal and 50–70 g protein/L.

POLYMERIC FORMULAS WITH FIBER The addition of dietary fiber to formulas sometimes improves bowel function and feeding tolerance. Fermentable (soluble) fibers such as pectin and guar are metabolized by colonic bacteria, yielding short-chain fatty acids that fuel colonicocytes. Nonfermentable (insoluble) fibers increase fecal bulk, improve peristalsis, and may improve diarrhea.

ELEMENTAL AND SEMI-ELEMENTAL FORMULAS The macronutrients in these formulas are partially or completely hydrolyzed. They were

designed for patients with known maldigestion and malabsorption but are sometimes used empirically for patients intolerant of a standard polymeric formula, especially when acutely ill, although without strong evidence of superiority.

IMMUNE-ENHANCING FORMULAS In addition to providing macronutrients and conventional amounts of micronutrients, these EN products contain large amounts of certain nutrients designed to favorably modulate the immune response: arginine and n-3 fatty acids especially have some clinical experimental support, but also various combinations of glutamine, nucleotides, and antioxidants for which evidence of benefit is limited or lacking.

PROTEIN-ENRICHED FORMULAS Most EN products provide energy and protein in a ratio appropriate for a healthy person. Protein-enriched formulas provide ~90 g protein and 1000 kcal/L. Originally marketed to meet the increased protein requirement of weight-reducing obese patients, these products are increasingly used to provide protein to catabolic patients with a more generous amount of protein without energy overfeeding. EN can be further protein-enriched by adding flushes of water-soluble powdered protein supplements.

OTHER FORMULAS Various disease-specific EN products are available for patients with diabetes or hepatic, renal, or pulmonary disease. Their use can improve some metabolic endpoints, without clear evidence that they improve clinical outcomes.

Parenteral Nutrition PN delivers a complete nutritional regimen directly into the bloodstream in the form of crystalline amino acids, glucose, triglyceride emulsions, minerals (calcium, phosphate, magnesium, and zinc), electrolytes, and micronutrients. Because of its high osmolarity (>1200 mOsm/L) and often large volume, PN is infused into a central vein in adults. Ready-to-use PN admixtures typically containing 4–7% hydrated amino acids and 20–25% glucose (with or without electrolytes) are available in two-chamber (amino acids and glucose) or three-chamber (amino acids, glucose, and lipid) bags that are intermixed with vitamins, trace minerals, and additional electrolytes then added just prior to infusion. Although convenient and cost-effective, these products have fixed nutrient compositions and are dosed according to the volume required to meet a patient's energy requirement but not necessarily their protein requirement. In some situations—especially ADM—a more sophisticated approach is justified that uses a computer-controlled sterile compounder to create combinations of amino acids and glucose that precisely meet the protein, energy, fluid, and acid-base regulatory requirements of individual patients.

Amino Acids The amino acids in PN admixtures provide sufficient amounts of the essential amino acids and total nonessential amino acid N. Unlike protein-bound amino acids, which are connected by peptide bonds, free amino acids are hydrated. This reduces their energy density from 4.0 (in formed protein) to 3.3 kcal/g and reduces the amount of protein substrate they provide by ~17%. Thus, 100 g of free mixed amino acids provides 83 g protein substrate.

Carbohydrate and Lipids The glucose in PN is dextrose monohydrate; this hydration state reduces its energy concentration from 4.0 kcal/g (as in formed carbohydrate) to 3.4 kcal/g. Lipid emulsions provide energy (~10 kcal/g) and the essential n-6 and n-3 fatty acids. Traditional lipid emulsions based solely on soybean oil are giving way to mixed emulsions that include medium-chain triglycerides, n-9 monounsaturated fatty acids, and n-3 fatty acids. Emulsions of pure soybean oil; or a mixture of 80% olive oil and 20% soybean oil; or a mixture of 30% soybean oil, 30% medium-chain triglycerides, 25% olive oil, and 15% fish oil are available in the United States. Fish oil (either as a component of a mixed emulsion or administered separately) may reduce the risk of infections and length of stay in critically ill patients. Some complex lipid emulsions are more highly enriched in n-3 fatty acids and/or contain fewer n-6 polyunsaturated fatty acids than soybean lipid, which is more prone to lipid peroxidation and could promote the formation of the proinflammatory n-6 derivatives. Standard lipid infusion rates should not exceed 8 g/h,

equivalent to 175 g (1925 kcal)/d for a 70-kg patient. Because of their longer chain length and slower tissue uptake, pure fish oil emulsions are infused at lower rates.

