Guidance for Supplemental Enteral Nutrition Across Patient Populations

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ABSTRACT

Enteral nutrition is preferred over parenteral nutrition as a result of the greater safety of enteral nutrition therapy and comparative convenience. A wide variety of enteral nutrition products have been developed, including disease-specific products to help manage the nutritional needs of patients with kidney failure, liver failure, lung disease, diabetes, and other conditions. An assessment of each patient's nutritional needs and digestive function should be conducted prior to initiation of enteral nutrition therapy. Other considerations in determining the appropriate route and method of enteral nutrition administration include the time and nursing involvement required for administration, potential complications of medication administration, and concerns related to pancreatic dysfunction in certain groups. Tailored guidelines and treatment considerations are reviewed in this manuscript the application of enteral nutrition in various patient populations.

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Enteral Nutrition

Enteral nutrition is administration of a specialized liquid food mixture that contains proteins, carbohydrates, lipids, vitamins, and minerals into the stomach or small bowel through tube-feeding.[1] Although enteral nutrition may be administered orally, enteral nutrition in hospitalized patients generally refers to products administered through a nasoenteric tube that delivers the enteral nutrition product directly to the stomach, duodenum or jejunum. Alternatively, enteral nutrition may be delivered via a surgically implanted tube, such as a gastrostomy tube or a jejunostomy tube, with the rate of administration controlled using an infusion pump, gravity drip system, or as boluses via a syringe.[2-4] For short-term enteral nutrition, a nasogastric or orogastric tube may be used to administer formula. However, long-term enteral nutrition is generally administered through a surgically placed gastrostomy or jejunostomy tube.[4]

Enteral nutrition is preferred over parenteral nutrition, as use of total parenteral nutrition (TPN) therapy is complex and has been associated with increased complications and higher costs.[5,6] Complications associated with TPN include line-associated infections, vascular thrombosis, cholestastic liver disease, metabolic bone disease, and cholelithiasis.[5,7] Additionally, close and frequent monitoring of patients on TPN is required due to the possibility of electrolyte imbalances and fluid overload.[5,8,9] Depsite these risks for certain patient groups, including patients with intestinal failure, short bowel syndrome, severe fixed intestinal obstructions, or fistulas not amenable to enteral nutrition, parenteral nutrition may be necessary to achieve adequate nutritional status.[2,8-12] Finally, TPN does not promote restoration of normal gastrointestinal digestive functions.[5,6]

Enteral nutrition products have become a preferred alternative to parenteral nutrition as a result of the comparative convenience, greater safety, and efficacy of enteral nutrition therapy.[2] Use of enteral feeding carries a low risk of serious complications, reduces bacterial translocation from the gut to the systemic circulation, reduces levels of circulating inflammatory cytokines, helps restore normal gut function, and reduces infectious complications and overall costs

of care.[3,6,11,13,14] There is some evidence showing improved outcomes of infection in critically ill, hospitalized patients receiving enteral nutrition compared with parenteral nutrition.[9] However, enteral nutrition therapy must be tailored to patient-specific needs; each patient's baseline nutritional status must be carefully assessed in the context of their anatomy, comorbid diseases, and present medical condition.[2,9]

KEY POINTS

- Enteral nutrition is administration of a specialized liquid food mixture that contains proteins, carbohydrates, fats, vitamins, and minerals into the stomach or small bowel through a feeding tube.
- Pancreatic exocrine insufficiency may pose a challenge when using enteral nutrition in certain patient groups, as pancreatic secretions are critical to the digestion of fats.
- Essential fatty acid deficiency may occur in patients receiving parenteral nutrition, patients with malnutrition, fat malabsorption syndromes, and patients receiving formulations of enteral nutrition that are very low in fat content.
- Pancreatic enzyme replacement therapy (PERT) may be needed when delivering enteral feeding to patients with chronic pancreatitis and cystic fibrosis, among other conditions associated with pancreatic hypofunction.
- PERT products generally contain a mixture of enzymes; none of these products are easy to administer via enteral feeding tubes.
- A recently approved in-line medical cartridge with immobilized lipase (RELiZORB) hydrolyzes fats in enteral formulas just prior to delivery into the patient with an enteral feeding tube.
- Enteral nutrition therapy must be tailored to patient-specific needs. Tailored guidelines have been developed for the use of enteral nutrition in special patient populations.

