Chapter 166: Enteral Nutrition

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CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Chapter 60, Nutrition Assessment and Support.

KEY CONCEPTS

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1. The gastrointestinal (GI) tract defends the host from toxins and antigens by both immunologic and nonimmunologic mechanisms, collectively referred to as the gut barrier function. Whenever possible, enteral nutrition (EN) is preferred over parenteral nutrition (PN) because it is associated with a lower risk of metabolic and infectious complications and is less expensive and invasive.

2. Candidates for EN are those with a sufficiently functioning GI tract to allow adequate nutrient absorption who cannot or will not eat and in whom enteral access can be safely obtained.

3. Critically ill patients benefit from early initiation of EN. It is acceptable to deliver EN at low rates (eg, trophic feeds) for the first week in most ICU patients. However, this method may not be appropriate for severely malnourished patients who should have their EN advanced to goal as quickly as tolerated.

4. The most common route for both short- and long-term EN access is directly into the stomach. The method of delivery may be continuous via an infusion pump, intermittently via a pump or gravity drip, or bolus administration via gravity or syringe.

5. Patients unable to tolerate tube feeding into the stomach because of impaired gastric motility may benefit from feeding tube placement into the duodenum or jejunum. When feeding into the small bowel, the continuous method of delivery via an infusion pump is required to enhance tolerance.

6. Selection of the enteral feeding formulation depends on nutritional requirements, the patient's primary disease state and related complications, and nutrient digestibility and absorption. A standard polymeric formulation is appropriate for the majority of adults.

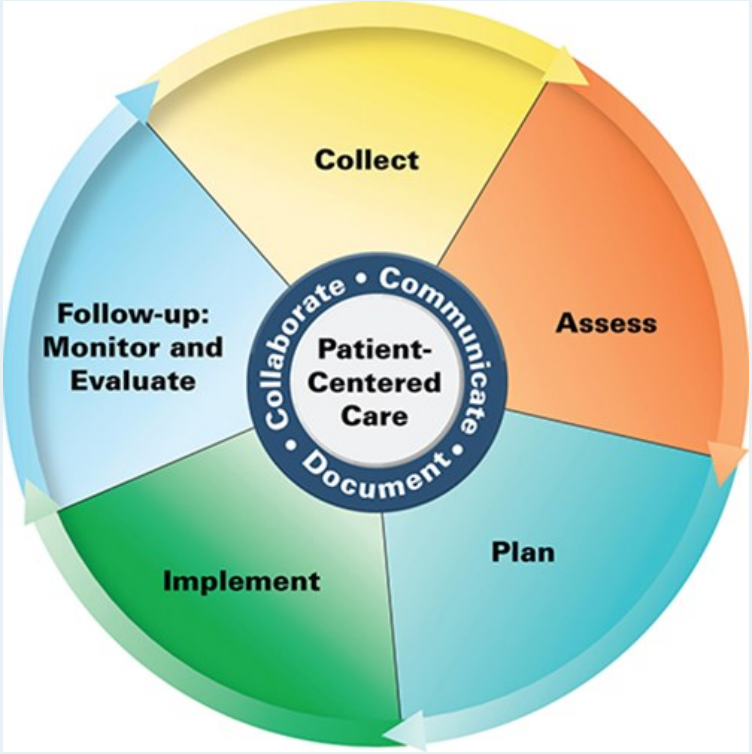
7. Management of diarrhea in patients receiving EN should focus on identification and correction of the most likely cause(s). Tube feeding-related causes include too rapid delivery or advancement, intolerance to the formula composition, and occasionally formula contamination.

8. Medication administration through a feeding tube requires selection of an appropriate dosage form and verification of appropriate enteral access. Medications that should not be crushed and administered through a tube include enteric-coated or sustained-release capsules or tablets and sublingual or buccal tablets.

9. The coadministration of medications with EN can result in alterations in bioavailability and/or changes in the desired pharmacologic effects. Numerous medications are known to interact with EN including phenytoin, warfarin, levothyroxine, select antimicrobials, antacids, and proton-pump inhibitors.

