22 NUTRITIONAL SUPPORT

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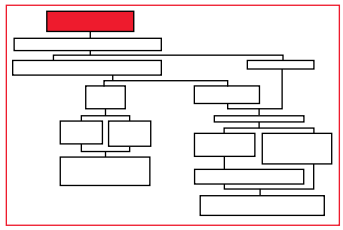
Nutritional Management of Hospitalized Patients

Evaluation of the Need for Nutritional Support



INDICATIONS FOR NUTRITIONAL INTERVENTION

Nutritional support is required in patients with various disease cprocesses who fall into one of the following general categories:

1. The patient has been without nutrition for 10 days. In a well-nourished person, body stores are generally adequate to provide nutrients during shorter periods of stress without compromising physiologic functions, altering resistance to infection, or impairing wound healing. The provision of nutrients becomes more important as body stores become eroded because of inadequate food intake and accelerated catabolism. In general, deficits occur in surgical patients after 7 to 10 days of partial starvation; nutritional intervention should be initiated before this time.
2. The duration of illness is anticipated to be more than 10 days. In patients whose illness is known to have a moderately prolonged course, nutritional support should be considered essential care. Thus, individuals with severe peritonitis or pancreatitis, major injury (injury severity score [ISS] > 15), or extensive burns (> 20% total body surface area [BSA]) are candidates for nutritional support because of the known duration of their illness. (The duration of illness in chronically malnourished patients also would be expected to exceed 10 days.)
3. The patient is malnourished (loss of > 10% of usual body weight over 3 months). Several nutritional assessment tools are available to screen patients for malnutrition, but in general, the degree of weight loss can be used as an index of nutritional deficiency. Recovery may be compromised in patients who do not have adequate body nutrient stores because of an existing nutritional deficit [*see Figure 1*]. The patient should receive nutritional support when the weight loss approaches or exceeds 15% of usual body weight:

$$\%\ \text{Weight loss} = (\text{Usual weight} - \text{present weight}) \times 100/\text{Usual weight}$$

Patients who do not meet one of these three general indications should be reassessed after 7 days to identify individuals

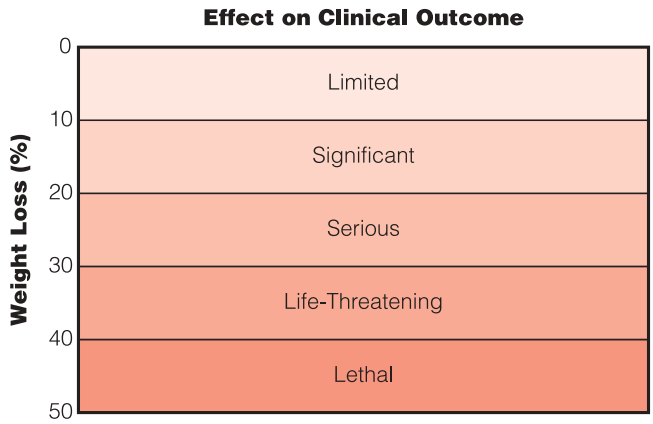
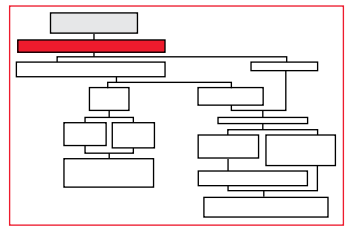


Figure 1 **The magnitude of weight loss is a rough predictor of its effect on clinical outcome.**

in whom complications develop after admission to the hospital and who require nutritional support. Serum proteins with a short half-life (e.g., prealbumin, transferrin, or retinol-binding protein) are useful markers for assessing the response to therapy.



PRIORITY OF CARDIOPULMONARY FUNCTION

Intensive care unit (ICU) patients are frequently candidates for nutritional support but often have a number of complex medical and surgical problems that may take precedence. In decreasing order of importance, the priorities are maintenance of airway, breathing, circulation, tissue oxygenation, acid-base neutrality, normal electrolyte concentrations, and adequate nutrition. The six functions that take priority over nutrition are usually impaired by acute and potentially life-threatening disorders that are often correctable over the short term. To optimize nutrient metabolism, circulation and tissue oxygenation must be adequate. In addition, hydrogen ion and electrolyte concentrations should be near normal in the extracellular fluid compartment, as reflected by blood or serum measurements.

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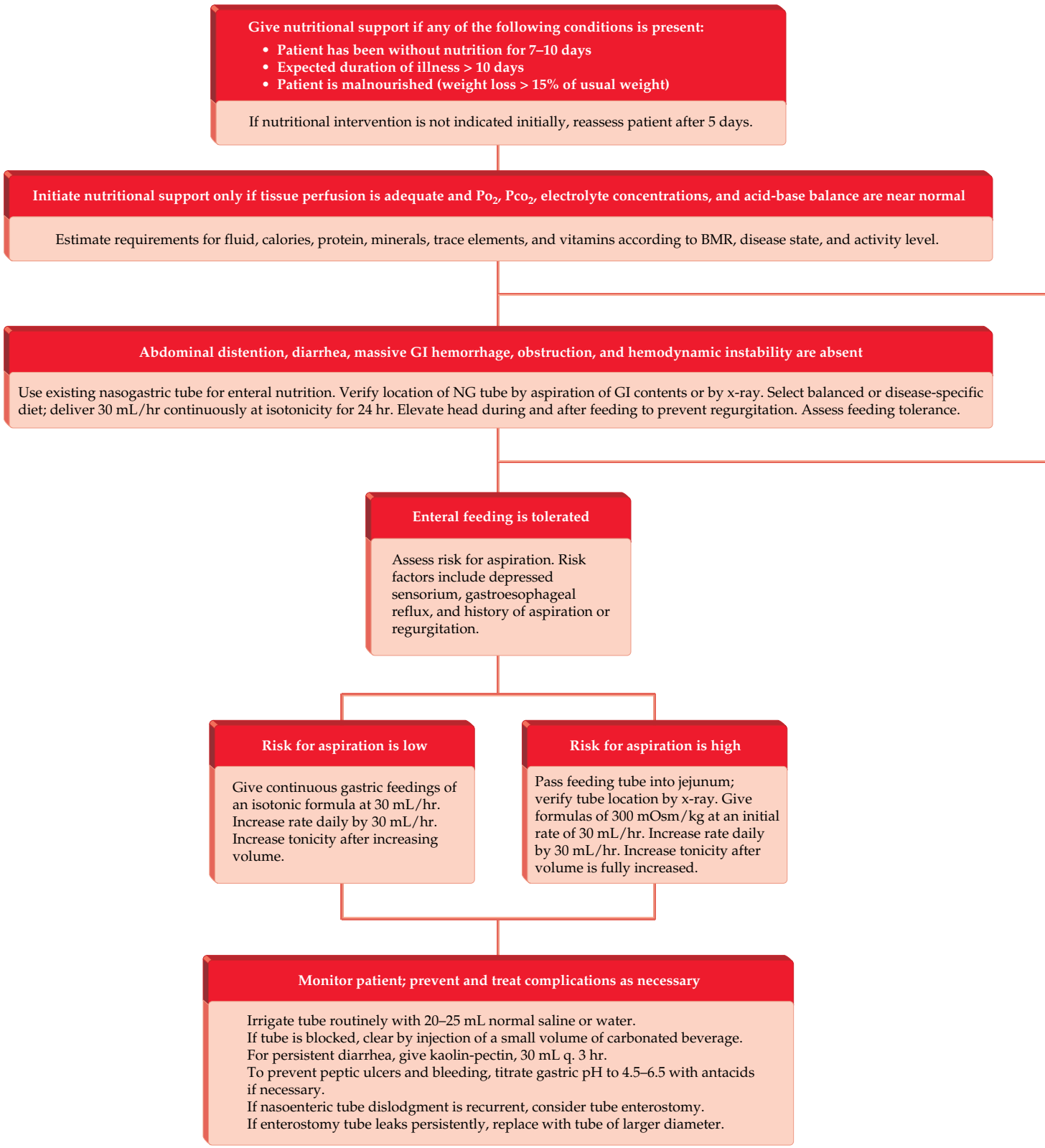
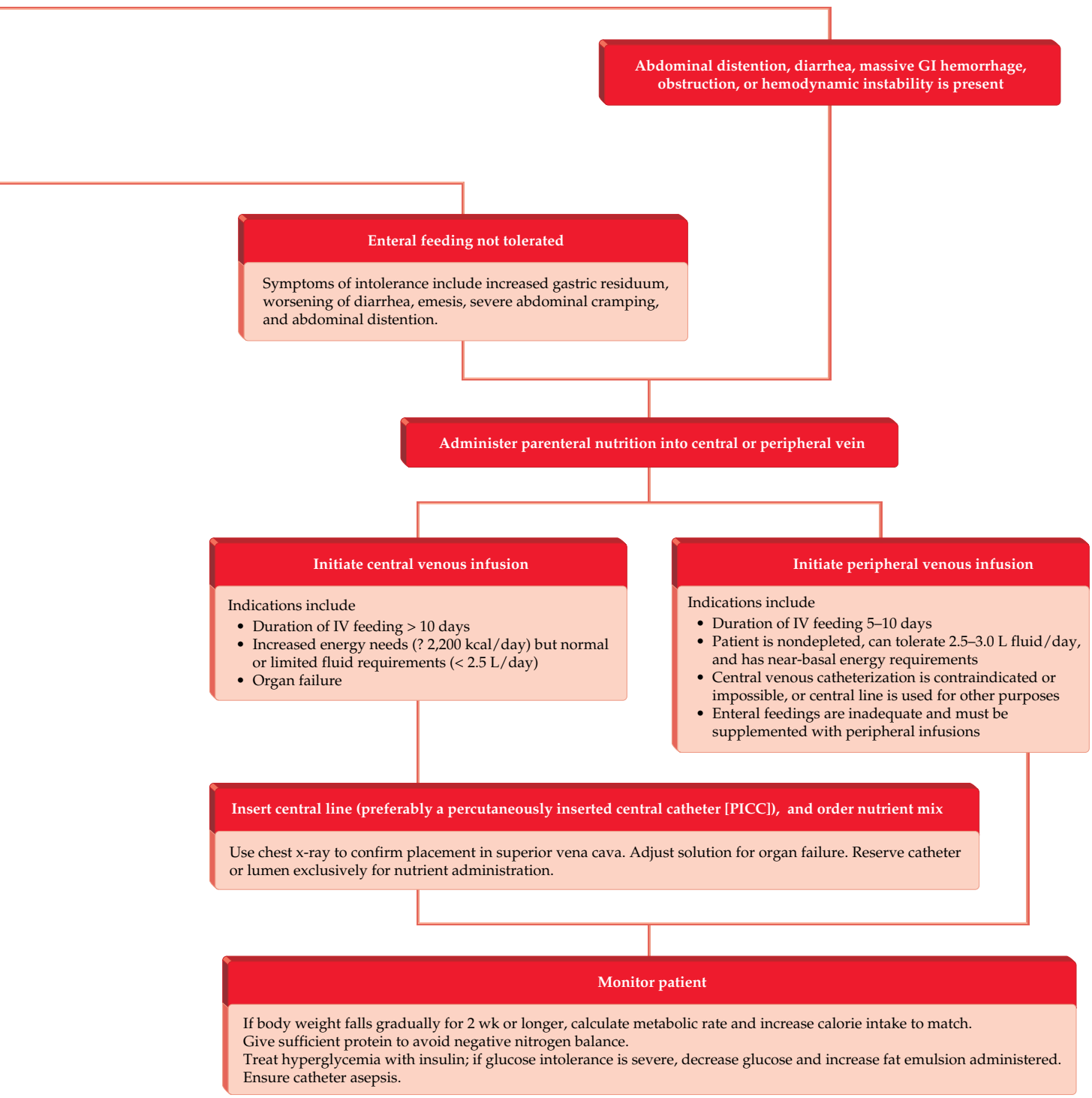

Give nutritional support if any of the following conditions is present:
• Patient has been without nutrition for 7–10 days
• Expected duration of illness > 10 days
• Patient is malnourished (weight loss > 15% of usual weight)
If nutritional intervention is not indicated initially, reassess patient after 5 days.
Initiate nutritional support only if tissue perfusion is adequate and Po_2, Pco_2, electrolyte concentrations, and acid-base balance are near normal
Estimate requirements for fluid, calories, protein, minerals, trace elements, and vitamins according to BMR, disease state, and activity level.
Abdominal distention, diarrhea, massive GI hemorrhage, obstruction, and hemodynamic instability are absent
Use existing nasogastric tube for enteral nutrition. Verify location of NG tube by aspiration of GI contents or by x-ray. Select balanced or disease-specific diet; deliver 30 mL/hr continuously at isotonicity for 24 hr. Elevate head during and after feeding to prevent regurgitation. Assess feeding tolerance.
Enteral feeding is tolerated
Assess risk for aspiration. Risk factors include depressed sensorium, gastroesophageal reflux, and history of aspiration or regurgitation.
Risk for aspiration is low
Give continuous gastric feedings of an isotonic formula at 30 mL/hr. Increase rate daily by 30 mL/hr. Increase tonicity after increasing volume.
Risk for aspiration is high
Pass feeding tube into jejunum; verify tube location by x-ray. Give formulas of 300 mOsm/kg at an initial rate of 30 mL/hr. Increase rate daily by 30 mL/hr. Increase tonicity after volume is fully increased.
Monitor patient; prevent and treat complications as necessary
Irrigate tube routinely with 20–25 mL normal saline or water.
If tube is blocked, clear by injection of a small volume of carbonated beverage.
For persistent diarrhea, give kaolin-pectin, 30 mL q. 3 hr.
To prevent peptic ulcers and bleeding, titrate gastric pH to 4.5–6.5 with antacids if necessary.
If nasoenteric tube dislodgment is recurrent, consider tube enterostomy.
If enterostomy tube leaks persistently, replace with tube of larger diameter.

Nutritional Management of Hospitalized Patients



If cardiopulmonary function is abnormal, nutrient administration may potentiate the abnormalities and create additional problems. For example, in a patient with respiratory insufficiency, infusion of moderate quantities of carbohydrate could increase carbon dioxide tension (P_{CO_2}) and lower serum potassium concentration. These changes could initiate a life-threatening cardiac dysrhythmia. The need for nutritional support in the ICU patient should always be evaluated with respect to other care problems; acute disorders of cardiorespiratory function, disturbed acid-base status, and altered electrolyte concentrations should generally be corrected before nutritional support is initiated.

NUTRIENT REQUIREMENTS

The energy requirements of an individual are primarily related to body size, age, gender, and energy expenditure of activity (muscular work). In hospitalized patients who are generally inactive, the basal metabolic rate (BMR) accounts for the greatest amount of energy expenditure. The BMR in normal individuals is about 25 kcal/kg/day but can be calculated more precisely according to the Harris-Benedict formulas:

$$\text{Males: BMR (kcal/day)} = 66 + (13.7 \times \text{weight [kg]}) + (5 \times \text{height [cm]}) - (6.8 \times \text{age [yr]})$$

$$\text{Females: BMR (kcal/day)} = 665 + (9.6 \times \text{weight [kg]}) + (1.7 \times \text{height [cm]}) - (4.7 \times \text{age [yr]})$$

The BMR is influenced by the disease process. Hypermetabolism occurs in surgical patients with moderate to severe infection or injury. In these patients, the magnitude of the increase in the BMR depends on the extent of injury or infection. Patients generally fall into one of four categories according to their metabolic requirements [*see Table 1*].