Available Forms of Enteral Nutrition Products

The carbohydrate and protein content of enteral nutrition formulas may be elemental, semielemental, or polymeric. Elemental formulas are composed of simple carbohydrates and amino acids, semielemental formulas contain short peptides and more complex carbohydrate, and polymeric formulas contain intact proteins and complex carbohydrates (**Table 1**[2,4,12,15-17]).[15] Products vary in terms of caloric density; protein, fat, fiber, and carbohydrate content; and osmolality.[3,4]

A wide variety of enteral nutrition products have been developed, including disease-specific formulas for the purpose of managing the nutritional needs of patients with kidney failure, liver failure, lung disease, diabetes, and other conditions (**Table 2**).[2,4,9,12,15,16,18] However, even with a wide variety of formulas available, specialized formulations may be tailored on a case-by-case basis using modular enteral nutrition recipes containing separate protein, carbohydrate, and fat sources to enable more flexibility. This greater flexibility carries the potential drawback of complexity of preparation and handling, which may increase the risk of contamination with bacteria.[3,4]

Key Components of Enteral Nutrition Formulas

As with any food source, the key components of enteral nutrition include proteins, carbohydrates, and fats. The characteristics of these macronutrient components vary, however. For example, nutrient components may be hydrolyzed or broken down to varying degrees to aid in digestion. The protein component of enteral nutrition may be composed of polypeptides, oligopeptides (partially hydrolyzed), or free amino acids (fully hydrolyzed). Although short-chain polypeptides and oligopeptides are easily absorbed, free amino acids may not be absorbed efficiently.[4,15]

The carbohydrate components of enteral nutrition may include polysaccharides, oligosaccharides, and fiber. Of these components, oligosaccharides can be absorbed. Carbohydrate polysaccharides, such as starch, may be broken down into simple sugars through enzymatic processes, while fiber may be fermented by gut bacteria to form short-chain fatty acids.[4]

The lipid component of enteral nutrition may include long-chain and medium-chain triglycerides. Of these fat sources, long-chain triglycerides require digestion by pancreatic lipase and are mixed with bile salts for absorption, whereas medium-chain triglycerides may be absorbed directly across the intestinal mucosa.[4] Linoleic acid and alpha-linolenic acid are essential fatty acids (EFAs). Importantly, EFAs cannot be synthesized by the human body and are obtained solely through dietary intake. These long-chain triglycerides cannot be absorbed in the absence of pancreatic enzymes.[4] To prevent EFA deficiency, approximately 5% to 10% of total calories ingested should be EFAs.[19,20]

Essential fatty acid deficiency may occur in patients receiving parenteral nutrition, patients with malnutrition, fat malabsorption syndromes, and patients receiving formulations of enteral nutrition that are very low in fat content.[19] Essential fatty acid deficiency may

TABLE 1. Characteristics of Enteral Nutrition Products[2,4,12,15-17]

Product Type	Primary Product Characteristics
Elemental	Low in fat; amino acid content is not well absorbed
Semielemental	Contains medium-chain triglycerides and partially hydrolyzed proteins and carbohydrates
Polymeric	Standard formula for patients with a functional gastrointestinal tract; contains intact proteins, carbohydates, and medium-chain triglycerides; intended for tube feeding, not direct oral intake

TABLE 2. Enteral Nutrition Considerations by Disease State[2,4,9,12,15,16,18]

Disease State	Enteral Nutrition Product Considerations
Malabsorption (including conditions involving exocrine pancreatic insufficiency, and irritable bowel disease)	Semielemental formulas may be used
High protein needs (eg, critically ill patients, trauma patients, and patients with other wounds)	High-protein formulas may be used in patients whose protein needs exceed 1.5 grams per kilogram of bodyweight per day
Kidney disease	Calorically dense formula low in electrolyte content; protein content may be adjusted to avoid overtaxing renal function in patients with advanced renal disease
Liver disease	Formulas contain branched chain amino acids, which are taken up directly by skeletal muscle, reducing metabolic production of ammonia to manage the risk of hepatic encephalopathy
Lung disease (eg, acute respiratory distress syndrome, acute lung injury)	Formulations with antioxidant content, lower carbohydrate content, and increased fat content may aid in management; however, no guideline recommendation supports their use
Diabetes mellitus	Reduced carbohydrate formulas with higher fat content may aid in management of hyperglycemia; however further evidence is needed before recommendations can be made
Immune-related conditions	Formulas may contain anti-inflammatory nutritional compounds, such as omega-3 fatty acids, arginine, and nucleotides

result in dermatitis, alopecia, impaired wound healing, anemia, thrombocytopenia, and impaired growth.[19]