PATIENT CARE PROCESS

Patient Care Process for the Use of Enteral Nutrition



Collect

- Patient characteristics (eg, age, sex)
- Patient history (past medical, surgical, family, social—alcohol use)
- Nutrition history (dietary history, weight history, dietary intolerance, prior enteral, or parenteral nutrition therapy)
- Current medications (including nutritional supplements)
- Current diet and current nutrition support regimen
- Procedures related to enteral access placement
- Objective data
  - Height, weight, body mass index (BMI)
  - Fluid balance (intake and output)
  - Labs (eg, serum electrolytes, SCr, blood urea nitrogen [BUN], glucose, albumin)
  - Other diagnostic tests when indicated (eg, abdominal imaging, gastric emptying study, swallow study)

Assess

- Appropriate time to initiate EN

- Presence of altered GI anatomy or function (eg, intestinal surgeries, delayed gastric emptying, pancreatic insufficiency)
- Nutritional status and risk of refeeding syndrome (eg, unintentional weight loss, prolonged-time period with poor nutritional intake, BMI <18 kg/m^2, low visceral proteins, muscle wasting)
- Nutrition requirements (goal protein, calories, fluid, and micronutrient intake)
- Appropriate enteral access (see Table 166-3)

Plan

- EN regimen includes specific enteral feeding formulation, method of administration (continuous, bolus), and initiation and advancement guidelines (see Table 166-5).
- Monitoring parameters for efficacy (weight, enteral intake), GI tolerance (stool output, nausea, vomiting, abdominal distension), and metabolic complications (serum electrolytes, SCr, BUN, glucose, liver function tests [LFTs]; see Table 166-6).

Implement

- Initiate EN when the oral route fails or is not possible, the GI tract is functional, and enteral access can be safely achieved
- Patient education when home EN is indicated

Follow-up: Monitor and Evaluate*

- Determine nutrition goal attainment
- Provide adjustments to the EN regimen when nutrition goals are not achieved and consider transition to PN if repeated adjustments fail or intolerance develops
- Transition off EN when nutrition needs are safely met by oral dietary intake
- Presence of adverse medication reactions and GI intolerance
- Plan for transitioning off EN

****Collaborate with patient, caregivers, and other health professionals.***

BEYOND THE BOOK

BEYOND THE BOOK

Visit the "Feeding Tube Awareness Foundation" Website <https://www.feedingtubeawareness.org> and navigate to "Tube Feeding Basics." The webpage contains information on each type of feeding tube. The information is presented in a patient education format and is useful to enhance student understanding of the types of feeding tubes available, how these appear when inserted into a patient, and general clinical and patient considerations for each tube. This will aid in the COLLECT and ASSESS steps in the patient care process.

INTRODUCTION

Enteral nutrition (EN) is defined as the delivery of nutrients by tube or by mouth into the gastrointestinal (GI) tract. This chapter focuses on nutrient delivery through a feeding tube rather than oral food ingestion. The terms *enteral nutrition* and *tube feeding* are thus used interchangeably in this context. The goal of EN is to provide calories, macronutrients, and micronutrients to those patients who are unable to achieve these requirements

from an oral diet. Increased recognition of malnutrition, along with improvements in enteral access techniques, feeding formulations, and methods to prevent and manage complications, have resulted in an increased use of EN across all healthcare settings. In this chapter, principles and practices related to the safe and successful use of EN therapy are described.

GASTROINTESTINAL TRACT PHYSIOLOGY

The GI tract plays a key role in the processing of ingested foods. Many of the processes involved in digestion, absorption, and utilization of nutrients are modifiable by the presence of acute and chronic illnesses.

Digestion and Absorption

Digestion and absorption are GI processes that generate the body's usable fuels.[1,2] Ingested nutrients are primarily large polymers that cannot be absorbed across the intestinal cell membrane unless they are transformed into an absorbable molecular form. Digestion consists of the stepwise conversion of a complex chemical and physical nutrient into a molecular form that is absorbable by the intestinal mucosa.[1] Absorption from the GI tract is a multistep process that includes the transfer of a nutrient across the intestinal cell membrane. The nutrient ultimately reaches the systemic circulation through the portal venous or splanchnic lymphatic systems, provided that the GI or biliary tract does not excrete it. In addition, a coordinated interplay of GI motility and neurohormonal secretion is required to facilitate adequate digestion and absorption.

Nutrient digestion involves the complex coordination of multiple mechanical, enzymatic, and physiochemical processes.[1,2] Mechanical dissolution of food occurs by chewing, then mixing and grinding the stomach contents. Food stimulates the secretion of numerous hormones and enzymes from the salivary glands, stomach, liver and biliary system, pancreas, and intestines (Table 166-1). As food traverses the gut lumen, these hormones modulate GI motility and the secretions from other organs of the digestive system. Nutrient absorption occurs within the gut lumen and is a specific function of the intestinal cell membrane, which is comprised of fingerlike projections called villi. Each individual villus is made up of epithelial cells called enterocytes. The enterocyte surface contains special luminal projections called microvilli, which provide an increased surface area that is referred to as the brush-border membrane.