Estimates that are based on normal basal metabolic requirements and adjusted only for the disease state of the patient reflect the energy needs of patients requiring mechanical ventilation or those at bed rest. However, further adjustments are necessary for patients who are out of bed and physically active: they should receive additional calories. To meet the energy needs of physically active patients, who are in a nonbasal state, calculated requirements should be increased an additional 15 to 20%. The metabolic response to stress and critical illness is complex and is mediated by interactions between the neuroendocrine system and circulating cytokines. This interaction produces a metabolic milieu in which the body cannot utilize supranormal amounts of nutritional substrates (i.e., hyperalimentation). In fact, administering excessive nutrients with the purported goal of acutely correcting nutrient deficits is often harmful, leading to an abnormal accumulation of hepatic glycogen, enhancing total energy expenditure, and causing increased urea production and elevation of the blood urea nitrogen (BUN).

Table 1 Alterations in Metabolic Rate

Patient Condition	Basal Metabolic Rate
No postoperative complications Fistula without infection	Normal
Mild peritonitis Long-bone fracture or mild to moderate injury	25% above normal
Severe injury or infection in ICU patient Multiorgan failure	50% above normal
Burn of 40–100% of BSA	100% above normal

Weight gain usually should not be a priority for ICU patients. Complications of nutrient delivery are minimized and nutrient metabolism is generally optimized if the ICU patient receives only the energy necessary for weight maintenance throughout a complex and complicated clinical course. (This quantity of energy rarely exceeds 35 total calories/kg body weight/day in most general surgical patients who are admitted to the ICU for non–trauma-related care.) With resolution of the disease process, the hormonal environment is altered to favor anabolism. In addition, increases in spontaneous activity and in planned exercise stimulate rebuilding of lean body mass.

Protein

After energy requirements are determined, protein needs are calculated. The protein requirement for most individuals is 0.8 g/kg body weight/day (about 60 to 70 g protein/day). Critically ill patients may need 1.5 to 2.0 g/kg/day. Most standard enteral and parenteral feeding mixtures provide this increased quantity of protein if sufficient volume of formula is delivered to meet the increased caloric requirements of these patients. The nitrogen-to-calorie ratio for most feeding formulas prepared for surgical patients is 1:150 (i.e., 1 g of nitrogen for every 150 kcal).

The contraindications to this increased quantity of protein (a daily total of 100 to 150 g, which is equivalent to the amount of protein in a lean 16 oz. steak) are renal failure before dialysis (BUN > 40 mg/dL) and hepatic encephalopathy. Patients with systemic inflammatory response syndrome (SIRS) often require increased quantities of dietary protein [*see 8:13 Multiple Organ Dysfunction Syndrome*]. Nutritional support reduces net nitrogen losses in such patients, but positive or even neutral nitrogen balance is generally not achieved, because of the disturbance in metabolism and the reduced intake of dietary protein.

Vitamins and Minerals

The requirements for vitamins, minerals, and trace elements are usually met when adequate volumes of balanced nutrient formulas are provided [*see Table 2 and Table 3*]. The requirements for most of the major minerals (sodium, potassium, chloride, phosphorus, magnesium, and zinc) are satisfied by monitoring serum concentrations of these elements and adjusting intake to maintain levels within the normal range. Some minerals and electrolytes are restricted in patients with renal failure. Although serum concentrations may not directly reflect total body deficits, sufficient quantities of these nutrients are available to support normal cellular functions if adequate blood concentrations are maintained. Most premixed enteral formulas provide adequate quantities of these substances if caloric needs are met. Vitamins and trace elements must be added to parenteral solutions.

Table 2 Vitamin Requirements					
Vitamin	**Units**	**Recommended Dietary Allowance (RDA) for Daily Oral Intake[1]**		**Tolerable Upper Intake Level[1]**	**Daily Requirement for IV Intake[99]**
		Male	**Female**		
Vitamin A (retinol)	µg	900	700	3,000	990
Vitamin D (ergocalciferol)	µg	5–15*	5–15*	50	5
Vitamin E (tocopherol)	mg TE	15	15	1,000	7
Vitamin K (phylloquinone)	µg	120*	90*	Unknown	150
Vitamin C (ascorbic acid)	mg	90	75	2,000	200
Thiamine (vitamin B_1)	mg	1.2	1.1	Unknown	6
Riboflavin (vitamin B_2)	mg	1.3	1.1	Unknown	3.6
Niacin	mg	16	14	35	40
Pyridoxine (vitamin B_6)	mg	1.3–1.7	1.3–1.5	100	6
Pantothenic acid	mg	5*	5*	Unknown	15
Folic acid	mg	0.4	0.4	1	0.6
Vitamin B_{12}	µg	2.4	2.4	Unknown	5
Biotin	µg	30*	30*	Unknown	60

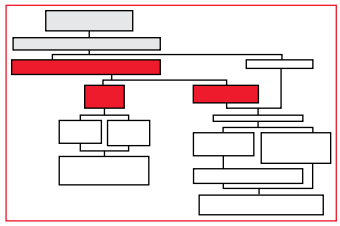
*Estimated to be safe and adequate dietary intakes.

Pharmacologic recommendations for stress in surgical patients The prescription of vitamins and minerals for therapeutic use should be based on the patient's nutritional history as well as on estimated requirements for the current disease state. These considerations are particularly important in prescription of the fat-soluble vitamins, which are stored in body fat and thus may become toxic at high levels. The upper levels of daily intake for vitamins and minerals have been published [*see Table 2 and Table 3*]. These are the maximum levels of intake from all sources likely to pose no risk of adverse effect.[1] Vitamins and minerals are sometimes given in large dosages to exert antioxidant effects. Vitamins A, C, and E and the minerals zinc and selenium can attenuate the tissue-damaging effects of free radicals. In fact, a randomized prospective trial involving mostly trauma patients demonstrated a significant reduction in organ failure with the administration of vitamins C (1,000 mg) and E (1,000 IU).[2] Many physicians are giving these vitamins and minerals as supplements to injured and infected patients[3]; supplementation with glutamine should also be considered because of its ability to enhance intracellular glutathione stores, which also play a major antioxidant role [*see* Discussion, *below*].

Table 3 Trace Mineral Requirements				
Mineral	**Recommended Dietary Allowance (RDA) for Daily Oral Intake[1] (mg)**		**Suggested Daily IV Intake[99] (mg)**	**Tolerable Upper Intake Level[1] (mg)**
	Male	**Female**		
Zinc	11	8	2.5–5.0*	40
Copper	0.9	0.9	0.3–0.5	10
Manganese	2.3†	1.8†	0.06–0.1	11
Chromium	0.03–0.035†	0.02–0.025†	0.01–0.015	Unknown
Iron	8	18	0	45

*Burn patients require an additional 2 mg.
†Estimated to be safe and adequate dietary intakes.

Enteral Nutrition



Enteral nutrition is the provision of liquid-formula diets by mouth or tube into the gastrointestinal (GI) tract. The GI tract is the preferred site for feeding the critically ill patient. Enteral nutrition maintains and restores intestinal epithelium, whereas starvation or parenteral nutrition causes villous atrophy. It cannot be used safely, however, in patients who are hemodynamically unstable or who have abdominal distention, intestinal obstruction, or massive GI bleeding. For patients who are able to receive enteral nutrition, either a balanced or a modified diet is selected on the basis of diagnosis and nutritional requirements. An isotonic (approximately 300 mOsm/kg) diet is given continuously for a trial period of 24 hours. If the patient tolerates this regimen but is at increased risk for aspiration, feeding is delivered into the jejunum rather than into the stomach. A standard protocol is helpful in reducing complications.

SAFE USE OF THE GASTROINTESTINAL TRACT FOR FEEDING

Enteral nutrition should be prescribed only if safety and a low complication rate can be ensured. To determine whether the critically ill patient can be fed safely via the GI tract, a clinical assessment of intestinal function is performed. A good determinant of safe tolerance of enteral nutrition is a GI output lower than 600 mL/24 hr. For the purpose of these guidelines, GI output is defined as the volume of effluent from a nasogastric tube, an ostomy, or a rectal tube. Examples of conditions in critically ill patients that produce excessively high (> 600 mL/24 hr) GI outputs and therefore preclude the use of enteral nutrition are gastroparesis, intestinal obstruction, paralytic ileus, high-output enteric fistulas, antibiotic-induced colitis, severe idiopathic diarrhea, and the initial phase of short-bowel syndrome (SBS). Selected patients with enteric losses exceeding 600 mL/24 hr may receive enteral nutrition, however, if carefully monitored by an experienced team.

Another major cause of increased GI output is massive GI bleeding. Conditions that produce bleeding of this magnitude include peptic ulcer disease, esophageal varices, diverticulosis, and angiodysplasia of the colon. Mild bleeding such as that produced by stress gastritis may actually resolve with the delivery of enteral nutrition into the stomach because the liquid diet buffers gastric acid.[4] Enteral nutrition does not exacerbate mild lower intestinal bleeding.

Although commonly used at the bedside as indicators of intestinal function, bowel sounds and passage of flatus are nonspecific and are unrelated to the eventual tolerance of enteral nutrition.

In the absence of excessively high GI output, abdominal distention, and massive GI bleeding, a trial of enteral nutrition is warranted to determine if the GI tract can be used safely for feeding.[5]

SELECTION OF DIET

Before delivery of enteral nutrition, the appropriate diet must be selected on the basis of the patient's nutrient requirements [*see* Indications for Nutritional Intervention, *above*]. Most liquid-formula diets consist of either a balanced or a modified formula.

Balanced diets contain carbohydrates, proteins, and fats in complex (polymeric) forms in proportions similar to those of a regular Western diet. Frequently, however, the fat content is reduced to 10 to 15% of total calories, and the carbohydrate content is increased. Carbohydrates are present as oligosaccharides, polysaccharides, or maltodextrins; fats consist of medium-chain triglycerides (MCTs) or long-chain triglycerides (LCTs). The nitrogen source is a natural protein, which may be either intact or partially hydrolyzed. In general, balanced diets are isotonic, lactose free, and available in ready-to-use, liquid form. Flavored balanced diets can be used for oral supplementation as well as for enteral tube feeding.

Selection of a balanced diet is based on nutrient and fluid requirements. The caloric density of balanced diets can be 1.0, 1.5, or 2.0 kcal/mL. The largest number of commercially available diets provide 1.0 kcal/mL. The nonprotein caloric content of these diets is derived from either carbohydrates or lipids. Balanced diets formulated with carbohydrates as the main caloric source have higher osmolarity than isocaloric diets containing lipids. These carbohydrate-based diets are well tolerated when administered directly into the stomach and may be helpful for patients with steatorrhea. Balanced diets that are fat based may be more appropriate for patients who have diarrhea caused by diet hyperosmolarity, especially when feedings are infused directly into the small intestine. However, fat malabsorption is common in critically ill patients when the fat content of the diet exceeds 30% of total calories.

In modified formulas, the proportions and types of nutrients differ from those of a regular Western diet. Manufacturers of enteral diets have introduced these modifications to meet the special nutrient needs of patients with renal failure or SBS. Modified diets are also known as elemental diets or chemically defined diets. These diets contain crystalline amino acids or short peptides in compositions that differ from the reference composition of proteins of high biologic value, such as egg albumin. The fat-to-carbohydrate ratio of these modified diets varies depending on the purpose of the modification. The source of carbohydrate is either dextrose or oligosaccharides; fats are usually in the form of MCTs, essential fatty acids, or both. Because they are not palatable, modified diets are rarely used as oral supplements. Modified diets are further characterized according to the conditions for which they are formulated: stress, immunomodulation, and hepatic, renal, respiratory, or GI dysfunction [*see Table 4*].

Diets for patients with GI dysfunction have modified nitrogen and fat composition. Transport of dietary nitrogen across the intestinal mucosa is enhanced when nitrogen is provided in the form of short peptides rather than free amino acids. It is also well documented that the small-bowel mucosa utilizes glutamine as the preferred fuel [*see* Discussion, *below*]. Consequently, some modified diets contain nitrogen in the form of short peptides, whereas others have an extra amount of glutamine. MCTs are more easily absorbed and metabolized than LCTs are. Diets modified for improved absorption contain a higher proportion of MCT oil. These diets may be efficacious when used during the transition phase after a

Table 4 **Composition of Modified Diets**

Formula	Protein (g/L)	Carbohydrate (g/L)	Fat (g/L)	Ratio of Nitrogen (g) to Nonprotein Calories (kcal)	Caloric Density (kcal/mL)	Product* (Manufacturer)
Elemental	50	127	34	1:100	1.0	Subdue (Mead Johnson Nutritionals)
	40	127	39	1:131	1.0	Peptamen (Nestlé Clinical Nutrition)
Stress	56	130	28	1:71	1.0	Impact (Novartis)
	66	177	37	1:97	1.3	Perative (Ross Laboratories)
Hepatic	44	168	36	1:148	1.2	Hepatic Aid II (B. Braun Medical Inc.)
Renal	19	365	46	1:800	2.0	Amin-Aid (R&D Laboratories)

* Partial listing.

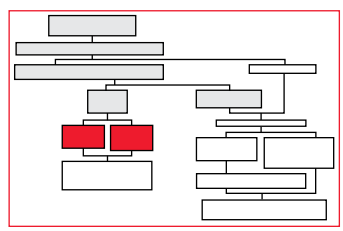
period of prolonged bowel rest or when the intestine is inflamed. Controlled trials are necessary to verify their clinical efficacy. Stress formulas are indicated for hypercatabolic patients whose nitrogen balance continues to be negative despite increased intake of a balanced diet. These diets usually contain more nitrogen and frequently have an altered amino acid composition. Little evidence supports the use of diets that provide branched-chain amino acids (BCAAs) in concentrations higher than 20 to 25% of total amino acid content for stressed patients.

The fat sources used for enteral diets are primarily omega-6 fatty acids (the arachidonic acid family). Published research suggests that supplementation with omega-3 fatty acids (the eicosapentaenoic acid family) results in the synthesis of eicosanoids (prostaglandins, leukotrienes, and thromboxanes) that enhance the immune response. Other substances that are said to be immunomodulating have also been added to enteral formulas [*see* Discussion, *below*].

ASSESSMENT OF FEEDING TOLERANCE

The selected formula is started at isotonicity and delivered continuously at 30 mL/hr for 24 hours. During this initial trial, the formula is delivered via a previously inserted Salem sump or rubber nasogastric (Levin) tube. If a nasogastric tube is not already in place, a soft tube made of either silicone rubber or polyurethane is inserted (see below).

Feeding tolerance is assessed for the first 24 hours. Poor tolerance is indicated by vomiting and severe abdominal cramps, gastric residuum greater than 50% of the volume administered during the previous 4-hour period of feeding, increased abdominal distention (a particularly important factor to assess in comatose patients and patients undergoing mechanical ventilation), and worsening of diarrhea. If any one of these conditions is present, parenteral nutrition is recommended. If there is no evidence of feeding intolerance, the patient is assessed for the risk of aspiration.



ASSESSMENT OF RISK OF ASPIRATION

Aspiration is a major complication in patients receiving enteral nutrition. The propensity to aspirate enteral feedings is often related to the patient's primary disease and neurologic status, as well as to the site of GI access and the method of delivery.

Important factors in assessing the risk of aspiration include depressed sensorium, increased gastroesophageal reflux, and history of previously documented episodes of aspiration. Depressed sensorium in the critical care setting is secondary to organic lesions of the central nervous system (CNS), metabolic encephalopathies, or medications. Head trauma, hypoxemia, hepatic and septic encephalopathies, and the use of H_2-receptor blockers are common causes of depressed sensorium in critically ill patients. Increased gastroesophageal reflux may be present in individuals with reduced lower esophageal sphincter (LES) pressure and increased intragastric pressure. Many medications used in the ICU, such as theophylline, anticholinergics, calcium channel blocking agents, beta-adrenergic agonists, and alpha-adrenergic antagonists, cause a reduction in LES pressure. Finally, a history of aspiration places the patient at increased risk for recurrent episodes.