Other components of enteral nutrition products are intended to exert immunomodulatory effects; omega-3 fatty acids, ribonucleic acids, and glutamine or arginine addition to formulas may modulate immune response.[2,4] Fiber is another important component of many enteral nutrition formulas. The presence of fiber helps to promote absorption of sodium and water in the colon and to support the colonic mucosa.[4] Fiber induces healthy changes in gut flora by promoting favorable bacterial growth.[2,12]

Defining Appropriate Patients for Enteral Nutrition

Because nutrition can have important effects on health outcomes, the Joint Commission requires accredited institutions to perform nutritional screenings for patients who enter hospitals, with such screenings typically completed within 24 hours of entry.[19] Nutritional assessment may include evaluation for the presence of disease states or patient-specific factors associated with malnutrition, an assessment of the risk of developing malnutrition, and an assessment of each patient's nutritional needs.[9,19]

Various scoring systems and biochemical tests are used to assess nutritional outcomes. One assessment tool for nutritional status is the Subjective Global Assessment.[19] Other tools include the Mini Nutritional Assessment, which is primarily used for elderly patients. Nutrition Risk in Critically Ill (NUTRIC) scoring may be used in the critical care setting to assess the risk of poor clinical outcomes in association with malnutrition.[9,19] In addition to scoring systems, biochemical markers including serum albumin levels, prealbumin levels, and transferrin levels may be indicators of physiologic stress (inflammation) to augment clinical assessment of nutritional needs, but should not be used solely as a marker of nutritional status.[2,19]

These scoring systems and biochemical markers must be assessed in the context of each patient's medical conditions and the corresponding nutritional needs of patients with these underlying disease states. Although there are some contraindications for use of enteral nutrition, scoring systems are important because these systems help identify patients with a wide range of disease states who may benefit from enteral nutrition therapy. including patients with dysphagia, oral or esophageal lesions, head and neck cancers, critically ill patients, neonates, patients with reduced gastric motility, patients with protein calorie malnutrition/sarcopenia, patients with intestinal failure, and patients with pancreatitis.[2,4,11,21] Assessing appropriateness of therapy in each patient through a scoring system may help standardize the approach to individualized nutritional therapy in a broad and heterogenous group of patients.

Timing and Administration of Enteral Nutrition Therapy

In critically ill patients, early initiation of enteral nutrition within 24 to 48 hours of hospital admission reduces the risk of medical complications associated with hospitalization, including infectious complications.[9] Biochemically, early administration of enteral nutrition is associated with a reduction in release of inflammatory cytokines, which may alter gut function.[4] Regardless of these advantages, use of enteral nutrition must be evidence-based and carefully considered, as with any therapy, taking into account each patient's total nutritional needs and pre-existing digestive dysfunction, and administration challenges associated with enteral nutrition.

Before administering enteral nutrition therapy, total caloric intake needs must be estimated and total protein intake as a proportion of all calories must be determined.[2] Although indirect calorimetry is touted as the ideal method for determining appropriate total caloric

TABLE 3. Conditions of Pancreatic Dysfunction Associated With Malabsorption[24]

Condition	Percentage of Patients with Malabsorption Syndromes	Potential Symptoms Related to Pancreatic Dysfunction
Cystic fibrosis	Approximately 90% of patients	• Flatulence • Abdominal discomfort • Exacerbation of malabsorption syndrome • Micronutrient deficiency • Cramping • Frequent defecation • Oily, clay-colored, or yellowish stool
Pancreatic cancer	22% to 45% of patients (4% experience steatorrhea)	
Pancreatitis	Following surgery, 50% to 75% of patients experience pancreatic exocrine insufficiency	
Gastrointestinal surgeries (eg, gastric and pancreatic surgeries)	Not reported	
Bowel obstruction	Not reported	
Small bowel intestinal overgrowth	Not reported	

requirement, most centers do not have access to this technology. In these centers, lean body mass and body composition indices such as body mass index (BMI), simple weight-based formulas, or other predictive equations may aid in determining appropriate intake levels.[2,9] Protein intake is an especially important consideration for critically ill patients, as enteral nutrition formulas higher in protein may contribute to improved outcomes in these patients.[2,9] When the total caloric intake need and macronutrient balance for enteral nutrition have been determined, administration considerations must be addressed.