Minerals, Micronutrients, and Trace Elements The default concentrations of electrolytes, minerals, and micronutrients in PN solutions are designed to meet the requirements of a healthy adult. These starting doses must be adjusted to meet the frequently abnormal and often-changing requirements of individual patients. Being unstable, multivitamin mixtures are injected into PN bags just prior to their delivery to the medical unit. Parenteral water-soluble vitamin requirements are greater than standard oral requirements, because hospitalized patients often have vitamin deficiencies or increased requirements and because intravenous administration of vitamins increases their loss in the urine. Ascorbic acid degrades spontaneously in PN solutions, even when protected from light.

APPROACH TO THE PATIENT Indications, Selection, and Provision of Specialized Nutritional Support Most hospitalized patients do not require SNS because they can and will eat enough with appropriate management of their primary disease. Others may have a terminal disease whose downward course will not be mitigated by SNS. Patients who are unable to eat and digest enough of the standard hospital diet and have or are at high risk of developing SRM or CDM are candidates for optimized voluntary nutritional support. Instrumental SNS is indicated when optimized voluntary nutritional support is inappropriate, impractical, or has failed. The decision to provide EN or PN is based on a combination of four factors: (1) the determination that nutrient ingestion will likely continue to be inadequate for many days; (2) there is important muscle loss (of any cause); (3) the patient's nutrient requirements are increased (as from inflammatory diarrhea, enterocutaneous fistulas or exudates, or an inflammatory protein-catabolic state); and (4) the reasoned judgment that SNS has a reasonable prospect of improving the patient's clinical outcome or quality of life.

EN THERAPY EN is indicated when the patient is unable to eat enough food and is unlikely to do so for a long time, their gastrointestinal tract is functional and accessible, and optimized voluntary nutrition is impossible or inappropriate. EN is commonly used for patients with impaired consciousness, severe dysphagia, or severe upper gastrointestinal tract dysfunction or obstruction, or who need mechanical ventilation. Equally commonly, situations arise in which a patient's voluntary food intake is seriously curtailed by anorexia, unappealing food, nausea, vomiting, pain,

distress, delirium, depression, chewing difficulties, mild dysphagia, physical and sensory disability (including dysgeusia), or undiagnosed thrush. In these complicated and difficult situations, the clinical diagnosis of SRM or CDM will tip the decision toward EN or PN. EN is contraindicated by intestinal ischemia, mechanical obstruction, peritonitis, and gastrointestinal hemorrhage. High-dose pressor therapy is a relative contraindication because of the rare but lethal risk of intestinal ischemic injury. Severe coagulopathy, esophageal varices, absent gag reflex, hypotension, paralytic ileus, diarrhea, and nausea and vomiting are not absolute contraindications, but they increase the risk of complications and make it less likely that EN will succeed in achieving its nutritional goal. In general, intensive EN is best avoided under conditions of very grave and unstable illness. Initiation, Progression, and Monitoring Nasogastric tube feeding may proceed when the patient's gastrointestinal function is adequate with respect to gastric contractility (e.g., nasogastric tube output <1200 mL/d) and intestinal function (no known or suspected intraabdominal pathologic process and a nondistended