For most enterally fed patients, safety demands that the head be elevated at feeding time and for some period thereafter to prevent regurgitation. If elevating the patient's head is not possible, an alternative site of nutrient delivery should be considered. Nasogastric intubation, in particular, requires elevation of the head because the tube may render the upper and lower esophageal sphincters incompetent and liable to reflux. Even the presence of a tracheostomy or endotracheal tube does not ensure that regurgitated gastric contents will not be aspirated. Liquid filling the pharynx will inevitably trickle past even an overinflated endotracheal tube cuff and into the lung. The lack of a truly reliable bedside method for detection of aspiration makes study of this complication difficult.

ACCESS FOR FEEDING

In most general and thoracic surgical patients, access for feeding is most commonly obtained via the stomach or the jejunum. Methods of access for intragastric feedings include nasogastric tubes and feeding gastrostomies placed through a laparotomy or percutaneously with the aid of endoscopy, fluoroscopy, or laparoscopy.

Nasogastric tubes provide the most common method of access for gastric feeding. Tubes made of polyurethane or silicone rubber are preferred because they are soft, nonreactive, and well tolerated by most patients. They are also less corrosive to the nasopharynx than tubes made of rubber or polyvinyl chloride. The soft consistency of these tubes often makes insertion into critically ill patients difficult and precludes the checking of gastric residuum. The difficulties of tube passage into the stomach are increased when thin, floppy tubes are inserted into obtunded patients. Useful aids include stylets, judicious use of gravity and positioning, and designation of especially experienced and certified nursing personnel to assist in this task [*see Table 5*].

Passage of a tube through the pylorus into the jejunum may be necessary if the patient is at increased risk for aspiration (see above). Our practice is to place the tube into the stomach, to position the patient on the right side for several hours once or twice in the next 24 hours, and then to obtain an abdominal x-ray. If the tube has not passed, metoclopramide, 10 mg IV, is given while the patient is still in the radiology department, and a repeat x-ray is obtained. If the location of the feeding tube is not evident, a small amount of contrast material can be injected through the tube to verify the position.

If the tube still has not passed through the pylorus, the aid of the fluoroscopist is enlisted. (Interventional radiologists take justifiable pride in their ability to cannulate almost any internal orifice.) Finally, if all else has failed and no alternative route for nutrition is appropriate, the endoscopist can capture the tube tip in the stomach with the biopsy forceps of the flexible endoscope (aided by a suture through the tube end) and guide the tube through the pylorus.

***Table 5* Procedure for Inserting Nasoenteric Tubes**

Provide privacy.
Explain procedure and its purpose.
Place patient in sitting position with neck flexed slightly and head of bed elevated to 45°.
Lubricate stylet and insert into feeding tube.
Inspect nares and determine optimal patency by having the patient breathe through one nostril while the other is temporarily occluded. Estimate the length of tubing required to reach into the stomach by measuring the distance from the tip of the nose to the earlobe and then from the earlobe to the xiphoid process. Add 25 cm to this length for nasoduodenal intubation.
If the patient seems uncooperative, instill generous amounts of lidocaine jelly into the nares and nasopharynx before tube insertion.
Lubricate the end of the tube and pass it posteriorly. Ask a cooperative patient to swallow water to facilitate passage of the tube.
Once the tube is beyond the nasopharynx, allow the patient to rest.
Have the patient continue neck flexion and swallowing while the tube is advanced.
If the patient begins to cough, withdraw the tube into the nasopharynx and then reattempt passage.
Confirm passage into the stomach by obtaining an abdominal x-ray.
Remove stylet.
Secure tube to bridge of nose or upper lip with nonallergenic tape and prevent undue pressure on external nares.

When any type of nasoenteric tube is placed to administer enteral nutrition, verification of the tube's location before feedings are started is mandatory. The simplest means of assessing proper tube placement in the GI tract is by the aspiration of gastric contents, the source of which can be confirmed by measuring the pH of the aspirate. Because small-bore, soft tubes tend to collapse under high negative pressure, a small syringe should be used to aspirate gastric contents. If gastric contents cannot be aspirated through the tube, radiographic confirmation of tube location is mandatory before enteral feedings are started. Because feeding tubes are often radiopaque, a simple plain film of the abdomen may be adequate. If the exact location of the tube is still in doubt, a small amount of contrast material can be injected through the tube. Placement of the distal tip of the tube in the duodenum is usually confirmed by an abdominal x-ray before transpyloric feedings are started. The tube should be inserted to a length sufficient to permit migration into the proximal jejunum.

Simple insufflation of air into the tube is not sufficient to verify the position of the tube. Auscultation over the stomach can detect sound transmitted through a tube that has been inadvertently passed into the bronchial tree. Many of these tubes are small enough to pass through the glottis and the trachea without markedly interfering with phonation or respiration. Enteral formulas delivered into the bronchial tree through a misplaced tube can cause severe pneumonitis and death.

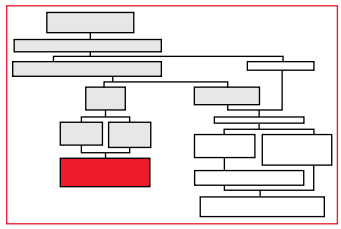
The development of percutaneous techniques for the placement of gastrostomies has been a major contribution to enteral nutrition. Percutaneous endoscopic gastrostomy (PEG) [*see 5:18 Gastrointestinal Endoscopy*] and Witzel techniques for these procedures are well documented.

Concurrent decompression of the stomach and feeding into the small intestine have been used to reduce the risk of aspiration in critically ill patients. This combination of procedures requires either the insertion of a multilumen nasojejunal tube, the surgical placement of combined gastrojejunal tubes, modification of PEG, or insertion of a nasogastric tube in conjunction with a surgical jejunostomy. Such access to the GI tract also provides a route for the delivery of crushed medications and the option to provide cyclic nocturnal enteral nutrition with gastric decompression (i.e., the patient receives nutrients by mouth during the day).

FEEDING REGIMENS

If the patient tolerates the initial trial of enteral nutrition, then the delivery site for future feeding is chosen according to the risk of aspiration, and the feeding regimen is gradually intensified. If the risk of aspiration is minimal, intragastric feedings are preferred. These feedings are better tolerated physiologically, easier to administer, and less restrictive for the patient than continuous feeding into the small intestine. Patients fed into the stomach receive an isotonic formula delivered continuously at a rate of 25 mL/hr. The delivery is advanced by 25 mL/hr every 8 hours until the goal rate is reached.[6] The level of gastric residuum that is of concern in the critically ill patient appears to be 400 mL.[7] If the risk of aspiration is increased, feedings are delivered via nasoduodenal or nasojejunal tubes. Patients fed into either the duodenum or the jejunum receive formulas of 300 mOsm/kg delivered at an initial rate of 30 mL/hr with the aid of a

peristaltic pump. The rate is increased daily by 30 mL/hr until the goal rate is reached. It should be emphasized that only isotonic feedings should be administered into the small bowel. Hypertonic formulations have been associated with small-bowel injury and necrosis.



MONITORING AND PREVENTION OF COMPLICATIONS

Patients who receive enteral nutrition should be as carefully monitored as those who receive parenteral nutrition. Particular attention is directed to the patient's metabolic status and fluid and electrolyte balance. A protocol should be established and followed to ensure that nutritional goals are met and complications minimized. A standard checklist is helpful in starting and maintaining enteral nutrition and prevents omission of important details [*see Table 6*].

Four types of complications are related to enteral nutrition: GI, mechanical, metabolic, and infectious. The two most common types are GI and mechanical complications.

The most frequent GI complication is diarrhea, which may occur in as many as 75% of critically ill patients receiving enteral nutrition. Diarrhea is best defined as stool weight greater than 300 g/24 hr or stool volume greater than 300 mL/24 hr; however, these measurements are impractical and difficult to obtain. A more practical definition of diarrhea is more than three loose bowel movements during a period of 24 hours. There are many causes of diarrhea in critically ill patients receiving enteral nutrition, and the most frequent association (about 80% of cases) is with receipt of antibiotics [*see Figure 2*]. The desired therapeutic approach is to adjust the enteral nutrition regimen accordingly rather than to discontinue it completely. Only one variable of the feeding regimen (i.e., osmolality, volume, rate, or type of diet) should be altered at a time. In our experience, critically ill patients tolerate a continuous feeding regimen better than intermittent feeding. If the patient still has diarrhea when being fed at a rate of 30 mL/hr and a concentration of 150 to 300 mOsm/kg, antidiarrheal treatment is indicated.

In many instances, antidiarrheal medication is given without a definite diagnosis; therefore, it is essential to select medications with both a wide therapeutic range and a low

Table 6 Standard Orders for Enteral Nutrition

Obtain abdominal x-ray to confirm tube location before feeding.
Elevate head of bed 45° when feeding into the stomach.
Record type and strength of diet and rate of infusion.
Check gastric residuum every 4 hr in patients receiving gastric feedings.
Withhold feedings if residuum is 400 mL or greater. Check gastric residuum every 2 hr after feedings held and restart gastric feedings when residuum is less than 400 mL.
Check for abdominal distention. Check frequency, consistency, and volume of stool output.
Weigh patient on Monday, Wednesday, and Friday. Record weight on graph.
Record intake and output daily. For every shift, chart volume of formula administered separately from water or other oral intake.
Change administration tubing and cleanse feeding bag daily.
Irrigate feeding tube with 20 mL of water at the completion of each intermittent feeding, when tube is disconnected, after the delivery of crushed medications, or if feeding is stopped for any reason.
When patient is ingesting oral nutrients, ask the dietitian to provide calorie counts daily for 5 days, then weekly thereafter.
On a weekly basis, obtain complete blood count with red blood cell indices, SMA-12, serum iron, and serum magnesium.
Obtain SMA-6 every Monday and Thursday.
Once a week, collect urine for 24 hours, starting at 8:00 am, and analyze for urea nitrogen.

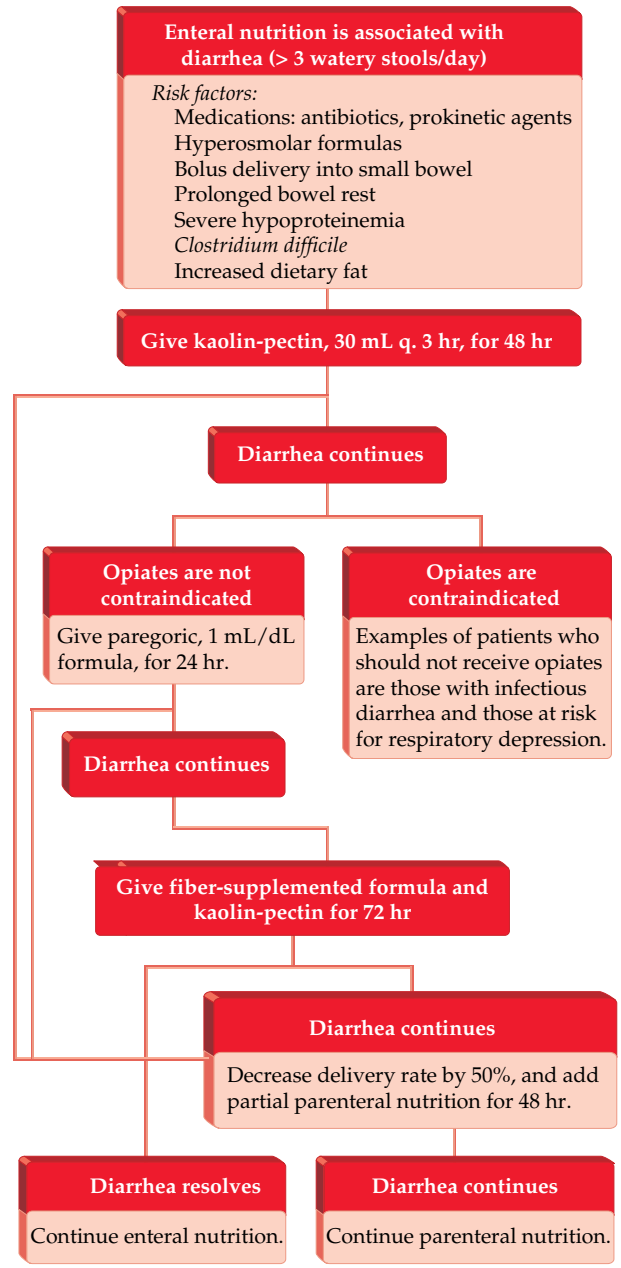


Figure 2 **The decision-making approach for pharmacologic and dietary treatment of diarrhea associated with enteral nutrition is shown.**

incidence of side effects. For these reasons, we prefer kaolin-pectin over opiates such as paregoric. Every 3 hours, 30 mL of kaolin-pectin solution is given through the feeding tube and followed by 25 mL of normal saline for irrigation. If this regimen is unsuccessful after 48 hours and opiates are not contraindicated, paregoric is added at a dose of 1 mL/100 mL of formula [*see Figure 2*]. Opiates act by slowing intestinal motility. Since the normal motility pattern is a defense mechanism for growth of bacteria in the small bowel, administering opiates to a patient with a contaminated small bowel can lead to bacterial overgrowth and worsen diarrhea. In addition, opiates are respiratory depressants and are also contraindicated in patients with infectious diarrhea.

Several diagnostic methods may help in identifying the cause of diarrhea associated with enteral nutrition. These include the assay of stool for *Clostridium difficile* enterotoxin, analysis of stool for fat malabsorption, the D-xylose test for carbohydrate malabsorption, and breath H_2 analysis for bacterial overgrowth. The D-xylose test and the breath H_2 analysis are more commonly used in non–critically ill patients with diarrhea associated with enteral feeding.

To prevent peptic ulcerations and bleeding, gastric acidity is controlled with H_2-receptor blockers in critically ill patients. Although these drugs help control hyperacidity, which is a cause of diarrhea, they also lead to bacterial overgrowth in the intestine.[8] Therefore, the use of H_2-receptor blockers should be avoided in patients who receive feedings into the stomach, because the presence of the liquid formula in the stomach already provides a physiologic means of buffering acid. If necessary, antacids rather than H_2-receptor blockers should be used to titrate gastric pH to 4.5 to 6.5. The amino acid glutamine is also utilized to prevent or treat ulceration of the upper GI tract.

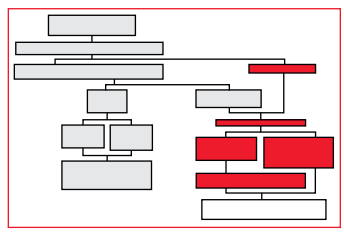
The most common mechanical complications that are related to enteral nutrition are tube dislodgment, clogging of the tube, and leakage of enteric contents around the exit site of the tube onto the skin. Tube dislodgment occurs more frequently in agitated patients and hypoxic patients. Inadvertent removal of the tube is usually prevented by adequate taping of the nasoenteric tube or, in agitated patients, by suturing the tube or using a Velcro abdominal wall binder.

Clogging or plugging of the tube often results from the failure to use saline irrigations after intermittent feedings or the inadvertent delivery of crushed medications through a small-bore tube. This complication is reduced by routine irrigations of 20 to 25 mL of normal saline or water after each intermittent feeding. Liquid medications may also help prevent this complication, although these medications are frequently hyperosmolar and may produce discomfort and diarrhea when delivered rapidly into the jejunum. The injection of a small volume of a carbonated beverage into a plugged tube will often clear the blockage. Occasionally, a guide wire and the help of the interventional radiologist will be needed.

The leakage of enteric contents onto the skin around the exit site of a tube enterostomy is often uncomfortable for the patient and may produce a moderate amount of skin irritation. One cause of such leakage is insufficient approximation of the end of the tube (balloon or mushroom head) to the gastric wall. Leakage around a tube is prevented by proper fixation of the end of the tube with a retention disk or "bumper" at the skin level. The assistance of an enterostomal therapist and the use of products such as karaya gum, zinc oxide, Stomahesive, and locally applied antacid are often helpful. Also problematic is the inappropriate use of urinary catheters for enteral access; these devices were not designed to function as gastrostomy or enterostomy tubes. The catheters currently preferred for these purposes are made of either silicone rubber or polyurethane and include a system designed to prevent migration of the tube into the stomach.