Administration of enteral feeding may be accomplished in any of 4 ways: through continuous feeding, cyclic feeding, bolus feeding, or intermittent feeding. While any method may be used with gastric delivery, continuous administration of enteral nutrition is reserved for enteral nutrition that is delivered directly to the small bowel.[4] Cyclic feeding is an alternative to continuous feeding, in which continuously administered enteral nutrition is delivered over a set number of hours during the day or overnight.[4] An alternative to continuous administration method is intermittent feeding, in which enteral nutrition is administered over 20 to 60 minutes through an enteral pump or gravity drip system. This mode of administration may be more similar to the physiological pattern of eating.[4] A further alternative to continuous, cyclic, and intermittent administration of enteral nutrition is bolus administration. Bolus feedings are typically given as 4 to 6 feedings of enteral nutrition formula into a gastrostomy tube using a syringe, with each administration lasting 5 to 10 minutes.[4]

Other considerations in determining the appropriate route and method of enteral nutrition administration include the time and nursing involvement required for administration, potential complications of medication administration. Complications of enteral feeding may include patient intolerance, a rate of feeding that is overly rapid, contamination concerns, and clogging of the feeding tube.[4,22] Clogging may result from incomplete crushing of certain medications. Additionally, the need to crush medication prevents use of extended-release and enteric-coated medications, which, if crushed, might lead to inappropriate rapid release of medication and feeding tube occlusion.[4,22]

In addition to administration-related considerations, certain patient groups pose a challenge when using enteral feeding and require special consideration such as those with pancreatic exocrine insufficiency, as pancreatic secretions are critical to the digestion of fats.[23] Pancreatic function is complex, is mediated by hormones and neurotransmitters, and involves release of pancreatic enzymes, which include amylase, lipase, trypsinogens, chymotrypsinogen A and B, and procarboxy peptidase A and B.[24] In a given day, the pancreas releases 500 mL to 1000 mL of fluid containing these enzymes, with release of pancreatic juices increasing 20 minutes after a meal, and continuing for hours after meal completion.[24]

Although the pancreas has some functional reserve in the production of pancreatic enzymes, when pancreatic exocrine function is reduced to less than 10% of normal function, clinically significant alterations may occur. However, in some patients, clinically significant effects may manifest even when pancreatic function is only slightly impaired.[24] Enzymes in pancreatic secretions are most important in the absorption of fats, but also affect the digestion of proteins and carbohydrates. As a result, pancreatic enzyme replacement is important to maintaining digestive processes in patients with certain conditions associated with functional deficits of pancreatic function.[24]

Pancreatic Enzyme Replacement Therapy for Patients Receiving Enteral Nutrition

Pancreatic enzyme replacement therapy (PERT) may be needed when delivering enteral feeding to patients with chronic pancreatitis and cystic fibrosis, among other conditions associated with pancreatic hypofunction (**Table 3**[24]).[24] In these patients, deficits of pancreatic function may lead to malabsorption of fats, including essential fatty acids and fat-soluble vitamins.[23]

PERT products generally contain a mixture of enzymes that include amylase, lipase, and protease, which are known collectively as pancrelipase.[24] These enzymes may be derived from porcine sources.

Currently available PERT products include several delayed-release products (trade names: Pertzye, Pancreaze, Zenpep, and Creon), and one immediate-release product (trade name: Viokace).[25-29] Although none of these products are indicated for use in enteral feeding tubes, and the products are not meant to be chewed or crushed, as previously described, the tablets or capsules are sometimes crushed and administered in feeding tubes, which may result in clogging. Preparing and administering these products may place a burden on caregivers in terms of time required.[24]

To administer enteral nutrition physiologically with currently available PERT products, various methods have been attempted that involve crushing product tablets or opening capsules (while wearing a mask and gloves) and mixing the resulting powder with fruit juice or bicarbonate.[16,24] In addition to difficulties related to PERT product preparation, the timing of administration of these extemporaneously compounded products may be challenging, as treatment should be administered either during enteral feeding, or within 30 minutes of feeding, and approximately every 2 to 3 hours during feeding.[16] Beyond the use of PERT for tube feeding, other strategies may include use of semielemental or elemental formulas for patients with gastrointestinal or pancreatic pathologies.[15]

To address the unmet need for PERT in patients receiving enteral feeding, a medical device with immobilized lipase has been developed to hydrolyze fats in enteral formula *ex vivo* (trade name: RELiZORB). The safety and efficacy of RELiZORB was evaluated in a total of 33 pediatric and adult patients with CF (5 to 34 years of age) who had a history of EN use for an average of 6.6 years. Patients receiving oral PERT also received enteral nutrition hydrolyzed by RELiZORB as an inline cartridge for 7 days and recorded their gastrointestinal (GI) symptoms. Patients reported a lower incidence and severity of GI symptoms with RELiZORB administration during this period as compared with EN supplemented with PERT during the initial 7 day run in phase. Administration of EN with RELiZORB improved stool-related GI symptoms of constipation and diarrhea by more than 50% compared with EN without RELiZORB. RELiZORB use was associated with fewer symptoms of abdominal pain, bloating, indigestion, steatorrhea, and nausea. Patients had mean baseline plasma concentrations of DHA and EPA below 60% of normal values, indicating fatty acid deficiency. Patients who were administered enteral formula hydrolyzed by RELiZORB achieved a significant ($P < .001$) increase in fat absorption, measured by 2.8 fold increase of DHA and EPA plasma concentrations compared with placebo after the first feeding.[30,31]