abdomen—mere absence of bowel sounds is not, by itself, a contraindication). After consent has been obtained and the appropriate feeding tube (usually a nasogastric tube for short-term feeding) has been placed and its position verified, the head of the patient's bed is raised to at least 30° and kept there to reduce the risk of regurgitation. The clinical dietitian ordinarily orders the formula and adjusts its rate. When a standard polymeric formula is infused, it normally commences at 50 mL/h and is advanced by 25 mL/h every 4–8 h until the goal rate is attained. Elemental formulas begin at a slower rate and progress more slowly. Intra-gastric bolus feeding is an option (200–400 mL feeding solution infused over 15–60 min at regular intervals with verification of residual gastric contents every 4 h). Complications The common complications of EN are aspiration of regurgitated or vomited formula, diarrhea, fluid volume and electrolyte derangements, hyperglycemia, nausea, abdominal pain, constipation, and failure to achieve the nutritional goal. Aspiration Patients with delayed gastric emptying, impaired gag reflex, and ineffective cough are at high risk of aspiration pneumonia. Ventilator-associated pneumonia is most often caused by aspiration of microbial pathogens in the mouth and throat past the cuff of an endotracheal or tracheostomy tube. Tracheal suctioning can induce coughing and gastric regurgitation. Ventilator-associated pneumonia can be prevented by elevating the head of the bed, good mouth hygiene and gastrointestinal decontamination, nurse-directed algorithms for formula advancement, and sometimes postpyloric feeding. EN need not be suspended for gastric residual volumes <300–400 mL in the absence of other signs of gastrointestinal intolerance (nausea, vomiting, abdominal pain, abdominal distention). Continuous EN is often tolerated better than bolus feeding and is the only option during jejunal feeding. Diarrhea Diarrhea commonly occurs when the patient's bowel function is compromised by disease or drugs (most often, broad-spectrum antibiotics). Once infection and inflammatory causes have been ruled out, EN-associated diarrhea may be controlled by using a fiber-containing formula or adding an antidiarrheal agent to it. H₂ blockers or proton pump inhibitors may help reduce the net volume of fluid presented to the colon. Luminal nutrients exert trophic effects on intestinal mucosa, so it is often appropriate to continue tube feeding despite moderate but tolerable diarrhea, even if it necessitates supplemental parenteral fluid support. Except in cases of impaired small-intestinal absorptive function, there are no well-established indications for elemental formulas; nevertheless, they may be tested empirically when diarrhea persists despite the use of fiber-enriched formulas and antidiarrheal drugs. Gastrointestinal Intolerance Abnormally high gastric residual volumes, abdominal distention, pain, and nausea are greatly distressing for patients, increase nursing workload, and slow the progression of EN. These

problems can be avoided or minimized by ensuring that the patient is in normal fluid and electrolyte balance, by preventing severe hyperglycemia, and, when nausea, vomiting, or abdominal distention develop, by the judicious prescription of antiemetic and prokinetic drugs (and sometimes proton pump inhibitors) on a regular—rather than as-needed—basis. Patients with gastroparesis require postpyloric feeding. Fluid Volume, Electrolyte, and Blood Glucose Abnormalities

EN's essential purpose is to provide macronutrients at an appropriate rate. EN also provides standard amounts of fluid, electrolytes, minerals, and micronutrients. Standard EN products are not designed to manage abnormal fluid volume, electrolyte, and mineral requirements, which vary considerably and can change rapidly. Blood glucose concentrations should be monitored regularly, and additional measures—including intravenous fluid, electrolyte, and insulin therapy—may be required to maintain homeostasis. Failure to Reach the Nutritional Goal EN is frequently delayed or interrupted by intolerance to the administered formula, CHAPTER 346 Enteral and Parenteral Nutrition