Parenteral Nutrition

CENTRAL VENOUS VERSUS PERIPHERAL VENOUS INFUSIONS



Central venous infusions [*see 6:26 Vascular and Peritoneal Access*] are indicated in most critically ill patients who receive parenteral nutrition because (1) patients in the ICU often require increased quantities of energy and cannot tolerate large fluid volumes, and (2) solutions of much greater caloric density and tonicity can be infused into central veins than can be infused into peripheral veins. Nonetheless, peripheral venous infusions may be indicated in certain situations [*see Table 7*] (see below).

CENTRAL VENOUS NUTRIENT INFUSION

Hypertonic nutrient solutions are infused into the superior vena cava, where they are rapidly diluted. Usually, these solutions contain hypertonic glucose (25%), amino acids (5%), and other essential nutrients. The tonicity of the hypertonic nutrient solutions is so great (> 1,900 mOsm/kg) that administration of the mixture into peripheral veins would cause severe thrombophlebitis and venous sclerosis. These solutions contain at least 1 kcal/mL, and thus, infusion of 2.0 to 2.5 L/day provides 2,000 to 2,500 kcal of energy and all essential nutrients. This calorie load is sufficient to meet energy requirements in more than 90% of surgical patients.

Table 7 **Indications for Central Venous or Peripheral Venous Infusions**

Central venous infusions
To provide adequate IV nutritional support for 10 days or more
To satisfy nutrient requirements in patients with increased energy needs and normal or decreased fluid requirements
To support the patient with single- or multiple-organ failure by infusing modified nutrient solutions in a limited fluid volume
Peripheral venous infusions
To provide initial feeding (< 5 days) before catheter insertion in a patient who will require central venous feedings
To infuse less concentrated solutions via a multiuse central catheter (i.e., a line for blood drawing, medication, and nutrients) into an individual in whom other venous access cannot be easily or safely obtained
To supplement enteral feedings that are inadequate because of GI dysfunction
To satisfy energy requirements that are near basal (1,500–1,800 kcal/day) in a nondepleted patient who can tolerate 2.5–3.0 L IV solution each day

Once positioned, the catheter is used exclusively for administration of the hypertonic nutrient solution. Drawing blood, monitoring central venous pressure, and administering medication through this dedicated lumen are to be avoided. Multiple-lumen central venous catheters are currently used in most patients; manufacturers suggest that at least one port be devoted to the infusion of hypertonic nutrient solutions and that other ports be used for drawing blood, monitoring pressure, and infusing medications. Reports suggest that the rates of catheter sepsis associated with use of these catheters are higher than the rates associated with single-lumen feeding catheters.[9,10] In our experience, the infection rate associated with multiple-lumen catheters was similar to that observed with single-lumen catheters (3.3% versus 1.0%), but the multiple-lumen catheters were in place for a shorter period than the single-lumen catheters (7 versus 14 days).[11] Removal of the multiple-lumen catheters was indicated when multiple central access ports were no longer required or when one of the lumens became clotted or malfunctioned. It appears that multiple-lumen catheters can be used in the ICU for central venous nutrient infusions if strict protocols are maintained to ensure that one lumen is dedicated to nutrient infusion, that other lumens are handled safely, and that the catheters are removed when they are no longer required.

Occasionally, a patient may require the infusion of a hypertonic nutrient solution in a situation where percutaneous puncture of central veins is impossible or contraindicated. In such cases, catheterization of an antecubital vein and insertion of a peripherally inserted central catheter (PICC) with the tip positioned in the superior vena cava should be considered. These catheters are readily inserted by the interventional radiologist, and they eliminate the complications associated with subclavian and internal jugular vein insertions. The PICC line has become the primary route of central venous access in many institutions.

Catheters made of Silastic have been safely kept in place for extended periods and provide an additional option for care of patients who require central venous infusions. Catheterization of the femoral vein may provide a route for central venous access in some situations. Because of the high density of skin pathogens in the groin area, these catheters should be replaced every 2 to 3 days. If the catheter tip is positioned in the iliac vein or the inferior vena cava, the concentration of solution infused through the catheter should not exceed 15%. Strict care of the entrance site should be maintained because of the high complication rate associated with lines placed in the groin.

Central Venous Solutions

Central venous solutions are formulated in the hospital pharmacy. These solutions are commonly combinations of 500 mL of 50% dextrose and 500 mL of a 10% amino acid mixture [*see Table 8*] to which electrolytes, vitamins, and trace elements are added (see below). Each day, 2 L of the solution can be infused. Administration of fat emulsion (500 mL, 20%) 1 day a week meets essential fatty acid requirements. Alternatively, the three major nutrients may be mixed together in a 3 L bag (triple mix or three-in-one) and the entire contents of the single bag infused during the 24-hour period [*see Table 8*]. Another innovation is the use of an automated mixing device (Automix; Baxter International, Deerfield, IL) that compounds various proportions of 70% glucose, 10% amino acids, and 20% fat emulsions into 3 L bags. This device allows the hospital pharmacy to manufacture a variety of nutrient combinations with minimal effort. More concentrated solutions can be made, and the computer will generate a label for the bag that allows nurses to verify the order.

Table 8 Composition of Central Venous Solutions

	Standard Solution	Triple-Mix Solution
Volume		
Amino acids 10% (mL)	500	1,000
Dextrose 50% (mL)	500	1,000
Fat emulsion 20% (mL)	—	250
Total (mL)	1,000	2,250
Contents		
Amino acids (g)	50	100
Dextrose (g)	250 (25%)	500
Total nitrogen (g)	8.4	16.8
Total calories (kcal)	1,050	2,600
Ratio of nitrogen to calories	1:125	1:154
Caloric density (kcal/mL)	1.0	1.15
Osmolarity (mOsm/kg)	1,970	1,900

Electrolytes and minerals are added to the base formula as required [*see Table 9*]. Sodium and potassium salts are added as chloride or acetate, depending on the acid-base status of the patient. The solution should usually consist of approximately equal quantities of chloride and acetate. If chloride losses from the body are increased, as in a patient who requires nasogastric decompression, most salts should be administered as chloride. Sodium bicarbonate is incompatible with the nutrient solutions, and acetate is administered when additional base is required (when metabolized, acetate generates bicarbonate). Phosphate is usually given as the potassium salt; sodium phosphate is used when potassium is contraindicated. Phosphate is also present in fat emulsions.

Commercially available preparations of vitamins, minerals, and trace elements are also added to the nutrient mix for

Table 9 Electrolytes Added to Central Venous Solutions

Electrolyte	Usual Concentration	Usual Range of Concentration
Sodium (mEq/L)	30	0–150
Potassium (mEq/L)	30	0–80
Phosphate (mmol/L)	15	0–20
Magnesium (mEq/L)	5	0–15
Calcium* (mEq/L)	4.7	0–10
Chloride (mEq/L)	50	0–150
Acetate (mEq/L)	70	70–220

*As gluconate.

daily administration unless they are contraindicated. A solution containing both fat- and water-soluble vitamins should be added. Vitamin K_1 (phytonadione), 10 mg, is given once a week to preparations without vitamin K but is contraindicated in patients receiving warfarin.

Trace elements are given daily. Usual requirements are satisfied by the addition of commercially available mixtures either to 1 L of standard solution or to the triple-mix bag each day. Trace elements are indicated for all patients receiving central venous nutrient solutions except those with chronic renal failure or severe liver disease. At especially high risk for zinc deficiency are alcoholics and patients who have pancreatic insufficiency with malabsorption, have undergone massive small-bowel resection, are in renal failure with dialysis, or have nephrotic syndrome; at high risk for copper deficiency are patients with SBS, jejunoileal bypass, malabsorptive conditions with severe diarrhea, or nephrotic syndrome. Copper and manganese are excreted primarily via the biliary tract. Therefore, in patients with biliary tract obstruction, excess retention of copper and manganese should be avoided by decreasing intake of these ions, monitoring blood levels, or both. Although the main excretory route for zinc and chromium is via the feces, renal excretion will minimize dangers from modest excesses of these elements. In patients with renal insufficiency, however, daily zinc and chromium administration may be contraindicated. ICU patients usually do not require iron. Iron is contraindicated in patients with sepsis because it supports bacterial growth. Iron may be required to treat iron deficiency anemia, particularly during convalescence from this condition. Rarely does the anemia that is associated with chronic disease and inflammation respond to iron therapy during the active stages of disease.

Like other invasive therapies, total parenteral nutrition (TPN) is associated with potential complications deriving either from central venous access or from the composition of the formula given. Most such complications are preventable with appropriate attention to detail [*see Table 10*].

PERIPHERAL VENOUS SOLUTIONS

Slightly hypertonic nutrient solutions (approximately 600 to 900 mOsm/kg) can be prepared for peripheral venous infusions from commercially available amino acid mixtures (5%), dextrose solutions (10%), and fat emulsions (20%). These nutrient mixtures have a low caloric density (approximately 0.3 to 0.6 kcal/mL) and thus provide only 1,200 to 2,300 kcal in 2,000 to 3,500 mL of solution. These solutions are particularly useful in patients who receive some but insufficient amounts of tube feedings; they must be supplemented with additional nutrients by venous infusion.

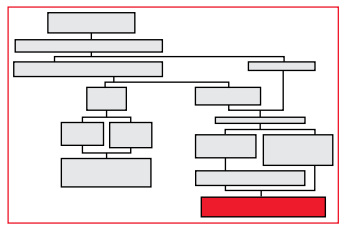
These dilute nutrient mixtures can be infused through plastic cannulas placed in large-bore peripheral veins. The catheter insertion site and surrounding tissue should be inspected periodically for signs of phlebitis or infiltration, and the infusion site should be rotated every 48 to 72 hours to prevent thrombophlebitis. Only fat emulsion can be administered simultaneously through the same IV site as a peripheral venous solution. The nutrient solution should be temporarily stopped if the catheter is used for administration of antibiotics, chemotherapeutic agents, blood, or blood products. The infusion line should then be flushed with saline and infusion of the nutrient solution resumed.

If the fat emulsion is infused in a piggyback manner, administration should be performed over a period of 8 to 12 hours and concluded in the early morning (3:00 am) to allow clearance of the emulsion from the bloodstream. Blood sampling should be avoided during short-term periods of fat infusion because the associated hypertriglyceridemia will interfere with many of the serum measurements. In patients who are receiving peripheral venous solutions by triple mix, hypertriglyceridemia is rare because the rate of infusion has been reduced and infusion extended over a 24-hour period.

Patients receiving peripheral venous feedings should be monitored as suggested for individuals receiving central venous feedings (see below). Mechanical and septic complications are uncommon. Fluid imbalances and alterations in serum electrolyte concentrations are similar to those seen in standard IV support, and corrections are made by altering the volume of the infusion or adding or omitting electrolytes. Hyperglycemia and glycosuria are rarely observed unless the patient is diabetic.

MONITORING THE PATIENT: OPTIMIZING NUTRITIONAL SUPPORT, PREVENTING COMPLICATIONS, AND RESOLVING COMMON PROBLEMS

General Measures



Patients receiving central venous feedings should be weighed daily, and accurate intake and output records should be maintained. Blood glucose should be monitored daily. Persistent abnormalities require that a more stringent schedule of monitoring blood glucose be instituted and specific therapy initiated (see below).

The quantity of energy administered to most ICU patients should minimize the loss of lean body mass and adipose tissues. Thus, variations in body weight usually reflect alterations in fluid balance. If sustained weight loss occurs (as characterized by a gradual fall in body weight over a period of 2 weeks or longer), caloric intake may be inadequate. Additional calories (500 to 1,000 kcal/day) should be administered to maintain weight. Alternatively, the metabolic rate could be calculated from the volume of oxygen consumed per minute ($\dot{V}O_2$) and calorie intake then matched to equal energy expenditure:

$$\text{Metabolic rate (kcal/hr)} = \dot{V}O_2 \text{ (mL/min)} \times 60 \text{ min/hr} \times 1 \text{ L}/1{,}000 \text{ mL} \times 4.83 \text{ kcal/L}$$

This calculation is required in only 5% of our patients.

In non–ventilator-dependent patients, oxygen consumption and, in turn, the metabolic rate can be derived from measurements of respiratory gas exchange. Equipment (e.g., the metabolic cart) is commercially available that can make these measurements at the bedside. In a patient with a Swan-Ganz catheter in place, oxygen consumption can be calculated from cardiac output determinations and simultaneous measurements of mixed venous oxygen content ($C_{mv}O_2$) and arterial oxygen content (C_aO_2):

$$\dot{V}O_2 \text{ (mL/min)} = \text{cardiac output (L/min)} \times (C_aO_2 \text{ [mL/dL]} - C_{mv}O_2 \text{ [mL/dL]}) \times 1 \text{ L}/10 \text{ dL}$$

Table 10 **Diagnosis, Treatment, and Prevention of Potential Mechanical and Metabolic Complications Associated with TPN**

Complications		Diagnosis	Treatment	Prevention
Mechanical	Pneumothorax	Dyspnea, chest x-ray	Tube thoracostomy Observation	Avoid emergency procedures Trendelenburg position
	Hemothorax	Dyspnea, chest x-ray	Remove catheter Observation	Insert catheter using appropriate technique
	Venous thrombosis	Inability to cannulate	Remove catheter Heparin therapy	Use silicone catheters Add heparin to solution
	Air embolism	Dyspnea, cyanosis, hypotension, tachycardia, precordial murmur	Trendelenburg position Left lateral decubitus position	Trendelenburg position Valsalva maneuver Tape IV connections
	Catheter embolism	Sheared catheter	Fluoroscopic retrieval	Never withdraw catheter through needle
	Dysrhythmias	Catheter tip in right atrium	Withdraw catheter to superior vena cava	Estimate distance to superior vena cava before insertion; confirm position with x-ray
	Subclavian artery injury	Pulsatile red blood	Remove needle Apply pressure Chest x-ray	Review anatomy
	Catheter tip misplacement	Chest x-ray	Redirect with a guide wire	Direct bevel of needle caudally
Metabolic	Hyperglycemic, hyperosmolar, nonketotic coma	Dehydration with osmotic diuresis, disorientation, lethargy, stupor, convulsions, coma, glucose 1,000 mg/dL, osmolarity 350 mOsm/kg	Discontinue TPN; infuse D5 in 0.45% saline at 250 mL/hr Insulin 10–20 U/hr Bicarbonate Monitor glucose, potassium, pH	Monitor glucose
	Hypoglycemia	Headache, sweating, thirst, convulsions, disorientation, paresthesias	D50W IV	Taper TPN by one-half for 12 hr; then 12 hr of D5W at 100 mL/hr
	CO_2 retention	Ventilator dependence, high respiratory quotient	Taper glucose	Provide 30–40% of calories with fat
	Azotemia	Dehydration, elevated BUN	Increase nonprotein calories	Monitor fluid balance
	Hyperammonemia	Lethargy, malaise, coma, seizures	Discontinue amino acid infusions Infuse arginine	Avoid casein or fibrin hydrolysate
	Essential fatty acid deficiency	Xerosis, hepatomegaly, impaired healing, bone changes	Fat administration	Provide 25–200 mg/kg/day of essential fatty acids
	Hypophosphatemia	Lethargy, anorexia, weakness	Supplemental phosphate	Treat causative factors; alkalosis, gram-negative sepsis, vomiting, malabsorption Provide 20 mEq/kcal
	Abnormal liver enzymes	Fatty infiltrate in liver	Evaluate for other causes	Provide balanced TPN solution
	Hypomagnesemia	Weakness, nausea, vomiting, tremors, depression, hyporeflexia	Infuse 10% $MgSO_4$	Supply 0.35–0.45 mEq/kg/day
	Hypermagnesemia	Drowsiness, nausea, vomiting, coma, dysrhythmia	Dialysis Infuse calcium gluconate	Monitor serum levels

BUN = blood urea nitrogen; D50W = dextrose 50% in water; TPN = total parenteral nutrition.

