MEDICAL INTELLIGENCE

CURRENT CONCEPTS

Nutritional Support of Hospitalized Patients

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AS limits of nutritional-support programs are tested, the tendency is to simplify regimens for nutrition, to exhaust means of enteral and peripheral-vein supplementation before resorting to central parenteral nutrition, and to scrutinize the advocacy of some uses of total parenteral nutrition; these policies guide our practice. Our chief index for advising nutritional support sufficient to meet or exceed a patient's basal energy requirements is the common definition of caloric malnutrition: loss of 10 per cent of usual weight, coupled with inability to eat or absorb enough food to reverse the depleted state.

Although otherwise normal patients might be expected to benefit from parenteral nutrition given after operation, little evidence supports this assumption. An overenthusiastic nutritional regimen can even worsen hypercatabolic states, for reasons to be discussed below. On the other hand, nutritional support may improve a patient's chances of completing a course of radiotherapy and chemotherapy by providing calories and protein to those who are unable to eat because of continual nausea, vomiting, esophagitis, or enteritis.[1] Reactivity to skin tests may be restored during total parenteral nutrition.[2] Nonetheless, nutritional support of patients with cancer has neither increased their response to radiotherapy and chemotherapy nor increased the length of their survival.[3]

Despite advocacy of elemental diets in the treatment of various intraabdominal disorders (including pancreatitis, Crohn's disease, ulcerative colitis, enterocutaneous fistulas, and short-bowel syndrome), the efficacy of these diets has not been proved in controlled trials.[4] Ordinary meal-replacement formulas may be equally effective. The response to parenteral nutrition is uneven[5-7]; the only controlled trial has shown no specific effect of total parenteral nutrition in acute colitis.[8]

For patients who have undergone extensive small-bowel resection, parenteral nutrition affords prolonged support, both on an inpatient and outpatient basis,[9] until maximal compensatory hyperplasia of the bowel occurs in response to eating.

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NUTRITIONAL ASSESSMENT BY TESTS

In our view, assessment based on anthropometric measurements, delayed cutaneous hypersensitivity to several antigens, and a battery of laboratory tests[10] is not required in everyday use. The validity of these methods is limited, and they do not replace perceptive history taking and physical examination. Although measurement of the skinfold thickness of the triceps correlates with the reserve of fatty tissue, and circumference of the arm muscles correlates with lean body mass, the 95 per cent confidence limits of these measurements are wide.[11] In addition, these measurements do not reflect improvements after repletion. Skin testing is a poor index of malnutrition because anergy also occurs in the presence of fever, sepsis, steroid therapy, tumors, shock, and circulating inhibitors of lymphocyte function.

Other indexes such as low serum concentrations of albumin and transferrin indicate only severe protein and calorie malnutrition, and their early response to enteral or parenteral refeeding is often unpredictable. The relative stability of serum albumin concentration despite low protein and caloric intake is partly explained by the large total albumin mass, by the capacity to maintain albumin synthesis at a high level as a result of diverting amino acids from muscle to liver, by mobilization of albumin from the extravascular pool to the intravascular pool during dietary restriction, and by the relatively long half-life of albumin (19 days).[12] In addition, because massive amounts of albumin can be lost through the gastrointestinal tract in inflammatory bowel diseases or through the kidneys in nephrotic syndrome, a low serum albumin level in these diseases is not necessarily related to malnutrition. The normal level of serum transferrin (half-life, eight days) also varies over a wide range, even in clinically obvious cases of malnutrition, and iron deficiency itself can induce transferrin synthesis in the absence of malnutrition.