by diagnostic tests and procedures (including dialysis), physical or occupational therapy, or a clogged or pulled out tube. The result can be a long delay in the progression of EN and ultimate failure to meet the patient's nutrient requirements. EN in the Intensive Care Unit Most critically ill patients cannot eat anything and hence depend entirely on SNS. EN serves two purposes in this setting. The first is to meet the patient's macronutrient requirements, especially their increased protein requirement. The second purpose is to infuse sufficient nutrients into the intestines to maintain their barrier and immunologic functions in the face of a systemic inflammatory response that threatens them. Current guidelines recommend starting EN soon after a critically ill patient has been fluid resuscitated and stabilized. Once EN is underway, its rate of delivery is gradually increased toward the nutritional goal. EN frequently falls far short of its protein provision target, even after a week or longer in the intensive care unit. Newer, highprotein EN products (and sometimes the addition of powdered protein supplements) can correct this protein shortfall. There is uncertainty about the timing and macronutrient composition of EN early in ADM. We continue to recommend early EN as a platform and preparation for later, more generous nutrient provision and to maintain intestinal function. PN THERAPY PN is more resource-intensive and requires more expertise than EN. It is used when invasive SNS is indicated and EN is impossible, inappropriate, or insufficient to meet the patient's nutritional needs. The risks of PN are those of inserting and maintaining a central venous catheter (traumatic injury from the insertion, serious infection, and venous thrombosis); allergy to some of its components; glucose, electrolyte, magnesium, phosphate, and acid-base balance abnormalities; and the adverse effects of the large intravenous fluid volumes. When prolonged for many weeks—and especially when it delivers excess energy—PN may cause or contribute to hepatic dysfunction. PART 10 Disorders of the Gastrointestinal System Initiation, Progression, Monitoring, and Discontinuation When indicated, PN should begin soon after the patient has been hemodynamically stabilized; glucose, electrolyte, and acid-base homeostasis has been established; and they are able to tolerate the fluid volume required to deliver it. Newer evidence indicates that the provision of energy equal to total energy expenditure in the first week of PN is not, in general, beneficial and can be harmful under certain conditions. The high osmolarity of adult PN solutions and the need for strict sterility require that they be infused through a dedicated port in a central venous catheter. Jugular or femoral vein catheters should not be used because of the difficulty maintaining a dry, sterile dressing over the

insertion site and the higher rate of complications. The initial dose of glucose should not exceed 200 g/d to avoid hyperglycemia (and—in susceptible patients with adapted SRM—the refeeding syndrome). Most non-critically ill patients do not require >500 g glucose (1700 kcal)/d—assuming in this example a normalized dry body weight of 70 kg. Patients with ADM should, in general, not receive

“ 350 g glucose (1200 kcal)/d during the intense phase of their critical illness. A glucose infusion rate of ~200 g/d is physiologic and rarely needs to be exceeded. When it eventually becomes appropriate to provide energy equal to total energy expenditure, this may be achieved by infusing a lipid emulsion. We recommend hypocaloric nutrition (limited in glucose, lipid, and fluid volume but generous in amino acids) for the first 2 weeks of SNS in fat-sufficient or obese patients with ADM. Energy provision may increase, if indicated, after the catabolic storm has abated. Lipids are commonly introduced after the first week of PN to make up energy shortfalls. Serum triglyceride concentrations are measured before commencing lipid infusions to detect preexisting hypertriglyceridemia (>400 mg/dL), a relative contraindication. Lipids may be infused daily or two or three times weekly. Lipid

infusions are not necessary to prevent essential fatty acid deficiency during hypocaloric nutrition of patients with a normal or excessive fat store, because the endogenous fat mobilized during energy deficiency provides essential fatty acids to the rest of their body. Capillary blood glucose concentrations are monitored several times daily. Subcutaneous regular insulin is added to the PN admixture as required to maintain average serum glucose concentrations <140 mg/dL and >80 mg/dL. (Upper and lower limits of 180 and 100 mg/dL appear to be appropriate for critically ill patients with diabetes mellitus.) The dose of regular insulin required on a given day can be added to the following day's PN solution. The insulin dose increases roughly proportionately to the glucose dose. Certain benchmarks are useful. Basal endogenous insulin secretion is ~30 units/d in normal people. When insulin is required for nondiabetic, noncatabolic patients, 10 units of regular insulin roughly cover 100 g infused glucose. Patients with non-insulin-dependent diabetes require ~20 units/100 g glucose. Noncatabolic patients with insulin-dependent diabetes usually require approximately twice their at-home insulin dose, because parenteral glucose stimulates insulin release more potently than oral carbohydrate and because some insulin adheres to the infusion bag. Biochemical Monitoring Serum urea, creatinine, electrolytes, glucose, magnesium, phosphate, calcium, and albumin concentrations are determined prior to commencing PN and most of them (not albumin) monitored for the first few days, then twice weekly or as required. Serum triglycerides and liver function indicators are measured at baseline and after PN is underway to verify tolerance to lipid infusions. An N balance determination may be useful at the outset to evaluate the severity of protein catabolism in patients with CDM or ADM, to identify patients who will benefit from more generous amino acid provision, and during the course of PN to determine whether N balance is improving with therapy. Discontinuation PN is tapered and discontinued when the patient can be adequately nourished by the enteral route. The PN dose is proportionately reduced as food intake increases. Once a patient can tolerate one-half to two-thirds of their requirement by the enteral route and there is no mechanical or other barrier to further increases,