Another objective of nutritional support in the ICU patient is the maintenance of lean body mass, which is reflected by nitrogen balance equilibration or positive nitrogen balance. Although complete nitrogen balance determination is a complex and sophisticated study, nitrogen equilibration can be estimated by using common analytic procedures. To estimate nitrogen balance, total nitrogen loss is subtracted from total nitrogen intake. Calculation of total nitrogen loss requires several steps. The urine urea nitrogen (UUN) concentration is multiplied by the total volume of urine output during a given day to yield the 24-hour UUN, that is, the total amount of urea excreted during that period. Because urea accounts for only approximately 80% of the nitrogen excreted in the urine, the value for the 24-hour UUN must be increased by an additional 20%. This quantity and an additional 2 g/day are added to the value for the 24-hour UUN to account for nonurea nitrogen, stool, and integumentary losses:

$$\text{24-hour UUN (g/day)} = \text{UUN (mg/dL)} \times \text{urine output (mL/day)} \times 1\ \text{g/1,000 mg} \times 1\ \text{dL/100 mL}$$

$$\text{Total nitrogen loss (g/day)} = \text{24-hour UUN (g/day)} + (0.20 \times \text{24-hour UUN [g/day]}) + 2\ \text{g/day}$$

Metabolic Monitoring

A wide variety of metabolic complications may occur during parenteral feeding [*see Table 11*]. These are minimized by frequent monitoring [*see Table 12*] and appropriate adjustment of nutrients in the infusion.

The most common metabolic problems occurring in ICU patients are hyperglycemia and glucosuria. The combination of excessive counterregulatory hormone release and overproduction of tumor necrosis factor–α (TNF-α), interleukin-1, and interleukin-6 characteristic of critical illness is a major factor responsible for stress-induced hyperglycemia in the nondiabetic host.[12] Hypergylcemia has been associated with infectious complications,[13,14] worsened outcome after head injury and stroke,[15] and increased proteolysis.[16] Moreover, prevention of hyperglycemia by aggressive insulin treatment has been associated with a reduced mortality in ICU patients.[17] Initially, elevated levels of blood glucose should be treated by the administration of subcutaneous insulin (5.0 U every 4 to 6 hours for glucose levels of 200 to 250 mg/dL; 7.5 U for 250 to 300 mg/dL; and 10.0 U for 300 to 350 mg/dL). When the nutritional solution is ordered for the next 24-hour period, half of the quantity of insulin administered subcutaneously is added to the mixture. At least 10 U of regular insulin per liter of solution should be given as the initial dose, and in some cases, as much as 40 U/L may be required. If larger doses of insulin are needed (> 100 U/day), a separate insulin infusion or drip should be used.

In most patients with severe glucose intolerance, the rate of glucose administered should not exceed 5 mg/kg/min (approximately 500 g/day). Additional calories should be administered as fat emulsion. The commercially available fat emulsions are all generally well tolerated by critically ill patients. Triglyceride levels should be monitored, and the rate of administration of the emulsion should be decreased or the emulsion temporarily discontinued if levels exceed 500 mg/dL. Fat emulsion should be used with caution in patients with known hypertriglyceridemia or in those with gram-negative bloodstream infection that is associated with hyperlipidemia.

The infusion of excess glucose or lipid energy may alter pulmonary function and, in some patients, prevent weaning from a mechanical ventilator. Excessive carbohydrate loads (usually > 500 g/day) increase CO_2 production. If the quantity of CO_2 produced exceeds the ability of the lungs to excrete this oxidative end product, hypercapnia results. Fat emulsion may also interfere with diffusion of gas across the alveolar membranes. This interference is generally related to the concentration of the emulsion in the bloodstream; hence, monitoring triglyceride levels and preventing hypertriglyceridemia will minimize this complication.

Catheter Care and Catheter Infection

The most serious problem associated with central venous feedings is catheter infection [*see 8:16 Nosocomial Infection*]. Primary catheter infection is defined as the presence of signs and symptoms of infection (usually a febrile episode), with the indwelling catheter being the only anatomic focus of sepsis. After removal of the catheter, the symptoms usually attenuate. Cultures of the catheter tip with semiquantitative techniques yield at least 10^3 organisms.[18] The organisms are the same as those recovered from cultures of blood drawn from a peripheral vein during the initial evaluation of the infection.

Secondary, as opposed to primary, catheter infection is associated with a second infectious focus that causes bacteremia and thus seeds or contaminates the catheter. The microorganisms cultured from the catheter tip are similar to those cultured from the primary source. The infection clears after specific treatment of the primary infection.

Primary catheter infection is prevented or at least greatly reduced by following strict protocols to govern the use and manipulation of the central venous feeding catheter and by employing a systematic method of care and surveillance of the catheter entrance site. Usually, catheter care and its supervision and certification are performed by a nurse with expertise in maintenance of long-term IV access (the nurse may be assigned to the nutrition support service or may be experienced in IV access or infection control). Every 48 to 72 hours, the dressing that covers the entrance site of the catheter is removed, the site inspected, the area around the entrance site cleaned, a topical antibiotic or antiseptic ointment applied, and the site redressed with a new sterile dressing. This procedure is documented in the clinical record; if drainage or crusting appears at the entrance site, appropriate cultures are taken. In addition, the dressing is changed if it becomes wet or soiled or no longer remains intact. In patients who have either draining wounds in close proximity to the catheter entrance site or tracheostomies, the entire dressing should be covered with a transparent barrier drape to minimize contamination.

If signs and symptoms of infection develop in a recipient of central venous parenteral nutrition, a history should be taken and a physical examination performed [*see Figure 3*]. Appropriate tests (e.g., complete blood count and urinalysis) and diagnostic studies (including radiography) should also be performed. If blood cultures are needed, they should be

Table 11 **Metabolic Complications of Total Parenteral Nutrition**

Problems	Possible Causes	Solutions
Glucose		
Hyperglycemia, glycosuria, osmotic diuresis, hyperosmolar nonketotic dehydration and coma	Excessive total dose or rate of infusion of glucose; inadequate endogenous insulin; increased glucocorticoids; sepsis	Reduce amount of glucose infused; increase insulin; administer a portion of calories as fat emulsion
Ketoacidosis in diabetes mellitus	Inadequate endogenous insulin response; inadequate exogenous insulin therapy	Give insulin; reduce glucose input
Postinfusion (rebound) hypoglycemia	Persistence of endogenous insulin production secondary to prolonged stimulation of islet cells by high-carbohydrate infusion	Administer 5–10% glucose before infusate is discontinued
Fat		
Pyrogenic reaction	Fat emulsion, other solutions	Exclude other causes of fever
Altered coagulation	Hyperlipidemia	Repeat study after fat has cleared bloodstream
Hypertriglyceridemia	Rapid infusion, decreased clearance	Decrease rate of infusion; allow clearance before blood tests
Impaired liver function	May be caused by fat emulsion or by an underlying disease process	Exclude other causes of hepatic dysfunction
Cyanosis	Altered pulmonary diffusion capacity	Discontinue fat infusion
Essential fatty acid deficiency	Inadequate essential fatty acid administration	Administer essential fatty acids in the form of one 500 mL bottle of fat emulsion every 2–3 days
Amino acids		
Hyperchloremic metabolic acidosis	Excessive chloride and monohydrochloride content of crystalline amino acid solutions	Administer Na^+ and K^+ as acetate salts
Serum amino acid imbalance	Unphysiologic amino acid profile of the nutrient solution; differential amino acid utilization with various disorders	Use experimental solutions if indicated
Hyperammonemia	Excessive ammonia in protein hydrolysate solutions; deficiency of arginine, omithine, aspartic acid, or glutamic acid, or a combination of these deficiencies in amino acid solutions; primary hepatic disorder	Reduce amino acid intake
Prerenal azotemia	Excessive amino acid infusion with inadequate calorie administration; inadequate free water intake, dehydration	Reduce amino acid intake; increase glucose calories; increase intake of free water
Calcium and phosphorus		
Hypophosphatemia	Inadequate phosphorus administration; redistribution of serum phosphorus into cells or bones, or both	Administer phosphorus (20 mEq potassium dihydrogen phosphate/1,000 IV calories); evaluate antacid or calcium administration, or both
Hypocalcemia	Inadequate calcium administration; reciprocal response to phosphorus repletion without simultaneous calcium infusion; hypoalbuminemia	Administer calcium
Hypercalcemia	Excessive calcium administration with or without high doses of albumin; excessive vitamin D administration	Decrease calcium or vitamin D
Vitamin D deficiency; hypervitaminosis D	Inadequate or excessive vitamin D	Alter vitamin D administration
Miscellaneous		
Hypokalemia	Potassium intake inadequate relative to increased requirements for protein anabolism; diuresis	Alter nutrient administration
Hyperkalemia	Excessive potassium administration, especially in metabolic acidosis; renal failure	Alter nutrient administration
Hypomagnesemia	Inadequate magnesium administration relative to increased requirements for protein anabolism and glucose metabolism; diuresis; cisplatin administration	Alter nutrient administration
Hypermagnesemia	Excessive magnesium administration; renal failure	Alter nutrient administration
Anemia	Iron deficiency; folic acid deficiency; vitamin B_{12} deficiency; copper deficiency; other deficiencies	Alter nutrient administration
Bleeding	Vitamin K deficiency	Alter nutrient administration
Hypervitaminosis A	Excessive vitamin A administration	Alter nutrient administration
Elevations in AST, ALT, and serum alkaline phosphatase	Enzyme induction secondary to amino acid imbalance or to excessive deposition of glycogen or fat, or both, in the liver	Reevaluate status of patient

ALT—alanine aminotransferase; AST—aspartate aminotransferase.

Table 12 **Variables to Be Monitored during Intravenous Alimentation and Suggested Frequency of Monitoring**

Variables	Suggested Monitoring Frequency	
	First Week	Later
Energy balance		
Weight	Daily	Daily
Metabolic variables		
Blood measurements		
Plasma electrolytes (Na^+, K^+, Cl^-)	Daily	3 × weekly
Blood urea nitrogen	3 × weekly	2 × weekly
Plasma osmolarity*	Daily	3 × weekly
Plasma total calcium and inorganic phosphorus	3 × weekly	2 × weekly
Blood glucose	Daily	3 × weekly
Plasma transaminases	3 × weekly	2 × weekly
Plasma total protein and fractions	2 × weekly	Weekly
Blood acid-base status	As indicated	As indicated
Hemoglobin	Weekly	Weekly
Ammonia	As indicated	As indicated
Magnesium	2 × weekly	Weekly
Triglycerides	Weekly	Weekly
Urine measurements		
Glucose	Daily	Daily
Specific gravity or osmolarity	Daily	Daily
General measurements		
Volume of infusate	Daily	Daily
Oral intake (if any)	Daily	Daily
Urinary output	Daily	Daily
Prevention and detection of infection		
Clinical observations (activity, temperature, symptoms)	Daily	Daily
WBC and differential counts	As indicated	As indicated
Cultures	As indicated	As indicated

* May be predicted from 2 × Na concentration (mEq/L) + [blood glucose (mg/dL) ÷ 18].

drawn from a peripheral vein. If trained nurses have maintained the catheter and no evidence of infection at the exit site has been noted, the catheter dressing should not be removed, and the catheter should not be manipulated. Blood cultures should never be taken through the catheter. The one possible exception to this rule is the case in which the initial presentation of infection is characterized by marked hyperpyrexia, hypotension, or both. (In this case, contamination of the catheter is immaterial because the catheter will be removed.) If no other infectious focus is identified, the physician may elect to remove all indwelling lines, including the feeding catheter. In addition, either drainage around the catheter or a previous positive culture from the catheter exit site may warrant immediate removal. If another primary source of the infection is diagnosed, then specific therapy should be instituted, and parenteral nutrition should be continued. If no source of infection is identified, the catheter should be removed and the catheter tip cultured.

A dilemma arises if another source of infection is identified and if signs and symptoms of infection persist despite what appears to be appropriate therapy. If blood cultures are positive, we favor removal of the catheter to prevent the complications that are associated with a contaminated indwelling catheter (e.g., septic emboli and endocarditis). If, however, peripheral blood cultures are negative, the catheter can be changed over a guide wire and the catheter tip cultured to confirm that no catheter infection exists. Central venous feeding can be continued during this interval. If the cultured catheter tip is positive ($\geq 10^5$ organisms), the catheter should be removed.

Changing the central venous catheter over a guide wire can aid in the diagnosis of primary catheter infection.[19] Because most ICU patients have multiple potential sources for infection, this technique allows culture of the catheter tip but minimizes the risks associated with reinsertion of a new central catheter. Strict aseptic technique is used. The area surrounding the catheter entrance site is sterilized, the IV tubing is disconnected from the catheter, a guide wire is passed into the catheter, and the catheter is removed over the guide wire. A new catheter is inserted over the wire and sutured in place. The tip of the old catheter is cut, placed in a transfer vessel, and taken to the microbiology laboratory for semiquantitative culture. With strict care of catheters, the incidence of catheter infection should be less than 6%.[20] Bloodstream infection is most commonly caused by growth and invasion of organisms along the catheter tract. Occasionally, bacteria are infused through the catheter because of a breach in sterility during care of the infusion apparatus. The most common bacterial organisms causing catheter infection are the skin contaminants *Staphylococcus epidermidis, Staphylococcus aureus, Klebsiella pneumoniae,* and *Candida albicans*. In some rare cases, the IV solutions may be contaminated. Moreover, most patients requiring central venous alimentation are immunocompromised hosts; their resistance is lowered further by disease, severe malnutrition, treatment, or some combination of these factors. Coexisting conditions (e.g., urinary tract infection, abscess, pneumonia, and mucositis secondary to chemotherapy) predispose these patients to bacteremia, which may contaminate the central venous catheter.

Immunosuppressed critically ill patients receiving multiple broad-spectrum antibiotics are also at risk for *Candida* bloodstream infection. Blood cultures positive for *C. albicans* in an ICU patient are an indication for catheter removal and treatment with fluconazole. An ophthalmologist should examine the eyegrounds of patients with proven candidemia to exclude the possibility of metastatic *Candida* ophthalmitis [*see 8:19 Fungal Infection*].

Home Nutritional Support

Home parenteral nutrition is indicated for patients who are unable to eat and absorb enough nutrients for maintenance. Most of the adult surgical patients who require home parenteral nutrition suffer from SBS caused by (1) extensive Crohn disease, (2) mesenteric infarction, or (3) severe abdominal trauma. Pseudo-obstruction, radiation enteritis, carcinomatosis, necrotizing enterocolitis, and intestinal fistulas are other indications for home nutritional support. Patients with these conditions cannot receive adequate nutrition enterally, though in some cases compensatory mucosal growth occurs that may either reduce or eventually eliminate the need for continued home parenteral nutrition.