TABLE 166-1

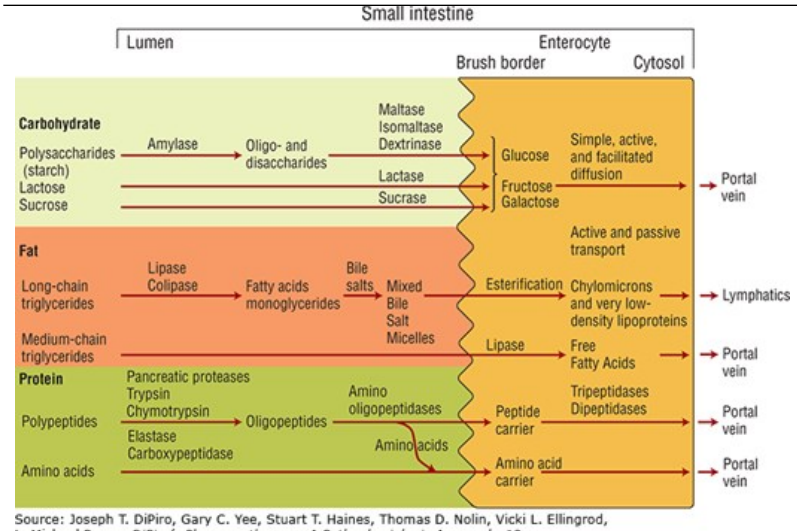
Gastrointestinal Enzymes and Hormones

Enzyme/Hormone	Site of Secretion	Main Actions
Amylase	Salivary glands, pancreas	Converts carbohydrates, starch, and glycogen to simple disaccharides
Cholecystokinin	Duodenum, jejunum	Stimulates pancreatic enzyme secretion and gallbladder contraction
Chymotrypsinogen	Pancreas	Breaks down proteins into peptides
Enteroglucagon	Duodenum, small intestine	Inhibits pancreatic enzyme secretion and bowel motility
Gastric inhibitory peptide	Small intestine	Decreases gastric motility and stimulates insulin secretion
Gastrin	Stomach, duodenum	Stimulates gastric acid secretion and mucosal growth
Glucagon	Pancreas	Stimulates hepatic glycogenolysis and inhibits motility
Lipase	Pancreas	Hydrolyzes dietary fat to release fatty acids
Pancreatic polypeptide	Pancreas	Inhibits gallbladder contraction and pancreatic and biliary secretion
Pepsinogen	Stomach	Converts large proteins into polypeptides
Secretin	Small intestine	Stimulates hepatic and pancreatic water and bicarbonate release
Trypsinogen	Pancreas	Breaks down proteins into peptides
Vasoactive inhibitory peptide	Small intestine, pancreas	Vasodilator; stimulates water and bicarbonate secretion, insulin and glucagon release, and small bowel secretions

The digestion and absorption of carbohydrates, fat, and protein within the small intestine are illustrated in Fig. 166-1. Carbohydrates are presented to the small intestine in either a digestible or a nondigestible form. Polysaccharides (starches) and oligosaccharides (sucrose and lactose) undergo enzymatic digestion to simple sugars. The simple sugars are absorbed via active and passive transport mechanisms and are eventually released into the portal vein. Polysaccharides, such as cellulose complexes and other fiber components, pass undigested to the colon, where they are digested by bacteria and enzymes to short-chain fatty acids. Colonic absorption of short-chain fatty acids stimulates sodium and water reabsorption. The short-chain fatty acids serve as a systemic energy source and provide nourishment for the colonic mucosa cells.

FIGURE 166-1

Schematic of carbohydrate, fat, and protein digestion.