PN should be terminated. The transition to oral nutrition can be difficult for some patients. In this situation, optimized voluntary nutrition, although labor-intensive, is much preferred to replacing PN with EN, for it is safe, effective, fosters well-being, and prepares the patient for discharge home. It is tempting to discontinue PN in hopes of stimulating the patient's appetite, but this impulse should be resisted. PN does not cause anorexia nor does discontinuing it stimulate appetite. Too-early discontinuation of PN may delay a patient's progression to full voluntary food consumption by inducing anxiety and recreating starvation conditions. A patient is most successfully weaned from PN by optimizing their voluntary nutrition (including food brought from home), providing emotional support, encouraging physical activity, and being patient. Some patients on the cusp of adequate oral nutrition will benefit from discharge to the security and pleasure of home life and homemade food; these patients are identified by observing, asking, and listening. Complications Patients receiving PN are at higher risk of blood stream infections than other patients with central venous catheters. Rigorously aseptic insertion technique, meticulous dressing care, one port dedicated solely to PN, and careful glycemic control reduce this risk. EN and PN carry equivalent overall risks and complication rates, apart from gastrointestinal side effects of EN. PN is much more prone to the error of inadvertent toxic overfeeding. Hyperglycemia The most frequent metabolic complication of PN is hyperglycemia in patients with insulin resistance due to non-insulin-dependent diabetes mellitus, high-dose glucocorticoid therapy, or severe systemic inflammation; the problem is exacerbated by excessive rates of glucose provision. Glucose

concentrations are most easily kept <140 mg/dL and with the least risk of hypoglycemia by infusing hypocaloric amounts of glucose and, when necessary, meeting the patient's energy requirement with intravenous lipid. In ADM, the benefits of using the lowest possible insulin dose—minimal hyperinsulinemia and a reduced risk of hypoglycemia—almost always outweigh the doubtful goal of rapidly matching energy provision to energy expenditure. Hypoglycemia Reactive hypoglycemia is uncommon but can occur immediately after high-glucose, non-insulin-containing PN is abruptly discontinued. It is prevented by slowing the PN infusion rate to 50 mL/h for 1 or 2 h prior to stopping, replacing it with 10% glucose, or when the oral route is available, providing a snack. More often, hypoglycemia occurs when the intensity of the patient's metabolic stress (or their glucocorticoid dose) decreases without an appropriate downward adjustment of the insulin dose. This problem is avoided by frequent capillary glucose determinations and careful attention to medication doses and the patient's general condition. Artefactual Hyperglycemia and Hyperkalemia Blood samples must be meticulously collected from a dual-port central venous catheter. The intermixing of sample with even a tiny volume of PN solution will falsely indicate hyperglycemia and hyperkalemia and can result in treatment error. This error is identified when the patient's apparent serum glucose (and potassium) concentration abruptly increases without reason, and the high glucose concentration is contradicted by a concurrent capillary glucose reading. Volume Overload Volume overload causes substantial morbidity and increases mortality. Total fluid provision should not normally exceed 2 L/d in the absence of abnormally high losses. Hypertonic intravenous glucose triggers a more intense insulin response than oral glucose, and it can increase urinary sodium and water retention. Volume overload can be prevented by using a compounder to prepare PN solutions, infusing glucose at the lowest appropriate rate, avoiding energy overfeeding, and monitoring the patient's volume balance. Hypertriglyceridemia This complication occurs when the rate of lipid infusion exceeds plasma triglyceride clearance capacity. Sepsis, renal failure, diabetes mellitus, high-dose glucocorticoid therapy, and multiple-organ failure reduce triglyceride clearance. An impaired immune response, increased risk of acute pancreatitis,