Truer indicators of subclinical malnutrition and of response to enteral and parenteral nutrition are probably plasma levels of thyroxine-binding prealbumin (half-life, two days) and retinol-binding protein (half-life, 12 hours).[12,13] Although these substances are sensitive to changes in both protein and calories and respond rapidly to refeeding, even they should not be assayed routinely. In patients with kwashiorkor, plasma levels of prealbumin and retinol-binding protein double after one week of refeeding.[13]

ESTIMATION OF ENERGY REQUIREMENT

A satisfactory estimate of basal caloric requirement or basal energy expenditure can be calculated from the formulas that Harris and Benedict derived over 60 years ago from the results of indirect calorimetry[14] (Table 1). Their results correlate well with the

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Table 1. Harris–Benedict Equations for Calculation of Basal Energy Expenditure (BEE).[14]*

WOMEN	
BEE = 655 + (9.6 × W) + (1.8 × H) − (4.7 × A)	
MEN	
BEE = 66 + (13.7 × W) + (5 × H) − (6.8 × A)	

*W denotes actual or usual weight in kilograms, H height in centimeters, and A age in years.

values obtained with contemporary techniques of continuous expired-air analysis.[15] The Harris–Benedict equations take into account sex, height, age, and weight. If the patient has recently lost more than 10 per cent of his weight, his usual weight is entered into the equation. Special slide rules are used to calculate quickly the value of the basal energy expenditure (Travenol Laboratories, Deerfield, Ill.).

GUIDELINES FOR NUTRITIONAL SUPPORT

In nondepleted postoperative patients the goal of nutrition is to prevent excessive loss of lean tissue.[16] If the patient is still unable to eat or absorb food properly one week after operation, parenteral nutrition providing 0.8 to 1 g of amino acids per kilogram of body weight per day and yielding a total number of calories about 20 per cent above the basal energy expenditure should be provided. Two liters of peripheral intravenous formulation and 0.5 to 1 liter of fat emulsion will meet these requirements. (The composition of solutions and emulsions is discussed below.) Although a needle-catheter jejunostomy placed during abdominal surgery for postoperative infusion of elemental diets could be useful in these circumstances, we have not been impressed with its utility as a routine measure.

In nutritionally depleted patients the goal is restoration of lean tissues with concomitant restoration of fat reserves. The amino acid intake should correspond to 1.5 to 1.8 g per kilogram, and the amount of calories should be 50 per cent above the estimated basal energy expenditure. An alternative is continuous-drip intragastric tube feeding alone or combined with peripheral intravenous formulation. Total parenteral nutrition delivered through a central venous catheter should be the method of supplementation if the enteral route is not available and if the course of parenteral nutrition is expected to last for more than two weeks.

In hypermetabolic patients the goal is to provide 2 g of amino acids per kilogram per day and a total energy intake of twice the basal energy expenditure — generally, about 50 kcal per kilogram. But these patients are not only hypermetabolic because their resting energy expenditure is increased by stress, sepsis, trauma, or severe burns; at the same time they are hypercatabolic because of increased loss of lean tissues, with increased nitrogen excretion (1 g of nitrogen corresponding to 32 g of lean tissue).[16]

Infusions via the central venous route are necessary in the majority of these patients. If the total energy requirements are not met with a total dextrose intake of 5 to 6 mg per kilogram per minute (or about 2.5 liters of 25 per cent dextrose for a 70-kg adult), consideration should be given to providing the extra calories as fat emulsions — not only to prevent fatty infiltration of the liver and glucose intolerance, but also to avoid excessive production of carbon dioxide.[9,17,18] An excess of carbon dioxide resulting from administration of too much parenteral glucose can compromise weaning of hypermetabolic patients from mechanical ventilation or can precipitate respiratory failure in patients with severe obstructive pulmonary diseases. Infusion of a solution containing 4 to 5 per cent amino acids and only 15 per cent of dextrose, combined with fat emulsions, may be indicated in these situations.

However, maintenance or restoration of lean body mass in hypercatabolic patients can be difficult because of the inevitable increased breakdown of muscle protein supplying amino acids for gluconeogenesis. At the same time, glucose tolerance is decreased, and conversion of fat stores to energy sources is limited.[17,19] During sepsis protein deficiency may not be reversible by nutritional therapy alone, because endotoxin can block protein synthesis. Trying to induce anabolism by infusing large amounts of carbohydrate increases the metabolic rate, the conversion of carbohydrate into fat, and the rate of carbon dioxide production; it does not promote increased protein synthesis, and thus it results in self-defeating hypermetabolism.[1,17,18,20]

ENTERAL FORMULAS

The intestinal tract should be the site used for nutritional supplementation whenever possible. Three types of enteral mixtures differing in osmolality, digestibility, caloric density, lactose content, fat content, and cost are available.[4,21] Since almost all clinical problems can be handled with a small number of mixtures, it is better to be familiar with the generic features of the formulas, instead of using myriad commercial products that are basically the same.