Enteral Nutrition Guidelines

Enteral nutrition guidelines for hospitalized adult patients were developed by the American College of Gastroenterology (ACG), and were published in 2016.[2] Also in 2016, guidelines for enteral nutrition in hospitalized patients and critically ill adult patients were developed by the Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN).[9] These guidelines emphasize the many advantages of enteral nutrition therapy versus parenteral nutrition therapy.

As noted in the ACG, SCCM, and ASPEN guidelines, enteral nutrition products became a preferred alternative to parenteral nutrition during the 1990s based on the results of studies showing superior outcomes in hospitalized patients receiving enteral nutrition therapy.[2] Further supportive data, including meta-analyses, have demonstrated reductions in mortality rates, rates of infectious morbidity, cases of pneumonia, and hospital length of stay when enteral nutrition is initiated promptly after ICU admission.[9] Evidence suggests that certain patient groups may especially benefit from enteral nutrition therapy rather than parenteral nutrition, including patients undergoing elective major surgery and patients with pancreatitis, traumatic injuries, burn injuries, or head injuries.[2]

Critical illness is associated with an inflammatory response and catabolic stress along with an increased risk of multiorgan dysfunction, morbidity, mortality, and hospitalization. Enteral nutrition therapy is a proactive strategy to reduce the risk of complications, reduce length of stay, and improve patient outcomes in these patient groups.[9] Patients at high risk of poor nutritional outcomes should be identified based on objective rating scales and nutritional markers.[9] In addition, indirect calorimetry may be useful in assessing nutritional needs, and scoring systems scoring systems such as Nutritional Risk Screening (NRS-2002) and NUTRIC may be useful in assessing nutritional risk.[2,9] Alongside scoring systems, as part of the nutritional assessment, comorbid conditions, gastrointestinal tract function, and the risk of aspiration should be evaluated.[9]

An appropriate assessment of nutritional status and nutritional needs should be pursued for all newly hospitalized patients, as administration of enteral nutrition soon after admission (ie, within 24 to 36 hours) is associated with reduced length of stay, lower infection rates, and reduced overall mortality rates.[2,9] Evidence for the benefits of early initiation of enteral nutrition have been documented in patients undergoing elective surgery, in patients receiving surgical treatment for pancreatitis, and in critical care patients.[2] Positive effects of prompt enteral nutrition therapy administration are thought to result from improved caloric intake, as well as effects of enteral feeding on supporting the gastrointestinal mucosa, maintaining the gut microbiome, and modulating inflammatory response.[2]

Mode of Administration

According to treatment guidelines, nasogastric or orogastric feeding tubes are preferred as the initial access device, with a post-pyloric feeding tube used in cases when nasogastric or orogastric feeding tubes are not well tolerated, or in patients at high risk of aspirating

stomach contents.[2,32] Monitoring for aspiration risk, adequacy of feeding, and tolerability of enteral nutrition are important in continuously assessing the appropriate route and type of enteral nutrition administered.[2]

Formula Selection

For most patients, a standard polymeric enteral nutrition formula or an enteral nutrition formula high in protein is recommended, whereas patients hospitalized in the intensive care unit or patients who have undergone major surgery may require specialized formulas, such as formulas supplemented with arginine and omega-3 fatty acids.[2,9] Selection of high-protein formulas should be considered for critically ill patients, as protein intake may be especially important in this patient population. In critically ill patients, guidelines advise monitoring protein intake on an ongoing basis, particularly in critically ill patients with major trauma or those undergoing major surgery. In these patients, up to 2.0 grams of protein per kilogram of bodyweight per day may be required, with adequacy of feeding calculated based on weight.[2,9]

Specialized Enteral Nutrition Formulations

Although a limited number of studies to date have evaluated the use of formulas specifically for immunocompromised critically ill patients, some meta-analyses demonstrate a potential benefit in reducing hospital length of stay.[9] However, other meta-analyses indicate no significant reduction in ICU length of stay, mechanical ventilation duration, risk of organ failure, or in-hospital mortality.[9]