and altered pulmonary hemodynamics are potential, but not well documented, complications of PN-induced severe hypertriglyceridemia. Lipid infusion rates should not usually exceed ~50 g (500 kcal)/d in ADM. Liver Disease Mild elevations of serum liver enzyme concentrations may occur within 2–4 weeks of initiating PN, but in most cases, they will return to normal even when PN is continued. Clinically important hepatic dysfunction, although common in children, is uncommon in adults for whom energy overfeeding with resultant fatty liver is avoided. Intrahepatic cholestasis occasionally develops after many weeks of continuous PN; it is most often multifactorial in origin. Cyclic PN—in which PN is infused for only 12 h of the day—may prevent or reduce the severity of this complication. PN in the Intensive Care Unit Current guidelines recommend starting EN soon after a critically ill patient has been resuscitated and stabilized and enteral access to an adequately functioning gastrointestinal tract has been established. If the protein goal has not been achieved after 7–10 days, PN may be added, especially if the protein-catabolic state has not yet abated. Soy-based lipid emulsions should be avoided during the first week of PN; alternative lipid emulsions may prove to be safe and beneficial. SPECIAL CLINICAL SITUATIONS The Critical Illness–Nutrition Paradox There is now good clinical trial evidence that confirms what was long indicated by a combination of physiologic reasoning, biologic plausibility, and formal

clinical observation—namely, that personalized nutritional interventions improve the clinical outcomes of starving, non-critically ill patients. The case for SNS would seem to be much stronger for patients with ADM, which induces rapid muscle loss and maintains or increases energy expenditure in people rendered incapable of eating voluntarily. Yet well-designed large-enrollment clinical trials have repeatedly failed to demonstrate short-term clinical benefits from nutritional interventions in critical illness. In fact, there is good evidence that, unlike in noncritical illness, early energy provision at a rate near or above the rate of energy expenditure not only fails to improve clinical outcomes but may be deleterious. The failure of formal clinical trials to show benefits from SNS in critical illness has several possible explanations: severe prolonged starvation is so obviously harmful that it is unethical to intentionally include such a treatment arm in a randomized clinical trial; critical illness is extremely heterogeneous, and not every critically ill patient is, or remains, severely protein-catabolic for long; and owing to generous admission criteria and thanks to the high quality of modern intensive care, many patients admitted to intensive care units rapidly improve and are discharged in a handful of days, while others are so mortally ill when admitted to the intensive care unit that their outcome is virtually predetermined. For these reasons, clinical trials that enroll and report the outcomes of all patients admitted to an intensive care unit could well fail to demonstrate an average benefit from SNS. More than that, in current practice, standard EN regimens prescribed for most critically ill patients commonly fail to deliver more than one-half the currently recommended amount of protein, and the low protein-to-energy ratio of most standard EN and PN products can make it impossible to provide critically ill patients sufficiently generous amounts of protein or amino acids without subjecting them to harmful energy overfeeding. We await the publication of large-enrollment clinical trials in which critical illness is diagnosed, not by where the patient is being treated, but using anatomic and pathophysiologic criteria and in which current standard care is compared with treatment arms that provide personalized SNS appropriate to patients' anatomy and pathophysiology. For now, along with other experts, we continue to recommend EN and PN for critically ill patients. Attempts to match energy provision to energy expenditure should be avoided as long as systemic inflammation remains severe. The dose of protein or amino acids should be guided by physiologic reasoning and a personalized evaluation of each patient's anatomic and metabolic condition. We recommend