Meal-replacement formulas (e.g., Isocal, Ensure, and Precision Isotonic) are used in patients who have almost normal proteolytic and lipolytic activity in their gastrointestinal tract. These formulas are polymeric mixtures containing proteins, fats, and carbohydrates in high-molecular-weight form; thus, they are lower in osmolality (350 mOsm per liter) than are formulas supplying equivalent amounts of calories in low-molecular-weight substrates. Approximately 30 per cent of the calories in meal-replacement formulas are provided by fat. Their lactose content is generally low, and they are "low-residue" products because the protein sources are casein, soy protein, or egg albumin instead of milk; milk contains lactose and starch, which contribute to fecal residue.

Theoretically, elemental diets (e.g., Vivonex Standard, Vivonex High Nitrogen, and Precision LR) are

helpful in patients who have an abnormal gastrointestinal tract (short-bowel syndrome, low enterocutaneous fistula, inflammatory bowel disease, and pancreatic insufficiency), because the proteolytic and lipolytic capacity of the gastrointestinal tract is not required for their absorption. These "monomeric" products use amino acids as the nitrogen source and oligosaccharides as the carbohydrate source; they usually contain little fat and no lactose (e.g., Vivonex and Vivonex HN). Because of their low viscosity they are the proper solutions for infusion through needle-catheter jejunostomy tubes. Their high osmolality (550 to 850 mOsm per liter) is often a cause of diarrhea.

For a daily intake of 3000 kcal an elemental diet costs from $12 to $25 daily, as compared with $5 for meal-replacement formulas and more than $100 for total parenteral nutrition. The recommended daily adult allowance for the various vitamins, however, can be fulfilled only by consumption of 1500 to 3000 ml of elemental diet per day. If diarrhea is triggered by these supplements, vitamin deficiency may occur unless vitamins are provided separately.

Feeding modules are concentrated sources of one nutrient (e.g., fat from Lipomul, carbohydrate from Polycose, and protein from Pro-Mix). These modules can be added to the formula diets to increase specific components that are deficient or to yield a small-volume, high-calorie mixture (1.5 to 2 kcal per milliliter) for patients in whom fluids should be restricted. Addition of 150 g of Polycose, for instance, to 1 liter of Isocal increases the caloric intake from 1 kcal per milliliter to 1.6 kcal, but also increases the osmolality of the resulting mixture by 160 mOsm per liter. The total osmolality then reaches more than 500 mOsm per liter, approaching the osmolality of elemental-diet formulas and risking the same kind of diarrhea as that induced by elemental diets.

These enteral feeding mixtures can be administered by mouth or through a tube. The small nasogastric Keofeed tube (9.6 French) (Health Development, Mountain View, Calif.) or Dobbhoff tube (8.0 French) (Biosearch Medical Products, Somerville, N.J.) is useful for long-term feeding because it is better tolerated than regular nasogastric tubes.

Continuous-drip infusion technique is the simplest and safest way to administer enteral feeding through these tubes. Infusion of enteral feeding mixtures is started at half strength and at a rate of 50 ml per hour. The rate is increased by 20 ml per hour every 24 hours until the required volume is achieved (generally 100 to 120 ml per hour). Only then is the concentration increased, first to three-quarter strength for another 24 hours and finally to full strength.

Types of Parenteral Solutions

When enteral intake is insufficient (short of 1500 kcal per day) or compromised for a limited period (up to two weeks), parenteral nutrition delivered through a peripheral vein is an easy and safe alternative. A solution containing 3 to 4 per cent amino acids (e.g., Travasol, Freamine, and Aminosyn) mixed with 5 to 10 per cent dextrose (as peripheral formulation) and given simultaneously with fat emulsion (Intralipid or Liposyn) will deliver between 1100 and 1800 kcal and 0.8 to 1 g of amino acids per kilogram of body weight daily.