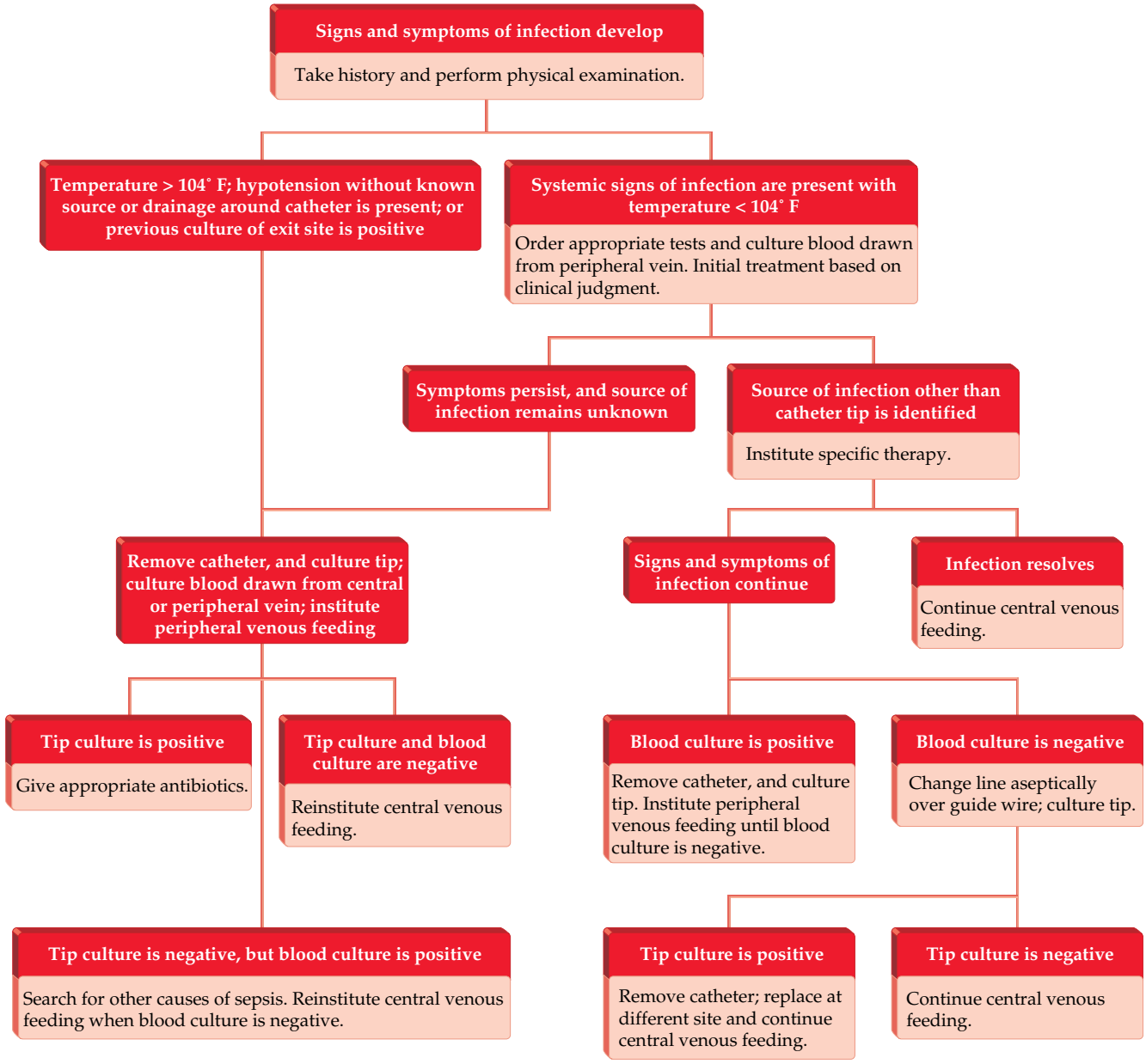


Figure 3 **Shown is an algorithm for evaluating a febrile patient receiving central venous parenteral nutrition.**

Patients must receive extensive evaluation, teaching, and training during hospitalization if home parenteral nutrition is to prove successful. These services should be provided by a team consisting of a physician, a nurse, a dietitian, a pharmacist, and a social worker. The team's instructions should be thorough and wide-ranging, covering the basic principles of parenteral nutrition as well as providing mechanical guidelines for catheter care, asepsis, and use of infusion pumps. Patients should be objectively evaluated before being discharged from the hospital to ensure that they have both an adequate understanding of the principles of IV nutrition and the technical ability to carry out home parenteral nutrition properly.

A patient who is judged by the nutrition support team to be a candidate for home TPN requires placement of a Silastic catheter designed for more permanent use than the central venous catheter employed during hospitalization.[21] The catheter is typically 90 cm long, with a thin 55 cm intravascular segment that is inserted either by venous cutdown into the internal or external jugular vein or the cephalic vein or directly into the subclavian vein by means of venipuncture. The intravascular portion of the catheter is cut so that its tip will lie at the junction of the superior vena cava and the right atrium. Placement of the catheter is carried out in the operating room by using local anesthesia (1% lidocaine) and adequate sedation. The catheter is tunneled subcutaneously from a small incision lateral to the sternum to the site of venous insertion. The catheter exit site is chosen on the basis of the patient's gender, physique, and hand dominance. In women, lower paraxiphoid or upper abdominal exit sites permit a more natural appearance. If the patient's coagulation status is abnormal, the cephalic vein is isolated in the deltapectoral

groove and tied distally, and the catheter is inserted proximally by means of venotomy. Otherwise, a percutaneous approach to the subclavian vein is taken. Proper positioning of the catheter is confirmed by fluoroscopy, and the incisions are closed with absorbable sutures. The catheter is sutured to the skin exit site, and the sutures are left attached for at least 2 weeks while tissue ingrowth into the Dacron velour cuff takes place. After the sutures are placed, sterile dressings are applied.

Calorie, protein, and fluid needs are carefully estimated for each patient, and the administration schedule is arranged so that the total volume may be infused nocturnally over 10 to 12 hours. Electrolytes, micronutrients, and trace minerals are added as indicated. Fat emulsions may be given either separately or admixed with glucose and protein and are used to reduce the requirement for dextrose calories and to prevent essential fatty acid deficiency.

The complications of home TPN are much the same as those of in-hospital TPN. They may be divided into four categories: mechanical, infectious, metabolic, and psychosocial. Mechanical complications, which are generally easy to remedy, include catheter occlusion and dislodgment and damage to the external portion of the catheter. Infectious complications that are superficial to the Dacron cuff usually respond well to antibiotics. Infections of the intravascular catheter may necessitate removal of the catheter after the diagnosis is confirmed by blood cultures obtained through the catheter, but the usual therapeutic approach is to initiate a trial of parenteral antibiotics. Metabolic complications related to individual nutrient deficiencies may be corrected by addition of the appropriate substance to the solution. The role of serum levels of trace minerals and micronutrients in the delineation of nutrient deficiency states remains unclear. In patients receiving insulin, hyperinsulinemia after infusion may be prevented by reducing the rate of administration gradually over the last hour of infusion. Psychosocial complications may vary from slight depression to suicidal tendencies, which must be treated with appropriate counseling.

The costs of a home TPN program may also be divided into four categories: patient training, equipment, supplies, and follow-up. It has been estimated that the average annual cost of home TPN is 70% less than that of in-hospital TPN. The growth of private companies that deliver equipment and supplies to the home, maintain inventory, bill patients, and help with health insurance reimbursement has considerably facilitated home care.

Home enteral nutrition is frequently employed either as the sole source or as a partial source of nutritional support. It is the preferred method when GI tract function is adequate. In patients undergoing surgery of the aerodigestive tract for cancer, jejunostomy feedings can supplement oral feedings, especially during periods of adjuvant chemotherapy and radiation treatment. Patients are taught to cycle the feedings over 12-hour periods, using an enteral pump system to provide 20 to 30 kcal/kg/day. Use of an appropriate feeding tube and immediate flushing of the tube after use reduce the incidence of clogging at home. If blockage occurs, proteases or carbonated beverages can be introduced into the tube in an attempt to open it. Jejunostomy feedings reduce the risk of aspiration and help maintain nutritional status during periods of inadequate oral intake. Use of inexpensive nutritionally complete commercial formulas is encouraged. For patients who have more permanent disabilities that prevent adequate oral intake, a gastrostomy (or PEG [*see 5:18 Gastrointestinal Endoscopy*]) may be preferable. It reduces the GI complications of feeding by making use of the reservoir and admixing functions of the stomach.

Discussion

EVIDENCE-BASED NUTRITIONAL SUPPORT

Early Oral Feeding after Elective Operations

Anesthetics, prolonged bed rest, and fluid shifts make the intestine susceptible to ileus after most types of surgery, particularly after abdominal surgery. In the past, patients underwent gastric decompression with a nasogastric tube until they began to show obvious signs of bowel function. In recent years, however, several authors have questioned the necessity of postoperative nasogastric decompression that impedes early oral feeding. A study of 110 postoperative patients randomly assigned to receive either intraoperative orogastric decompression or postoperative nasogastric decompression found that patients in the latter group had more subjective complaints relative to the tube and more febrile morbidity, as well as longer times to passage of first flatus and tolerance of a diet.[22] In another randomized study, 80 abdominal aortic aneurysmectomy patients had their nasogastric tubes either removed immediately upon tracheal extubation or left in place until passage of flatus. No intergroup differences were noted with regard to length of stay, time to tolerance of a clear-liquid or regular diet, or necessity of replacing the nasogastric tube.[23]

Other studies have suggested not only that nasogastric decompression is unnecessary but also that patients perhaps should be fed earlier than is traditionally practiced. In one study, 161 patients undergoing elective colonic or small-bowel resection without nasogastric decompression were randomly assigned to an early feeding group (clear-liquid diet on postoperative day 1, followed by regular diet as tolerated) or a traditional feeding group (nihil per os [NPO] until passage of flatus).[24] The early feeding group was able to tolerate a regular diet earlier, without any increase in nausea or need for reinsertion of a nasogastric tube.[24] Two similar studies documented shorter hospital stays among patients who were fed early.[25,26]

Traditionally, the initial diet given in the postoperative period has been either a clear-liquid diet or a full-liquid diet. Patients have generally been kept on these diets until they exhibit consistent flatus or pass bowel movements, then switched to regular diets. However, there is no evidence to suggest that this stepwise progression is justified or that this

approach leads to better outcomes. In fact, one randomized study of 254 patients who received either clear liquids (which were subsequently advanced to a regular diet) or a regular diet as the initial postoperative meal failed to show any significant differences in time to diet tolerance, complication rates, or hospital stays.[27]

The use of opioids in the perioperative period (or, indeed, at any time when the patient is in pain) can have substantial deleterious effects on nutrition. Opioid-induced constipation can lead to lower abdominal discomfort, fecal impaction with diarrhea, nausea, and inadequate absorption of oral drugs. The resulting bowel dysfunction is attributable both to CNS-mediated alteration in autonomic flow to the gut[28] and to the direct local effect of opioids on the bowel.[29] Opioid receptor antagonists (e.g., naloxone and naltrexone) have the ability to reverse these changes, but this ability is limited by the inherent reduction in analgesia. Newer agents, such as methylnaltrexone (a quaternary derivative of naltrexone), are poorly lipid soluble, do not penetrate the CNS, and therefore do not antagonize the central effects of opioids.[30] A study involving healthy human volunteers demonstrated that IV methylnaltrexone could prevent opioid-induced delays in bowel motility without affecting analgesia.[31] Such drugs may be particularly useful as adjunctive medications to minimize the side effects of opioids in those patients in whom their use is necessary.

Finally, early feeding has been combined with other therapies to enhance recovery [*see 1:9 Ambulatory and Fast Track Surgery*]. With the use of epidural anesthesia in conjunction with early oral feeding and an active exercise program, patients may experience much shorter periods of convalescent recovery and require less hospitalization.[32]

ELECTRONIC ORDERING TO OPTIMIZE NUTRITIONAL SUPPORT

Nutritional care is often standardized in a hospital setting to optimize formula composition and delivery. An approach to nutritional prescription has been developed that may be reviewed at <http://epen.kumc.edu>.

PREOPERATIVE TPN

Multiple studies have been conducted to evaluate the effects of preoperative TPN, most of them involving patients with GI cancer who were considered to be at least moderately malnourished on the basis of weight loss, decreased plasma protein levels, or abnormal prognostic indices.[33] A pooled analysis of the data showed that patients who received preoperative TPN experienced 10% fewer postoperative complications than the control group did (i.e., the complication rate dropped from approximately 40% to 30%); in five studies, these differences reached statistical significance. The pooled analysis found no significant differences in mortality between the TPN groups and the control groups.

INTRAOPERATIVE TPN

Although intraoperative TPN has not yet been tested in clinical trials, our view is that it should be avoided. The stress associated with surgery and anesthesia results in hyperglycemia even without the infusion of dextrose. When infused during surgery, the dextrose in the TPN solution can elevate blood glucose levels severalfold above normal values. These extreme levels of hyperglycemia have been associated with impaired immune function. Furthermore, experimental data has shown that hypotension or cardiac arrest during concentrated dextrose infusion results in more irreversible damage to the CNS.

POSTOPERATIVE TPN

Use of TPN in the immediate postoperative period without preoperative TPN has also been evaluated in multiple trials.[33] These studies included mostly patients with GI cancer who were considered to be at least moderately malnourished on the basis of weight loss, decreased plasma protein levels, or abnormal prognostic indices. In contrast to the pooled analysis of the preoperative data, a pooled analysis of the postoperative data showed that patients who received TPN after operation had an approximately 10% higher risk of ensuing complications (i.e., the complication rate rose from approximately 30% to 40%).

PERIOPERATIVE ENTERAL NUTRITION

Multiple trials have evaluated perioperative enteral nutrition, but the number of patients involved has been relatively small.[33] Two studies compared preoperative enteral nutrition with an ad libitum oral diet,[34,35] and in one,[35] postoperative complication rates were significantly lower in patients who received enteral tube feeding. Other studies compared early postoperative jejunal tube feeding with a standard oral diet that was advanced as tolerated[36–39]; no consistent differences in postoperative morbidity or mortality were identified. One study evaluated the use of postoperative jejunostomy tube feeding with a special formula enriched with arginine, ribonucleic acids, and omega-3 fatty acids after operation for upper GI tract cancer.[40] When only patients who were successfully fed were evaluated, those who received the enriched formula had fewer complications and shorter hospital stays than those who received the standard formula.

CANCER PATIENTS

Trials addressing perioperative nutritional support have been conducted in patients undergoing surgery for pancreatic, hepatocellular, GI, and head and neck malignancies. Many of those trials addressed the newer immunoenriched diets. In one, patients undergoing major pancreatic resection were randomly assigned either to a group that received TPN on postoperative day 1 or to a non-TPN group.[41] No significant benefit from the use of adjuvant TPN could be demonstrated, and the incidence of complications (primarily those associated with infection) was significantly greater in the TPN group. It was concluded that routine use of postoperative TPN in patients undergoing major pancreatic resection for malignancy could not be recommended.

Another trial examined the effects of cyclic versus continuous enteral nutrition on postoperative gastric function after pylorus-preserving pancreaticoduodenectomy.[42] Patients were evaluated with respect to gastric emptying, resumption of normal diet, and length of hospital stay. Nasogastric intubation was maintained for a shorter period in the enterally fed group than in the control group (6.7 days versus 9.1 days). The first day of normal diet came earlier for the enterally fed

group (12.2 days after operation versus 15.7 days). Hospital stay was shorter in the cyclic enterally fed group (17.5 days versus 21.4 days). It was concluded that cyclic enteral nutrition was clinically efficacious in this selected group of patients.

Studies using experimental models have shown that nutritional support reduces the catabolic response, improves protein synthesis, and enhances liver regeneration. One trial examined 64 patients who were randomly selected to receive perioperative IV nutritional support in addition to their oral diet, along with 60 patients (33 with cirrhosis, 12 with chronic active hepatitis, and 15 with no associated liver disease) who were randomly assigned to a control group.[43] The perioperative nutritional therapy consisted of an IV solution enriched with 35% BCAAs, dextrose, and a lipid emulsion (50% MCTs) that was given for 14 days perioperatively. Overall postoperative morbidity was lower in the perioperative nutrition group (34% versus 55%), mainly because the rate of infection-related complications was lower (17% versus 37%). These benefits were seen predominantly in patients with underlying cirrhosis who underwent major hepatectomy. It was concluded that perioperative nutritional support could reduce complications after major hepatectomy for hepatocellular carcinoma associated with cirrhosis.