bearing in mind that people who survive critical illness become non-critically ill people for whom the benefit of appropriate nutrition, together with other components of medical and surgical care, is not in question. Accordingly, we recommend a long-view approach to the design of nutritional support regimens for critically ill patients that aims both to increase their likelihood of short-term survival and anticipates their post-critical illness phase, which will be improved by measures that mitigate muscle loss, avoid toxic energy overfeeding, and prevent or correct micronutrient deficiencies. Iron and PN Iron deficiency is common in hospitalized patients. It has many causes: preexisting deficiency, insufficient food, macro- or microscopic gastrointestinal blood loss, and repeated blood sampling. Even though it is common, the diagnosis is often missed because the anemia of systemic inflammation is even more common, and it confounds interpretation of the usual indicator of iron deficiency, serum ferritin. Serum ferritin and fasting serum transferrin saturation should be part of the patient's initial nutritional evaluation. Current evidence suggests that a fasting transferrin saturation <20% is the most reliable indicator of functional iron deficiency, even in the absence of anemia. In principle, all micronutrient deficiency states should be prevented and corrected. In-hospital iron deficiency causes and prevents recovery from anemia and increases postoperative blood transfusion requirements. Subclinical iron deficiency could contribute to cognitive and immune dysfunction. CHAPTER 346 Enteral and Parenteral Nutrition

Iron is not added to PN mixtures. Iron dextran is incompatible with lipid emulsions, and although it appears to be chemically compatible with aqueous solutions of amino acids and glucose, there is realistic concern that interactions between iron molecules and certain vitamins and amino acids in PN solutions could catalyze the formation of free radicals that degrade vitamins and exert subtle adverse systemic effects. Intravenous iron is usually necessary to treat in-hospital iron deficiency, but it should be delayed if there is known or suspected bacterial infection, and possibly not during the intense phase of ADM. A substantial rise in the serum iron concentration could increase susceptibility to gram-negative (and possibly other microbial) infections, as well as catalyze the formation of free radicals that increase the intensity of the catabolic response to major tissue injury. Zinc One liter of secretory diarrhea contains ~12 mg of zinc. Patients with intestinal fistulas or high-volume chronic diarrhea require this amount of zinc in addition to their daily requirement of 15 mg to avoid zinc deficiency. Zinc may be provided parenterally or enterally. Because of its low bioavailability, 12 mg of parenteral zinc is equivalent to 30 mg of oral zinc. Old Age In addition to their other frailties, elderly people commonly suffer from age-related muscle loss (sarcopenia) compounded by disuse muscle atrophy. These factors place them at high risk of the consequences of starvation disease and make them candidates for earlier SNS. Inactivity Physical activity and adequate nutrition interact intimately. Reduced physical activity reduces appetite, and physical rehabilitation and its associated emotional benefits restore optimism and appetite. Full nutrient provision will maintain or normalize many physiologic functions in bedridden patients, but without exercise, they will not increase their muscle mass. PART 10 Disorders of the Gastrointestinal System Renal Failure Protein provision should not be reduced in patients with renal failure unless renal replacement therapy is unavailable. Renal replacement therapy removes large amounts of amino acids, vitamins, and trace elements from the circulation, so protein and micronutrient provision should be increased to compensate for these losses. Liver Failure Patients with severe hepatic disease are relatively intolerant to starvation and commonly have CDM when admitted to hospital, so they are prime candidates for SNS. Their SNS should be generous both in energy and protein, despite an increased risk of hepatic encephalopathy. The risk of encephalopathy can be reduced by meticulous attention to fluid balance, acid-base balance, and electrolyte status and by