If the parenteral route is the only usable one, and if the patient requires more than 2000 kcal daily for longer than two weeks, a vein catheter should probably be inserted in the subclavian vein for infusion of a hypertonic solution (1900 mOsm per liter) containing 4 to 5 per cent amino acids and 25 per cent dextrose (as "central formulation"), together with electrolytes, vitamins, and trace elements. The administration of 2 to 3 liters of this solution will meet the requirements of the majority of patients needing total parenteral nutrition for several weeks or months.

A less hypertonic central formulation may be used in patients who have poor glucose tolerance, as a means of preventing both fatty infiltration of the liver during long-term total parenteral nutrition[9,17] and excessive carbon dioxide production — a particular problem in patients with compromised respiratory function.[18,22] Infusion of each liter of a solution containing 4 to 5 per cent amino acids and 15 per cent dextrose (1400 mOsm per liter) can be combined with 500 ml of fat emulsion. This combination provides the same amount of amino acids and calories as regular central formulations; however, 50 per cent of the calories come from dextrose and 50 per cent from fat emulsions.

Vitamin deficiency is prevented by the provision of B-complex vitamins and 550 mg of ascorbic acid, as well as by 0.5 mg of folic acid in each liter of central parenteral solution. Once a week 3.5 ml of a multivitamin preparation (the B group and Vitamins A, D, and E) is also added to the solution, and 10 mg of Vitamin K and 150 μg of Vitamin B_{12} are administered intramuscularly.

Fat emulsions (Intralipid and Liposyn) supply essential fatty acids and a concentrated source of energy (1.1 kcal per milliliter). With an osmolality of 280, they can be infused through a peripheral vein. The usual clearance of fat emulsions is 3.8 g per kilogram of body weight per day, increasing threefold in cases of trauma or starvation,[23,24] but probably decreasing during severe sepsis. Even in patients with advanced alcoholic cirrhosis, fat emulsions are cleared from the plasma at a normal rate by extrahepatic tissues.[25] Although the recommended limits in the United States are 2.5 g of fatty acids per kilogram per day and a suggested maximum ratio of fat as 60 per cent of total daily caloric intake, these restrictions are routinely exceeded in Europe, where an even more concentrated fat emulsion (Intralipid 20%) has been used with few deleterious effects. (This emulsion is now available in this country.) Furthermore, in the initial study demonstrating that intravenous fat is as effective as dextrose in sparing protein or promoting positive nitrogen balance during parenteral nutrition, the pro-

portion of nonprotein calories given as fat was 83 per cent.[26]

Whenever possible, however, it seems better to provide balanced parenteral nutrition by administration of 50 per cent of the nonprotein calories as fat and 50 per cent as dextrose, because this proportion is close to that of normal dietary intake in most Western civilizations. This proportion prevents problems related to infusion of large amounts of glucose (hypertonic solution, requirement of exogenous insulin, fatty infiltration of the liver, and excessive carbon dioxide production), while avoiding hyperlipidemia and deficiency of essential fatty acids. Furthermore, infusing glucose simultaneously with fat lowers the plasma concentration of fatty acids by enhancing their plasma clearance.[27] A solution developed in Europe (Trivé 1000) contains 100 g of carbohydrate, 45 g of lipid, and 70 g of amino acid per liter (1 kcal per milliliter).[28,29]

Special Formulations

The Giordano–Giovannetti diet for parenteral administration, which provides direct precursors for protein mainly as essential amino acids,[30] should be used in patients with chronic or acute renal failure if the gastrointestinal route is unavailable. The solution (e.g., Nephramine) is mixed with hypertonic dextrose in water in order to yield a net concentration of 45 per cent dextrose and 1.7 per cent essential amino acids ("renal formulation").[31] The infusion is started at 30 ml per hour, which is then increased by 10 ml per hour to a maximum of 60 to 70 ml per hour, depending on the patient's water balance and glucose tolerance.