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

Fat is most often presented to the small intestine as long-chain triglycerides. Fat digestion requires pancreatic lipase release and formation of mixed bile salt micelles, which are then absorbed across the intestinal enterocyte. Within the enterocyte, triglycerides are reesterified and packaged into chylomicrons that are then transported into the lymphatic system. Medium-chain triglycerides (MCTs) can be absorbed intact by the mucosal membrane and are acted on by intracellular lipase within the enterocyte to release free fatty acids that pass directly into the portal vein.[3]

Protein is presented to the small intestine primarily as large polypeptides and to a lesser extent as free amino acids because of protein denaturation in the stomach. Polypeptide digestion generates oligopeptides, which are further hydrolyzed to dipeptides and tripeptides. Peptide absorption occurs via a peptide transport system while free amino acids are absorbed via specific amino acid transporters. These peptide carriers are efficient, whereas free amino acid absorption is free amino acid absorption is less efficient.[2]

Understanding the mechanisms involved in digestion and absorption can greatly enhance the rational use of EN in patients with normal or altered GI anatomy and/or function. Various circumstances may alter the efficacy of nutrient digestion and absorption. For example, pancreatic insufficiency may result in malnutrition associated with inadequate absorption of fat and fat-soluble vitamins.

Gut Host Defense Mechanisms

1 Besides digesting and absorbing nutrients to maintain nutritional health, the GI tract is actively involved in defending the host from toxins and antigens by both immunologic and nonimmunologic mechanisms.[4] These gut host defense mechanisms are collectively referred to as the gut barrier function. The gut barrier acts to prevent the systemic spread of intraluminal bacteria and endotoxins to other organs and tissues. Hydrochloric acid secreted by the stomach kills most of the bacteria ingested with food. Under normal circumstances, a mucus layer coats the intestinal epithelium and thereby alters the adherence of bacteria to the cells of the GI tract but provides a favorable environment for anaerobic bacteria. Anaerobic bacteria, which normally colonize the mucus layer, aid in preventing tissue colonization by potential pathogens. Small bowel peristalsis further prevents bacterial stasis and overgrowth. The gut barrier function is also maintained by the intestinal immune system, known as the gut-associated lymphoid tissue (GALT). GALT regulates the local immune response to antigens within the GI tract. Specific immunoglobulins are secreted to kill the remaining organisms and neutralize any toxins they produce. The liver Kupffer cells help to maintain gut barrier function by clearing the portal blood of gut-derived bacteria and endotoxins. Gut barrier integrity may be affected negatively by numerous pathogenic insults, such as physiologic stress and ischemia, and a variety of medications, including chemotherapeutic agents. The administration of certain probiotics can modify intestinal flora and may have beneficial effects in various disease states and patient populations by positively affecting the maintenance of gut barrier function and intestinal immune function.[5,6]

INDICATIONS FOR ENTERAL NUTRITION

2 The decision to initiate EN is based on a variety of factors. Suitable candidates are those who cannot or will not eat a sufficient amount to meet their nutritional requirements, those who exhibit a sufficient functioning GI tract to allow for nutrient absorption, and those in whom a method of

enteral access can be safely initiated.[7,8] Thus, EN may be indicated in a variety of conditions or disease states (Table 166-2). For example, patients who have difficulty swallowing due to stroke, altered mental status, or obstruction in the head, neck, or esophagus due to cancer may benefit from EN.

TABLE 166-2

Potential Indications for Enteral Nutrition

Neoplastic disease
- Chemotherapy
- Radiation therapy
- Upper GI tumors
- Cancer cachexia

Organ dysfunction
- Liver disease/failure
- Kidney disease/failure
- Cardiac cachexia
- ARDS/ALI
- Bronchopulmonary dysplasia
- Congenital heart disease
- Organ transplantation

Hypermetabolic states
- Closed head injury
- Burns
- Trauma
- Postoperative major surgery
- Sepsis

GI disease
- Inflammatory bowel disease
- Short bowel syndrome
- Esophageal motility disorder
- Pancreatitis
- Fistulas
- Gastroesophageal reflux disease (severe)
- Esophageal or intestinal atresia

Neurologic impairment
- Comatose state
- Cerebrovascular accident
- Demyelinating disease
- Severe depression
- Cerebral palsy

Other indications
- AIDS
- Anorexia nervosa
- Complications during pregnancy
- Failure-to-thrive
- Geriatric patients with multiple chronic diseases
- Inborn errors of metabolism
- Cystic fibrosis

AIDS, acquired immune deficiency syndrome; ALI, acute lung injury; ARDS, acute respiratory distress syndrome.