Challenges With Enteral Nutrition Therapy

Although enteral nutrition therapy is associated with improved outcomes over parenteral nutrition therapy in many patients, certain challenges remain, including the risk of aspiration pneumonia, administration difficulties, and enteral feeding–associated intolerance. Strategies to assess the risk of aspiration pneumonia, infection, and administration challenges are important in implementing and monitoring continued enteral nutrition therapy. An awareness of common gastrointestinal side effects and methods for awareness and prevention of these potential adverse events is important in implementing effective enteral nutrition therapy.[2,9]

In managing the risk of aspiration pneumonia, gastric residual volumes (GRVs) may be used to assess patients in some ICU settings, although this practice has been largely discontinued due to poor evidence in support of its value. Importantly, guidelines note that feedings should not be held in cases of GRVs less than 500 mL, as GRVs do not correlate with risk of pneumonia or aspiration.[9] Additional practical strategies for reducing the risk of aspiration pneumonia in high-risk patients include using a prokinetic agent, moving the feeding tube lower in the gastrointestinal tract, reducing the volume infused by using continuous-infusion enteral nutrition over bolus administration, and administering a chlorhexidine-containing mouthwash twice daily.[2,9] One of the most important strategies for reducing the risk of aspiration involves elevating the head of the patient's bed to 30 degrees to 45 degrees above the horizontal position while enteral nutrition is administered.[9]

Beyond aspiration, many other challenges may complicate administration of enteral nutrition. One of the most common issues is clogged feeding tubes. As patients may be receiving multiple medications through enteral feeding tubes, particles of crushed medications may agglomerate, blocking the entry of further medication or enteral nutrition. In unclogging feeding tubes, in addition to mechanical agitation, guidelines recommend use of a solution of a sodium bicarbonate tablet and non–enteric coated pancreatic enzyme tablet mixed with warm water or a carbonated soft drink to help clear the line.[2]

Diarrhea is commonly associated with enteral feeding. A lack of control of diarrhea may necessitate discontinuation of enteral nutrition therapy.[2,9] In patients experiencing diarrhea, it is important to consider the enteral nutrition product formulation. Factors as fiber content, osmolality, mode of delivery, contamination, and presence of short-chain carbohydrates (including fermentable carbohydrates) should be evaluated.[2] Although these factors may increase the risk of diarrhea, it is important to assess alternative causes such as diarrhea related to medication use or diarrhea of infectious origin.[2,9] The addition of soluble fiber to formula may help address enteral nutrition-associated diarrhea in certain individuals.[2]

Enteral Nutrition in Special Populations

Tailored guidelines have been developed for the use of enteral nutrition in pediatric patients, patients with obesity and metabolic disease, as well as renal disease, inflammatory bowel disease, and chronic pancreatitis. Special considerations for these populations are reviewed here.

Pediatric and Adolescent Patients

Guidelines published by The Task Force on Nutrition Support in 2013 addressing the use of enteral nutrition in pediatric patients and adolescent patients emphasize that meeting the nutritional needs of hospitalized children is critical to medical success. As in adults, in the pediatric population, poor nutritional status is associated with longer hospital stays, morbidity, and mortality.[33] However, children have different nutritional needs from adults. Adjusting for weight, pediatric patients tend to have higher caloric requirement than adults as a result of higher resting energy requirements and the caloric demands of growth.[33] In pediatric patients, it is important to consult with experts from several disciplines when formulating a care plan, to consider the patient's gastrointestinal function when selecting an appropriate enteral nutrition formulation, and to use growth progress as an additional outcomes indicator.[33]

> *"In the absence of clinical trials,* ***no specific recommendations can be made*** *regarding the use of pancreatic enzyme therapy with enteral feeding...*
>
> *Some centers suggest crushing or dissolving pancreatic enzymes in the formula; there is no evidence this is effective, and it is against manufacturer guidelines."*
>
> *—Cystic Fibrosis Foundation Evidence-Informed Guidelines*