spreading protein provision over the day to accommodate the liver's reduced capacity to clear amino acid- derived ammonia. Perioperative SNS Patients with SRM or CDM awaiting elective major surgery will benefit from 7-10 days of preoperative SNS. Optimized voluntary nutrition is always preferred, but when a patient has been admitted to hospital in a semi-urgent condition, EN or PN is usually required to quickly meet the patient's nutritional goal. Preoperative SNS improves immunity and reduces postoperative complications, but it will not increase serum albumin concentrations, and it should not be provided for >7-10 days with the expectation that it will do so. More prolonged preoperative EN or PN may confer slight additional nutritional benefits, but they are counterbalanced by their risks and the consequences of prolonged hospitalization and delayed surgery. Surgery should not be delayed for starving patients whose muscle mass is normal or only mildly depleted and who are not experiencing systemic inflammation, for they are well able to withstand the trauma of even major uncomplicated surgery. The need for urgent surgery often precludes otherwise indicated preoperative SNS. Early postoperative PN is usually indicated for these patients, for they are

at increased risk of postoperative complications and are unlikely to consume much food over the next many days. Patients with only mild muscle loss, no systemic inflammation, and no postoperative complications do not require postoperative PN unless (1) adequate feeding by mouth has not been achieved by day 5-7 after surgery or (2) there are indications that voluntary feeding will be further delayed. There is evidence that perioperative immuneenhancing EN reduces morbidity in patients undergoing major elective gastrointestinal surgery. Cancer SNS plays a crucial role in cancer therapy. Many malignant neoplasms (especially those that involve the gastrointestinal tract or induce systemic inflammation) and their cytotoxic therapies create the conditions for starvation and commonly lead to SRM or CDM. The prevention or treatment of these starvation diseases will improve patients' quality of life and their tolerance to anticancer therapy. EN and PN are generally not prescribed to patients with advanced cancer for which effective anticancer therapy is unavailable, because the side effects and complications of instrumental SNS are not counterbalanced by an improved disease trajectory. In some cases, the disease progresses so slowly that the patient will die of starvation long before they succumb to their primary disease. EN or PN is obviously appropriate in such cases. Advanced Dementia Optimized voluntary nutrition is the key approach in this situation, and it can be used to deal with problems such as disability and dysphagia in patients who get pleasure from eating. There is no evidence that EN or PN improves quality or length of life in patients with advanced dementia who show little or no interest in food, and the side effects and complications are unpleasant and sometimes dangerous.

REFEEDING SYNDROME The refeeding syndrome can occur in patients with successfully adapted SRM during the first week of nutritional repletion when carbohydrate and sodium are introduced too rapidly. Carbohydrate stimulates insulin secretion, which, owing to its antinatriuretic effect, expands the ECF volume, especially when excessive sodium is provided. Refeeding edema can be minimized by severely limiting sodium provision and increasing carbohydrate provision slowly. Carbohydrate refeeding may stimulate intracellular glucose-6-phosphate and glycogen synthesis sufficiently to seriously lower serum phosphate concentrations, impairing skeletal and cardiac muscle function, and can trigger hemolysis. Abrupt carbohydrate provision increases the downregulated metabolic rate of patients with adapted SRM and stimulates N retention, new cell synthesis, and cellular rehydration. Because phosphorus, potassium, and magnesium deficiencies occur and are dangerous during refeeding, their serum concentrations should be measured frequently and appropriate supplements provided. Left heart failure may occur in predisposed patients; it has three causes: (1) an abrupt increase of intravascular volume due to the administration of fluids and

of glucose, which stimulates insulin-mediated renal sodium retention; (2) increased cardiac demand on an atrophic left ventricle created by an insulin-mediated increase of resting energy expenditure; and (3) myocardial deficiencies of potassium, phosphorus, or magnesium. Cardiac arrhythmias may occur. Acute thiamine deficiency encephalopathy is a devastating preventable complication of refeeding, even with simple glucose infusions. ■ ■ FURTHER READING Berger MM et al: ESPEN micronutrient guideline. Clin Nutr 41:1357, 2022. Berger MM, Pichard C: When is parenteral nutrition indicated? J Intensive Med 2:22, 2022. Compher C et al: Guidelines for the provision of nutrition support therapy in the adult critically ill patient: The American Society for Parenteral and Enteral Nutrition. JPEN J Parenter Enteral Nutr 46:12, 2022.

Revision #1

Created 2026-01-06 16:34:39 UTC by Omar Ayman

Updated 2026-01-06 16:34:39 UTC by Omar Ayman