An Italian study was designed to determine whether preoperative supplementation with a specialized diet improves outcomes in comparison with a standard formula.[44] In this study, 305 patients with a GI malignancy and preoperative weight loss were randomly assigned to three groups: (1) a group that received 5 days of preoperative oral supplementation and no postoperative nutritional support, (2) a group that received 5 days of preoperative oral supplementation with postoperative supplementation; and (3) a group that received no artificial nutrition before or after surgery. The results showed that preoperative nutritional support decreased the length of hospital stay and the incidence of postoperative infections.

A similar study done in China enrolled 468 malnourished GI malignancy patients and compared the outcomes of preoperative combined with postoperative nutrition with those of postoperative nutrition alone.[45] The results showed that the addition of preoperative nutrition decreased the duration of hospitalization and the incidence of postsurgical complications while also reducing mortality.

A study from Switzerland then addressed the question of whether the duration of preoperative nutrition was of any significance with respect to its effect on postoperative complications.[46] The investigators compared 2 days of a preoperative immunoenriched diet with 5 days of the same diet. They concluded that perioperative administration of an immunoenriched diet significantly reduces systemic perioperative inflammation and postoperative complications in patients undergoing major abdominal cancer surgery when compared to a postoperative diet alone; they also concluded that a 2-day preoperative feeding regimen is as effective as a 5-day regimen.

Patients with head and neck malignancies who undergo surgery have a high incidence of postoperative complications. A study was carried out to determine whether an arginine-enriched diet could improve outcomes.[47] In this study, 47 patients were randomly assigned to two groups, of which one received an arginine-based formula and the other a standard formula. Fistulas were less frequent in the enriched-nutrition group. Wound infection was more frequent in the standard-formula group, but the difference was not statistically significant. The length of hospital stay was also shorter in the enriched nutrition group. It was concluded that enriched-formula diets improve local wound complication rates in postoperative head and neck cancer patients.

EARLY POSTOPERATIVE ENTERAL NUTRITION

A nonrandomized, uncontrolled study of 38 patients who underwent colorectal surgery over a 3-month period found that 31 of the 38 were able to tolerate an early feeding regimen.[48] Patients who tolerated early feeding had shorter postoperative stays (5.7 versus 10.6 days); those who did not had longer operative procedures and lost more blood intraoperatively. (Longer operating time and increased intraoperative blood loss may indicate a more difficult operation, which may in turn result in prolongation of recovery and decreased tolerance of early enteral feeding.) The investigators concluded (1) that early postoperative feeding is safe and is tolerated by the majority of patients and (2) that if early feeding is tolerated, it shortens hospital stay and may decrease health care costs.

In a study of 28 patients undergoing esophagectomy or pancreaticoduodenectomy who received either immediate postoperative enteral feeding via jejunostomy (13 patients) or no feedings during the first 6 days after operation (15 patients),[49] hand-grip strength, vital capacity, forced expiratory volume in 1 second (FEV_1), and maximal inspiratory pressure were measured before operation and on postoperative days 2, 4, and 6.[49] Postoperative vital capacity and FEV_1 were consistently lower in the fed group than in the unfed group, whereas there were no significant differences in grip strength and maximal inspiratory pressure. Postoperative mobility was lower in the fed group, and these patients tended to recover less rapidly. There were no significant differences in fatigue or vigor between the two groups. The investigators concluded that immediate postoperative jejunal feeding is associated with impaired respiratory mechanics and postoperative mobility and does not influence the loss of muscle strength or the increase in fatigue occurring after major surgery; they further concluded that immediate postoperative enteral feeding should not be routine in well-nourished patients who are at low risk for nutrition-related complications.

A 2005 study from Japan assessed 28 patients who underwent esophagectomy.[50] All of the patients received enteral nutrition immediately after the operation, but they were randomly assigned to two groups, of which one received a conventional enteral formula and the other a formula rich in omega-3 polyunsaturated fatty acids (PUFAs). The investigators found that early enteral nutrition with a large amount of omega-3 PUFAs resulted in reduced platelet aggregation, coagulation activity, and cytokine production. These effects would be expected to be beneficial in esophagectomy patients, but their clinical significance remains to be established.

A 1997 trial evaluated early enteral feeding after resection of upper GI malignancies.[51] The purpose of the study was to determine whether early postoperative enteral feeding with an immune-enhancing formula could decrease morbidity, mortality, and length of hospital stay. A total of 195 patients with upper GI cancer were randomly selected to receive either

the immune-enhancing formula (supplemented with arginine, RNA, and omega-3 fatty acids) via jejunostomy or standard IV crystalloid solutions. There were no significant differences between the two groups with respect to the number of minor, major, or infectious wound complications; the length of the hospital stay; or mortality.

A similar study was published in 2005,[52] involving 66 gastric cancer patients who were given early postoperative nutrition with either the immune-enhancing formula used in the previous study or a standard formula; the effect on the wound healing process was then examined. The investigators found that early postoperative enteral nutrition with a formula supplemented with arginine, omega-3 fatty acids, and RNA increased hydroxyproline synthesis and improved surgical wound healing in patients undergoing gastrectomy for gastric cancer.

Another trial investigated the effects of early postoperative enteral feeding in 43 patients with nontraumatic intestinal perforation and peritonitis.[53] After laparotomy, patients were randomly assigned to either a control group (22 patients) or a study group (21 patients). The study group received a feeding jejunostomy, and enteral feeding was started 12 hours after operation. Mortality was high in both groups (18% for the control group versus 19% for the study group). The control group had more septic complications than the study group (22 versus 8).

A 2008 study investigated early enteral feeding of septic patients with a pharmaconutrition supplement containing glutamine dipeptides, antioxidative vitamins and trace elements, and butyrate.[54] A total of 55 critically ill, septic patients from the adult ICU were enrolled. These patients received either an enteral supplement containing conditionally essential nutrients along with an immunoenriched formula or a standard formula. The study concluded that in medical patients with sepsis, early enteral pharmaconutrition with glutamine dipeptides, vitamin A and E, beta-carotene, selenium, zinc, and butyrate in combination with an immunoenriched formula results in significantly faster recovery of organ function.

ICU PATIENTS

A meta-analysis of 26 relevant randomized clinical trials involving 2,211 patients cared for in ICUs demonstrated that the administration of parenteral nutrition did not reduce morbidity or mortality, though the data did suggest that there might be some benefit in the most malnourished groups of patients.[55] Therefore, use of this expensive therapy, which is often associated with complications if appropriate policies and procedures are not in place, should be reserved for ICU patients who have specific nutritional needs and cannot accept enteral feedings.

A 2002 study examined 60 ICU patients who were fed either via a nasogastric tube or via a nasojejunal tube.[56] The results led to the conclusion that gastric feeding is not associated with a higher incidence of aspiration or other adverse outcomes than small-bowel feeding is. In addition, gastric feeding can be started and advanced to the desired goal sooner and with fewer placement attempts than small-bowel feeding can.

CONCLUSIONS

Parenteral and enteral nutritional support is a valuable adjunctive—and sometimes life-saving—therapy in the management of selected types of surgical patients. It is generally agreed that patients who are unable to ingest adequate nutrients for a prolonged period require nutritional therapy to prevent the adverse effects of malnutrition. It is not entirely clear, however, precisely how "adequate" and "prolonged" should be defined. In practice, the definitions are likely to vary from patient to patient, depending on the amount of body energy stores and lean body mass, the presence or absence of preexisting medical illnesses, the number and severity of postoperative complications, and the nature of the surgical procedure. Summation of the data from numerous trials suggests that perioperative administration of immunoenriched diets attenuates the perioperative inflammatory response and decreases postoperative infection complications. Severely malnourished patients (defined on the basis of percentage of body weight lost or nutritional risk index score) may derive greater clinical benefit from preoperative nutritional support, but this conclusion is based largely on retrospective analysis of prospective data. In addition, there are subsets of patients who may derive particular benefit from nutritional support, such as patients undergoing hepatic resection for hepatocellular carcinoma and elderly patients with hip fractures [*see* Guidelines, *below*]. The higher complication rates in patients given postoperative TPN and the case reports of small-bowel necrosis in patients who receive early postoperative enteral nutrition are evidence that nutritional support has risks and should not be given indiscriminately. Questions also remain as to the length of diet administration and the composition of the diet.

Nutritional Pharmacology and Immunonutrition

The role of nutrient administration to surgical patients has evolved from the maintenance of a positive energy and nitrogen balance to the use of nutrients to modulate tissue metabolism and organ system function. This new role is referred to as nutrition pharmacotherapy. Like other forms of adjuvant therapy, nutrition pharmacotherapy is usually a multitargeted therapeutic modality. For instance, one form of nutrition pharmacotherapy, immunonutrition, makes use of combinations of specific amino acids, fatty acids, and, in some enteral formulas, nucleotides. Another form, so-called bowel rehabilitation, uses an amino acid (glutamine) in combination with growth hormone and a modified diet. Inclusion of a specific nutrient as part of a plan of nutrition pharmacotherapy is based either on clinical studies or, more often, on extrapolations from experimental observations.

In what follows, we discuss each of the nutrients used, or proposed for use, in nutrition pharmacotherapy, with emphasis on chemical characteristics, physiologic effects, available forms for exogenous administration, and, if available, clinical data supporting its use for this purpose.

GLUTAMINE

Glutamine is the most abundant amino acid in the body and appears to be the most versatile. Most free glutamine is synthesized and stored in skeletal muscle, where

its concentration is 30 times greater than it is in plasma.[57] Skeletal muscle releases net glutamine for transport to the gut, immune cells, and the kidneys. The cells of the gut and those of the immune system proliferate rapidly, and glutamine acts as the main source of fuel and as a biosynthetic precursor. One of the compounds derived from glutamine is glutathione, a tripeptide (glutamate-cysteine-glycine) with potent antioxidant effects. Finally, glutamine participates in acid-base regulation via the release of ammonia, which combines with H^+ to form NH_4^+ and is lost in urine.

Catabolism induced by major injury, surgery, sepsis, or burns results in increased release of glutamine from skeletal muscle.[58] This output of glutamine into the circulation is associated with increased uptake and consumption by the gut, the immune system, the liver, and the kidneys. The net effect is a profound fall in intracellular muscle stores of glutamine. This deficit exceeds all other amino acid deficits and persists even when stores of all other amino acids have already been replenished.[59]

Standard amino acid formulations have always included all of the essential amino acids and most of the nonessential ones. For a long time, glutamine was excluded from parenteral formulations because of its instability in aqueous solutions. As more knowledge of the potential benefits of glutamine became available, the pharmaceutical industry began to develop ways of keeping glutamine stable in an aqueous solution. For instance, Glamin (Fresenius Kabi, Bad Homburg, Germany), an amino acid formulation that is already commercially available in Europe, includes the dipeptide glycyl-L-glutamine, which is readily hydrolyzed to free glutamine in plasma and tissues. These dipeptide formulations are not yet approved for use in the United States.

Glutamine has been shown to promote the recovery of small-bowel and colon mucosa. In one human study, patients with high-output fistulas were given either TPN alone or TPN along with oral glutamine.[60] The multivariate regression analysis showed that resolution of the fistula was 13 times greater in the patients who received oral glutamine.

Several clinical studies addressing supplementation of parenteral formulas with glutamine have been published. The most striking results have been reported in patients undergoing bone marrow transplantation and in patients with SBS. The first randomized, double-blind, controlled study to investigate the effects of glutamine on metabolic parameters and clinical outcome in patients undergoing bone marrow transplantation was published in 1992.[61] A total of 45 adults receiving allogeneic bone marrow transplants for hematologic malignancies were randomly selected to receive either L-glutamine, 0.57 g/kg/day, or a standard glutamine-free isonitrogenous formula for an average of 4 weeks after operation. The patients who received the glutamine-supplemented formula had a better nitrogen balance than the control group (-1.4 g/day versus -4.2 g/day); more important, they also had a lower incidence of microbial colonization and clinical infection and a shorter hospital stay. Subsequently, these findings were confirmed by a study performed by a different group of investigators.[62]

One of the most challenging pathologic conditions for surgeons is SBS developing after massive small-bowel resection. Fortunately, the advent of parenteral nutrition has improved survival for many patients with this condition who previously would have died of dehydration and malnutrition; however, it has also created a dependency on this therapy, which in the long term can have life-threatening complications. For this reason, many surgical scientists have searched for ways of augmenting these patients' intestinal absorption capacity so that their need for parenteral nutrition can be eliminated or at least greatly reduced. Having achieved a better understanding of the roles of glutamine, dietary fiber, short-chain fatty acids, and growth factors in the process of intestinal adaptation, investigators designed clinical trials with the aim of evaluating the effects of supplementation of these substances on patients with SBS.

In a randomized, double-blind, prospective multicenter trial, 41 SBS patients were given an optimal diet and then randomly selected to receive (1) oral glutamine (30 g/day) and placebo growth hormone, (2) placebo glutamine and growth hormone (0.1 mg/kg/day), or (3) both active agents.[63] The patients were weaned from TPN according to standard criteria based on daily measurements and laboratory values. At the end of 4 weeks, all subjects had lower IV nutrient requirements, with the glutamine–growth hormone group showing a greater reduction than the growth hormone group, which in turn showed a greater reduction than the glutamine group. These results demonstrate that specific growth factors and nutrients can be used to enhance nutrient absorption and adaptation after massive intestinal resection.

All of these studies were conducted according to research protocols that employed L-glutamine, which is not practical for IV use. As noted, glutamine is now commercially available (in Europe) in a dipeptide form that is stable in an aqueous solution. A recent meta-analysis of all the relevant studies involving IV glutamine showed that there was a significant reduction in postoperative infection associated with a decreased length of stay. In critically ill patients, there was a reduction in long-term (6-month) mortality, a finding that has not been recently associated with the administration of other specific nutrients.[64]

ARGININE

Arginine is a nitrogen-dense amino acid that is considered a semiessential amino acid because it is required for growth.[65] The effect of arginine on growth seems to be mediated by its role in polyamine and nucleic acid synthesis. In addition, arginine is a potent secretagogue of growth hormone, insulin, glucagon, prolactin, and somatostatin.[66–68] When the secretagogic effect of arginine is abolished by hypophysectomy, the stimulatory effect on wound healing is lost.[69] Supplemental dietary arginine has thymotrophic effects and enhances the responsiveness of thymic lymphocytes to mitogens in rats.[70] A similar response occurs in peripheral blood mononuclear cells of healthy human volunteers[71] and postoperative patients,[72] as evidenced by an enhanced response to concanavalin A and phytohemagglutinin.

Arginine enhances cellular immunity, as demonstrated by an increased delayed hypersensitivity response in animals with burns.[73] Dietary supplementation with arginine improves the response to dinitrofluorobenzene (DNFB) and enhances the survival of guinea pigs with burns on 30% of their BSA. In a model of acute peritonitis in guinea pigs, however,

supplemental arginine did not improve DNFB response or survival.[74]

Studies using arginine in humans have yielded confounding results because the amino acid is often administered with other active substances (such as RNA and omega-3 fatty acids). However, oral arginine supplementation has been shown to enhance markers of wound healing in human volunteers.[75] Other small studies show that immunologic measures improve with both enteral and parenteral arginine administration.[76] Although this amino acid has shown antitumor properties in animals, the only relevant study done on humans to date demonstrated that supplementation stimulated growth of breast cancer.[77] Because there is currently some controversy over increased mortality in critically ill patients receiving arginine (see below), careful patient selection and full informed consent are essential when the use of this agent is planned.