Cystic Fibrosis

Evidence-based guidelines developed by the Cystic Fibrosis Foundation in 2016 highlight the enteral nutrition administration challenges in patients with cystic fibrosis. Continuous nightly feedings are the preferred delivery method for patients with cystic fibrosis who receive enteral nutrition. As opposed to bolus feedings, administration of enteral feedings overnight improve absorption, provide more nutrients, and allow time off of pump feeding during the day. Intermittent bolus feeds as meal replacements and following suboptimal meals may also be used for patients who do not have adequate oral intake. Enteral nutritional needs must be assessed at each visit in order to calculate nutritional needs and optimize feeding; 30% to 65% of the total estimated caloric and nutritional needs should be provided by enteral feeding. As a part of goal management, patients with cystic fibrosis should be monitored for efficacy of enteral nutrition on measures of growth and BMI, as well as ongoing tolerance to enteral tube feeding. The Cystic Fibrosis Foundation does not recommend for or against a pancreatic enzyme supplement during enteral feeding in patients with CF. Patients with CF receiving EN may take enzymes orally at the start of a nocturnal feed and at the end; if possible, PERT is given in the middle of the feed. Patients with cystic fibrosis should not receive more than 2500 lipase units per kilogram of body weight for each meal (10,000 lipase units per kilogram body weight daily) or less than 4000 daily lipase units for every gram of dietary fat consumed.[34] Although some centers suggest crushing or dissolving pancreatic enzymes in the formula, there is no evidence this is effective, and it is against manufacturer guidelines.[16,34] To eliminate the challenges of PERT administration, the Cystic Fibrosis Foundation indicates RELiZORB may be used to deliver enteral formula in this population.[34]

Obesity in Critical Illness

Guidelines for the management of enteral nutrition therapy in patients with obesity developed by Choban et al were published in 2013. In patients with obesity, nutritional assessment and development of a nutrition support plan should be completed within 48 hours of ICU admission, and may include assessment of BMI and nutritional risk.[35] In these patients, enteral nutrition should meet 65% to 70% of target energy requirements.[9] Although obesity is not consistently associated with an increased risk of mortality, in the ICU setting, patients with obesity are at increased risk of complications versus persons without obesity.[35]

Feedings with high-protein hypocaloric enteral nutrition (ie, enteral nutrition supplying 1.2 grams to 2.5 grams of protein per kg of ideal body weight and while supplying <14 kcal/kg of actual bodyweight, or 50% to 70% of estimated energy needs) may be attempted in patients with obesity who do not have severe renal or hepatic dysfunction.[35] It is important to ensure that critically ill obese patients do not receive low-protein enteral feedings in the setting of hypocaloric feedings, as low-protein hypocaloric feedings are associated with unfavorable clinical outcomes in this population.[35] Vitamin and micronutrient supplementation is especially important in obese patients, and in patients who have undergone bariatric surgery.[35]

Metabolic Disease

Other metabolic issues that often accompany obesity, such as hyperglycemia or insulin resistance require certain additional considerations for enteral nutrition selection. In 2013, guidelines for enteral nutrition management in patients with hyperglycemia published by the American Society for Parenteral and Enteral Nutrition (ASPEN) noted that hyperglycemia (blood glucose level >180 mg/dL) in patients receiving enteral nutrition is associated with adverse outcomes, both in diabetic and nondiabetic patients.[36] Glycemic control should be pursued to achieve a target blood glucose level between 140 mg/dL and 180 mg/dL, with avoidance of hypoglycemia (blood glucose level <70 mg/dL).[36] Importantly, guideline authors do not make any recommendation about use of diabetes-specific enteral formulas in patients with hypoglycemia, citing a need for further research.[36]

Renal Disease

The management of enteral nutrition therapy is needed for patients with renal disease, which includes patient populations with declining renal function, acute kidney injury, or chronic kidney disease.[18] Indirect calorimetry, if available, should be used to assess energy requirements, or individualized intake goals should be established in cases when indirect calorimetry is not available.[18] Because protein and energy wasting are common features of kidney disease, it is important to adjust feeding based on loss of protein in dialysis, ongoing catabolic processes, and renal function.[18]

Inflammatory Bowel Disease

As with patients with renal disease, patients with inflammatory bowel disease (IBD) have specific and unique requirements for appropriate enteral nutrition therapy. As malnutrition and vitamin and mineral

TABLE 4. Elements of Nutritional Assessment Scoring Algorithms[37-40]

Scale	Population	Elements	Rating
Subjective global assessment	General adult population (hospitalized)	• Weight change • Dietary intake • Gastrointestinal symptoms • Functional capacity • Comorbidities related to nutritional needs	**A** (well nourished) **B** (moderately malnourished or suspected of being moderately malnourished) **C** (severely malnourished)
NRS-2002	General adult population	*Initial assessment:* • BMI level • Time (in months) to exhibit a >5% weight loss (1 month, 2 months, or 3 months) • Reduced dietary intake in the past week • Severe illness *Secondary assessment (as indicated after initial assessment):* • Assessment of nutritional status by level weight loss over the past 3 months, BMI, and food intake level • Assessment of severity of disease	**1** (mild) **2** (moderate) **3** (severe)
Mini Nutritional Assessment	Elderly patients	• Food intake over past 3 months • Weight loss during past 3 months • Mobility • Psychological stress or acute disease during past 3 months • Neuropsychological problems • Body mass index or calf circumference	• Normal nutritional status • At risk of malnutrition • Malnourished
NUTRIC	Critically ill patients	• Age • APACHE-II score • SOFA score • Comorbidities • Days hospitalized before ICU admission • IL-6 levels	• **High score** (associated with worse clinical outcomes; aggressive nutritional therapy is indicated) • **Low score** (patients are at low risk of malnutrition)