Parenteral feeding of patients with compromised cardiac function is associated with the risk of congestive heart failure due to fluid overload and with the risk of sepsis from the central venous catheter, which can be lethal in patients who have endocardial lesions or cardiovascular prostheses. Therefore, as often as possible, patients with cardiac disease should be given enteral supplements or tube-feeding formulas combined with peripheral intravenous solution. When the central venous route is the only alternative, a very concentrated solution (2500 mOsm per liter) containing 3.5 per cent amino acids and 40 per cent dextrose per liter ("cardiac formulation")[32] should be used to restrict the total volume load.

Fat emulsions represent another valuable source of energy for parenteral feeding of patients with cardiac disease. Although one study[27] showed that fatty acids could harm the hearts of ischemic dogs, the rate of infusion corresponded to a daily infusion volume of almost 5 liters of 10 per cent fat emulsion — a high rate never used in human beings.

Complications

Metabolic Complications

Episodes of hypoglycemia are often related to a sudden decrease in the rate of infusion because of mechanical problems with the central line (kinking or clotting of the line). Hyperosmolar hyperglycemic nonketotic coma is usually precipitated by latent or unknown diabetes, pancreatitis, sepsis, peritoneal dialysis, steroid medication, or concomitant use of phenytoin.

Hyperchloremic metabolic acidosis may occur because of the liberation of hydrochloric acid during the metabolism of the synthetic amino acids in most parenteral-nutrition solutions; it can be prevented by the routine addition of 15 to 30 meq of acetate to each liter of parenteral solution. Prerenal azotemia is the response of dehydrated patients to a sudden and excessive nitrogen load; dehydrated patients should be rehydrated with 5 per cent dextrose in water or with 0.45 per cent sodium chloride solution before central parenteral nutrition is begun. Deficiency of essential fatty acids usually occurs after two weeks of fat-free parenteral nutrition.[33] Infusion of 500 ml of fat emulsion every other day prevents this complication and should be routine; minor untoward responses to infusion are reversible.

Deficiencies in several trace elements[34] may be prevented by the addition of 1 mg of zinc, 0.5 mg of copper, 0.005 mg of chromium, and 0.028 mg of iodide to each liter of total-parenteral-nutrition solution. Because zinc and chromium are eliminated through the gastrointestinal tract and the kidneys, they are not added routinely to the renal formulation used for patients with renal failure. The minimal daily requirements for other trace elements such as arsenic, cesium, cadmium, molybdenum, and rubidium are probably not supplied in total-parenteral-nutrition solution,[35] and some day deficiencies in these elements may be recognized. Deficiencies in selenium[36] seem so likely that this element is already supplied in total-parenteral-nutrition solutions in some hospitals.

Mechanical Complications

The incidence of local vascular, neural, and pleural complications of central-line placement is related to the experience of the physician performing the procedure.[37,38] Air embolism can be avoided by placing the patient in the Trendelenburg position, by rehydrating the hypovolemic patient before catheterization, and by securing every junction in the tubing with adhesive tape to prevent accidental disconnections.

Thrombosis of the vena cava or its main tributaries should be treated by removal of the catheter and institution of heparin therapy, unless there is a contraindication. Use of streptokinase should also be considered. If recanalization occurs, the symptoms of superior vena cava thrombosis (swelling of the ipsilateral arm and shoulder and tenderness of the supraclavicular fossa) will subside after two or three weeks. Although the use of soft silicone catheters has been recommended to diminish thrombosis, the incidence of thrombosis in the central vein, as detected with routine phlebography, is the same (59 per cent)

whether silicone catheters, Teflon catheters, or polyethylene catheters are used.[39]

Septic Complications

Catheter-related sepsis is defined as an episode of sepsis that does not have a discernible anatomic locus and that resolves on removal of the catheter.[38] A rate of sepsis of 3 per cent or lower is acceptable, but when catheters are placed in patients who have episodes of transient bacteremia from septic foci in the urine, the wound, or the lungs, the rate of colonization of the catheters increases from 4 to 19 per cent.[40] The colonized catheter can become a source of reseeding infection. In the presence of unexplained fever and sepsis, the central venous catheter should be withdrawn and submitted for bacteriologic culture. If possible, a blood sample for culture should be drawn from the catheter before its removal.

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