NUCLEOTIDES

Purines and pyrimidines are precursors of DNA and RNA, which are essential for cell proliferation. Purines and pyrimidines are synthesized by the liver de novo from amino acids and reutilized by salvage pathways. Reduction of dietary nucleotides results in suppression of cellular immune responses and prolongation of allograft survival.[78] The mechanism of immunosuppression associated with nucleotide restriction seems to be an inability of T cells to undergo blastogenesis. Dietary supplements containing RNA or uracil (but not adenine) maintain resistance to infection by *C. albicans* or *S. aureus* in rodents.[79,80] However, the immune response is not enhanced in comparison with a standard control diet.

On the basis of the immunosuppressive effect of dietary restriction of nucleotides, it has been postulated that nucleotide supplementation could provide an immunostimulant effect. This postulate has been tested in studies of the RNA–fish oil–arginine formula now available [*see* Enteral Formulations to Counteract Immunosuppression, *below*].

FATTY ACIDS

Fatty acids in the systemic circulation can be used in two forms: as fuels to be stored and oxidized as needed by the organism and as precursors for other essential compounds, such as eicosanoids (i.e., prostaglandins, leukotrienes, and thromboxanes). The eicosanoids are 20-carbon compounds derived from the essential fatty acids. They function as regulatory compounds in various physiologic processes, such as the immune response. Although organisms can oxidize other compounds to meet caloric needs, fatty acids in minimal amounts are essential as precursors for the synthesis of eicosanoids.

Fatty acids are classified in many different ways. One classification is based on chain length: short (two to five carbons), medium (six to 11 carbons), and long (12 to 26 carbons). Another classification is based on the presence of double bonds in the carbon chain: those with double bonds are called unsaturated and are further classified either as monounsaturated fatty acids or as PUFAs, depending on the number of double bonds. Another classification that has gained popularity is the omega classification, which indicates where the first double bond is located when the carbons are counted from the noncarboxyl end of the chain (e.g., omega-3, omega-6, and omega-9).

Humans can synthesize only fatty acids with double bonds at position 7 (counting from the noncarboxyl end toward the carboxyl end). Therefore, fatty acids with double bonds at position 6 or position 3 must be supplied exogenously. Because humans can elongate and desaturate linoleic acid and α-linolenic acid to produce the remaining omega-6 and omega-3 PUFAs, these are considered the essential fatty acids. Providing 2% to 4% of total calories as fat prevents humans from developing essential fatty acid deficiency. The requirements for omega-6 PUFAs exceed the requirements for omega-3 PUFAs by a ratio of approximately 5:1.

PUFAs of the omega-6 series are abundant in vegetable oils, such as corn oil and soybean oil, and PUFAs of the omega-3 series are abundant in fish oils, such as menhaden oil. Other oils rich in omega-3 PUFAs are seed oils, such as black currant oil and canola oil (canola oil is derived from rape seeds and genetically modified to optimize the fatty acid composition).

The availability of 20-carbon PUFAs—arachidonic acid in the omega-6 series and eicosapentaenoic acid in the omega-3 series—is the determining factor for the synthesis of eicosanoids. There are two major metabolic pathways for the synthesis of eicosanoids. The cyclooxygenase pathway results in the production of prostanoids. Inasmuch as prostanoids contain two double bonds in the carbon side chain, they are also called dienoic products. These include prostaglandin E_2 (PGE_2), prostaglandin D_2 (PGD_2), prostaglandin F_2 (PGF_2), prostaglandin I_2 (PGI_2, also called prostacyclin), and thromboxane A_2 (TXA_2). The lipoxygenase pathway yields trienoic products (with three double bonds in the carbon side chain), such as thromboxane A_3 (TXA_3) and prostaglandin I_3 (PGI_3). All nucleated cells, with the exception of lymphocytes, can synthesize eicosanoids. Platelets are the major sources of thromboxanes, and the leukocytes mainly produce leukotrienes. Prostaglandins have various effects on the tone of blood vessels and the aggregation of platelets. Leukotrienes promote leukocyte migration (chemotaxis) and degranulation, release of lysosomal enzymes, and superoxide production.

Cells obtain arachidonic acid and eicosapentaenoic acid from degradation of phospholipids by phospholipase A_2 and phospholipase C or by elongation and desaturation of linoleic acid and α-linolenic acid. Mature immune cells, such as monocytes, macrophages, lymphocytes, and polymorphonuclear cells, lack D6 desaturase, the critical rate-limiting enzyme for transformation of 18-carbon PUFAs into 20-carbon PUFAs.[81] Therefore, the availability of precursors for eicosanoid synthesis in immune cells depends largely on their lipid composition. Because lipid intake influences the lipid composition of immune cells, the type of PUFAs ingested can influence the immune response.[82,83] Eicosanoids, especially PGE_2 and the lipoxygenase products leukotriene B_4 (LTB_4), 5-hydroxyeicosatetraenoic acid (5-HETE), and 15-hydroxyeicosatetraenoic acid (15-HETE), are immunomodulatory; when produced in excess (as in posttraumatic states), they are generally immunosuppressive.[84] Dietary supplementation with omega-3 PUFAs has improved survival of endotoxic shock in guinea pigs.[85] The reduced intake of

omega-6 PUFAs seems to be as important as the enrichment with omega-3 PUFAs. When animals are made deficient in linoleic acid, they have only a 24% mortality after endotoxin challenge; however, the mortality reaches 100% when arachidonic acid is given 2 days before endotoxin challenge.[86] Similar results have been reported in guinea pigs recovering from flame burns covering 30% of BSA.[87] When compared with animals fed dietary safflower oil (74% linoleic acid) or linoleic acid alone, animals fed fish oil had less weight loss, better skeletal muscle mass, lower resting metabolic expenditure, better cell-mediated immune responses, better opsonic indices, higher splenic weight, lower adrenal weight, higher serum transferrin levels, and lower serum C3 levels.

In conclusion, high intake of omega-6 PUFAs (e.g., linoleic acid) is associated with increased synthesis of PGE_2, which is immunosuppressive. A reduction in the intake of omega-6 PUFAs appears prudent in patients who are immunocompromised or in posttraumatic states. Dietary supplements with omega-3 PUFAs are associated with incorporation of eicosapentaenoic acid into leukocytes and with concurrent decreases in the incorporation of arachidonic acid. When these cells are challenged, there is significantly lower production of LTB_4, which exacerbates undesirable immune responses such as those seen in trauma and autoimmune diseases. Formulas for nutritional support should include omega-3 PUFAs, though the exact amount of omega-3 PUFAs and the precise ratio of omega-6 PUFAs to omega-3 PUFAs remain to be determined.

The fat emulsions currently available for IV use in the United States are made with LCTs derived either from soybean oil alone or from soybean oil and safflower oil. All of the fatty acids in LCTs are in the form of PUFAs, which include the essential fatty acids (i.e., linoleic and linolenic acids). As noted (see above), an excess of omega-6 PUFAs can have an immunosuppressive effect. Intravenously administered LCT emulsions are cleared in part through the reticuloendothelial system (RES).[88] When such emulsions are used as a calorie source, they may impair the ability of the RES to clear bacteria if given too rapidly or in excessively large amounts.

Moreover, the PUFAs in LCT emulsions require carnitine-mediated transport to cross the mitochondrial membrane for oxidation. Carnitine is a quaternary amine derived from two essential amino acids, lysine and methionine. During sepsis, urinary excretion of free carnitine rises significantly, and the plasma acylcarnitine level falls.[89] One way of circumventing these problems is to use emulsions that contain MCTs.

MCT-containing emulsions have long been used in enteral nutrition for their absorptive advantage over LCT-containing emulsions: whereas LCTs are absorbed via lacteals and the lymphatic system, MCTs are absorbed via the portal system. MCTs are obtained from coconut oil and contain saturated fatty acids (with octanoic acids predominating). Because MCTs are smaller than LCTs, they are more water soluble; they are also poorly bound to albumin and diffuse more easily across body compartments.

Several reports on IV administration of MCT fat emulsions have been published. One study evaluated the effect of a 75% MCT/25% LCT emulsion on RES function as demonstrated by technetium-99m–sulfur colloid (Tc-SC) clearance. Clearance of Tc-SC was significantly higher after 3 days of MCT/LCT administration than after 3 days of LCT administration.[90] Another study investigated the metabolic effects of MCT-containing emulsions on surgical patients.[91] The main finding of this study was the appearance of β-hydroxybutyrate in association with infusion of the MCT emulsion, which was indicative of a ketogenic effect. A tendency toward improved nitrogen balance was also observed but was not statistically significant.

In summary, specific fatty acids have significant potential for use in nutrition pharmacotherapy. Omega-6 fatty acids are potential immunosuppressants, whereas omega-3 fatty acids are potential immunostimulants. In the United States, the only emulsions commercially available for IV use at present are made of LCTs containing omega-6 fatty acids. MCTs offer some metabolic advantages over LCTs and obviate the side effects resulting from an excess of omega-6 fatty acids. Enteral diets containing omega-3 fatty acids appear to benefit stressed surgical patients, particularly those who are immunosuppressed as a result of therapy for cancer.

ENTERAL FORMULATIONS TO COUNTERACT IMMUNOSUPPRESSION

Impact (Sandoz Nutrition, Minneapolis, MN), a commercially available enteral formula enriched with omega-3 fatty acids, arginine, and RNA, was shown to reduce infectious complications in postoperative patients[92,93] and in some critically ill patients.[94] Furthermore, it has been shown to reduce hospital stay in selected patient groups.[95] Concerns were raised, however, by data from a large meta-analysis of studies using these diets, which suggested that mortality was increased in patients exposed to these formulations.[96] The authors of the meta-analysis suggested that immunomodulation with the use of this diet may be beneficial in some patients (generally the less seriously ill) but may be harmful in others (generally the more critically ill patients who require nutritional support).[97] Until this issue becomes resolved, patient selection is extremely important if this diet is to be administered to surgical patients.

Guidelines

In 2002, the American Society for Parenteral and Enteral Nutrition (ASPEN) published an updated version of its guidelines for the use of nutritional support.[98] The following comprises brief excerpts from these guidelines.

GENERAL RECOMMENDATIONS

A nutrition screening incorporating objective data such as height, weight, weight change, primary diagnosis, and presence of comorbidities should be a component of the initial evaluation of all patients in ambulatory, hospital, home, or alternate care settings. A formal nutrition assessment should be carried out in any patient, independent of the care setting, who is identified by a nutrition screen as being nutritionally at risk.

Specialized nutrition support (SNS) should be used in patients who cannot meet their nutrient requirements by oral intake. When SNS is required, enteral nutrition should generally be preferred to parenteral nutrition. When SNS is indicated, parenteral nutrition should be used in patients whose GI tract is not functional or cannot be accessed and in

patients who cannot be adequately nourished by oral diets or enteral nutrition. SNS should be initiated in those patients whose oral intake has been inadequate for 7 to 14 days or in whom inadequate oral intake is expected over a 7- to 14-day period.

RECOMMENDATIONS FOR SPECIFIC DISEASE STATES

Cardiac Disease

Patients who have cardiac cachexia or experience complications after cardiopulmonary bypass are at nutritional risk and should undergo nutrition screening. In the cardiac surgery patient, enteral nutrition should be deferred until hemodynamic stability is achieved.

Pulmonary Disease

Patients with chronic obstructive pulmonary disease (COPD) or acute respiratory distress syndrome (ARDS) are at nutritional risk and should undergo nutrition screening. Energy intake should be kept at or below estimated needs in patients with pulmonary disease and demonstrated carbon dioxide retention. Routine use of modified carbohydrate and fat nutrition formulations is not warranted. Provision of a modified enteral formulation containing omega-3 fatty acids may be beneficial in patients with early ARDS. A fluid-restricted nutrient formulation should be used in patients with ARDS whose hemodynamic status necessitates fluid restriction. Serum phosphate levels should be monitored closely in patients with pulmonary disease.

Liver Disease

Patients with liver disease are at nutritional risk and should undergo nutrition screening. Nutrition assessment in patients with liver disease should include screening for deficiencies of micronutrients, including vitamins A, D, E, K, and zinc. Patients with cirrhosis should divide their meals into 4 to 6 meals per day, including a late evening snack. Protein restriction should be implemented for the acute management of overt hepatic encephalopathy. Protein restriction should not be implemented on a long-term basis in patients with liver disease. Use of BCAA-enriched diets and SNS formulas is indicated only in the setting of chronic encephalopathy unresponsive to pharmacotherapy. Perioperative nutritional support should be employed in patients undergoing liver resection for hepatocellular carcinoma associated with cirrhosis.

Renal Disease

Patients with renal failure are at nutritional risk and should undergo nutrition screening. Well-monitored patients who have advanced chronic renal insufficiency but are not on dialysis should receive diets restricted to 0.6 to 0.8 g protein/kg/day. Patients with chronic renal failure on hemodialysis or peritoneal dialysis should receive 1.2 to 1.3 g protein/kg/day. Patients undergoing continuous hemofiltration should receive at least 1.0 g protein/kg/day. Patients with acute renal failure should be given a balanced mixture of both essential and nonessential fatty acids. Patients with acute renal failure who are severely malnourished or hypercatabolic should receive 1.5 to 1.8 g protein/kg/day. Intradialytic parenteral nutrition should only be considered in the event of gut failure or other unusual circumstances where enteral and parenteral nutrition are not feasible. Water-soluble vitamin supplementation is required for patients treated with dialysis. Vitamin A status should be carefully monitored in patients with chronic renal failure.

Pancreatitis

Patients with pancreatitis are at nutritional risk and should undergo nutrition screening. SNS should not be used routinely in patients with mild to moderate acute pancreatitis. SNS should be used in patients with acute or chronic pancreatitis to prevent or to treat malnutrition when it is anticipated that oral energy intake will be inadequate for 5 to 7 days. IV lipid emulsions are safe in acute pancreatitis, provided that triglyceride levels are monitored below 400 mg/dL.

Short-Bowel Syndrome

Patients with SBS are at nutritional risk and should undergo nutrition screening. Patients with SBS and an intact colon should receive diets rich in complex carbohydrates and low in fat. A low oxalate diet should be given to patients with SBS and an intact colon. Monthly vitamin B_{12} injections should be given to patients in whom more than 100 cm of the terminal ileum has been resected.

Inflammatory Bowel Disease

Patients with inflammatory bowel disease (IBD) are at nutritional risk and should undergo nutrition screening. Enteral nutrition should be used in Crohn disease patients who require SNS. In cases of fistula associated with Crohn disease, a brief course of bowel rest and parenteral nutrition should be attempted. Perioperative SNS is indicated in patients with IBD who are severely malnourished and in whom surgery may be safely postponed. SNS and bowel rest should not be used as primary therapies for ulcerative colitis or Crohn disease.

Solid-Organ Transplantation

Patients in any stage of the transplantation process are at nutritional risk and should undergo nutrition screening. In the perioperative transplant period, patients should receive 1.5 to 2.0 g protein/kg/day. SNS should be provided to malnourished patients with complications or delayed oral intake after solid organ transplantation. Metabolic and nutritional complications of transplantation, including obesity, hypertension, diabetes mellitus, hyperlipidemia, and osteoporosis, should be treated with appropriate dietary and pharmacologic interventions.

Burns

Patients with second- or third-degree burns are at nutritional risk and should undergo nutrition screening. Adequate calories must be provided to address the hypermetabolism associated with acute thermal injury. When possible, the energy requirements of burn patients should be measured with indirect calorimetry. Severely burned patients require increased intake of protein until significant wound healing is achieved. There is no current role for the routine use of specific nutrients and anabolic agents (e.g., arginine, glutamine, omega-3 fatty acids, vitamins, trace minerals, antioxidants, growth hormone, and oxandrolone) in burn patients. Enteral nutrition should be initiated as soon as possible in patients with moderate to severe burns.

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Acknowledgments

Figure 2 Talar Agasyan.