APACHE-II indicates Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; IL-6, interleukein-6; NUTRIC, Nutrition Risk in Critically ill; NRS, nutritional risk screening; SOFA, Sequential Organ Failure Assessment.

deficiencies are common features of IBD, protein-supplemented enteral nutrition formulas may be used in these patients.[12,15] On an outpatient basis, enteral nutrition may be considered as a possible alternative to corticosteroid therapy in patients with Crohn's disease, as use of formulas supplemented with omega-3 fatty acids has been shown to reduce the risk of relapse over the course of 1 year of therapy.[12] Although long-term use of semielemental enteral nutrition may be used in maintenance of Crohn's disease symptoms, challenges to implementation include tolerability of semielemental formulas and continued insurance coverage for semielemental nutritional therapies.[12]

In addition to use of enteral nutrition as part of corticosteroid-sparing therapy in patients with IBD, enteral nutrition has been shown to improve postsurgical outcomes in patients with IBD. Following surgical intervention in patients with IBD, use of enteral nutrition helps improve rates of clinical remission, improves healing of the gastric mucosa, and has been shown to reduce levels of proinflammatory cytokines in patients with Crohn's disease.[12] Some evidence indicates that preoperative treatment with enteral nutrition is associated with a reduction in postoperative complications.[12]

Pancreatitis

In addition to its use in patients with IBD, patients with acute and chronic pancreatitis may benefit from enteral nutrition therapy to reduce steatorrhea and achieve adequate energy intake. Approximately 10% to 15% of patients with chronic pancreatitis will require oral nutritional supplementation, and enteral tube feeding may be required long-term in approximately 5% of patients. In mild acute pancreatitis, enteral nutrition is generally not necessary unless normal oral nutrition is not possible due to pain. However, in severe necrotizing pancreatitis, enteral nutrition is indicated, if possible, and may be supplemented with parenteral nutrition. Use of enteral nutrition may be initially limited in patients with chronic pancreatitis due to abdominal pain, although caloric intake may be adjusted after pain is reduced. In an effort to improve the absorption and tolerability of enteral nutrition in patients with pancreatitis, semielemental formulas with medium-chain triglycerides and low fiber are often used.[21] A new strategy has become available to clinicians, a product that can hydrolyze enteral formulas as they are infused into the patient. In a recent study, 5 patients with chronic pancreatitis received enteral nutrition hydrolyzed by the iLipase bead complex of RELiZORB. After a single

enteral feeding, patients who received formula prehydrolyzed with RELiZORB had a 19% increase in fat absorption (P = .054), measured by plasma essential fatty acids (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) concentration 8 hours after administration.[30]

Assessing Outcomes in Enteral Nutrition Therapy

A variety of nutritional scoring assessments are available in enteral nutrition therapy. Algorithms have the common goal of improving outcomes through assessment and appropriate reassessment of patients. Patient-specific factors should be considered, including the patient's comorbidities, and the effect of these comorbidities on nutritional needs. The intended population for use and elements for scoring of enteral nutrition therapy quality are reviewed in **Table 4**.[37-40] Evaluating and assessing patients using these systems is an important element of ensuring appropriate nutrition, both in ensuring that the initial enteral feeding regimen meets patient needs, and that continuing therapy is appropriate given each patient's changing clinical situation.[37-40]

Summary

Enteral nutrition encompasses a variety of formulas that may be administered orally or through feeding tubes, including surgically implanted feeding tubes. Optimizing enteral nutrition therapy includes considering a patient's nutritional status at baseline, the patient's disease-specific nutritional needs, and the appropriate duration of therapy. Because use of enteral nutrition is associated with improved clinical outcomes versus parenteral nutrition, enteral nutrition should be used whenever possible. Formulation-specific issues related to palatability, tolerability, macronutrient balance, and macronutrient characteristics should be considered. Patient-specific factors (eg, pancreatic function) may also play a role in selection and administration of appropriate treatments. ■

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