Critically ill patients who are endotracheally intubated represent a large percentage of hospitalized patients requiring EN. Traditionally, EN in the critically ill population was regarded as supportive care designed to provide nutrients during the period of time the patient was unable to maintain adequate oral dietary intake. EN may also be used as a tool to modulate the stress response to critical illness and improve patient outcomes. Nutrition guidelines support the initiation of EN in critically ill adults who are unable to maintain volitional intake, and this can usually be achieved by feeding directly into the stomach.[9-11] Some of these patients may have reduced gastric emptying caused by sepsis, GI surgery, anesthetic agents, opioid analgesics, and underlying pathology, such as diabetic gastroparesis and burns. However, successful EN can often still be achieved by advancing the tip of the feeding tube beyond the pylorus into the duodenum, or preferably into the jejunum. Small bowel feeding may also be appropriate for patients with gastric outlet obstruction, those with pancreatitis, those with moderate-to-severe gastroesophageal reflux, or those with high aspiration risk.

Contraindications to EN use are distal mechanical intestinal obstruction, bowel ischemia, and necrotizing enterocolitis. Contraindications to tube

placement include active peritonitis and uncorrectable coagulopathy.[1,12] Conditions that may result in challenges to EN use include severe diarrhea, protracted vomiting, enteric fistulas, severe GI hemorrhage, hemodynamic instability, and intestinal dysmotility.

BENEFITS OF ENTERAL NUTRITION

The importance of maintaining nutrient delivery through the GI tract in patients without a contraindication to its use is well supported. The beneficial effects of EN, specifically in the critically ill patient, are further enhanced if EN is initiated within 24 to 48 hours of admission to an intensive care unit (ICU).[9-11]

Enteral Versus Parenteral Nutrition

Historically, comparisons of EN and parenteral nutrition (PN) in critically ill adult patients have demonstrated a decrease in infectious complications with the use of EN.[13] Infectious complications are thought to be less common with EN in part because EN supports functional gut integrity by stimulating bile flow and the release of endogenous trophic agents, such as cholecystokinin, gastrin, and bile salts. Provision of enteral nutrients help maintain the intestinal mucosal villous height and support the mass of secretory immunoglobulin A (IgA)-producing immunocytes that comprise the GALT. In the setting of critical illness or severe injury, adverse changes in gut permeability and gut barrier function that result in increased risk for systemic infection and multiorgan dysfunction syndrome have been noted. By supporting gut integrity, the enteral feeding route is thought to lower infection risk and minimize organ failure.[9]

The use of EN in patients with abdominal trauma, burns, severe head injury, major surgery, and acute pancreatitis is generally thought to lower infectious complications compared to PN. This reduction in infectious complications is primarily associated with a lower incidence of pneumonia and catheter-related bloodstream infections and a decrease in abdominal abscess in trauma patients.[13] However, the use of EN as the preferred route for early nutritional support in critically ill patients has been challenged.[14-16] EN is more physiologic than PN in terms of nutrient utilization and therefore is generally associated with fewer metabolic complications, such as glucose intolerance and elevated insulin requirements.[17] Enteral formulations contain both complex and simple carbohydrates, which results in slower carbohydrate absorption compared with the simple carbohydrate, dextrose, used in PN. In addition, enteral formulations that contain fiber and/or a high-fat content will further slow carbohydrate absorption and reduce blood glucose elevations by delaying gastric emptying, accounting for better blood glucose control when carbohydrates are given via the enteral route. An additional physiologic benefit of enteral feeding is that it stimulates bile flow through the biliary tract and thus reduces the risk of developing cholestasis, gallbladder sludge, and gallstones, conditions that have been associated with long-term PN and bowel rest.[18] EN avoids the potential infectious and technical complications associated with the placement and the use of a central venous access device required for PN. Finally, EN is less costly than PN when all factors associated with the therapy are considered.

Timing of Initiation

The timing of initiation of EN in the critically ill patient is of clinical significance. Initiating EN in the first 24 to 48 hours following admission to the ICU is associated with decreased disease severity and infectious complications when compared with the initiation of feedings after 48 hours.[9-11] Early EN has also been associated with a decrease in the release of inflammatory cytokines and fewer effects on gut permeability.[9] In addition, a trend toward reduction in mortality associated with early EN has been noted.[9-11]

In critically ill patients who are hemodynamically unstable, there is concern that EN may result in bowel necrosis because of poor gastric perfusion and increased oxygen demand. It is recommended that initiation of EN be delayed until the patient is fluid resuscitated and vasopressors are being withdrawn or are infusing at low, stable doses.[9] EN is well-tolerated in patients receiving lower doses of vasopressors, and early EN has been associated with decreased mortality in patients receiving vasopressors.[19,20] Therefore, early EN (within 24-48 hours after hospital admission) can safely be initiated in most critically ill adult patients.[9-11] Early EN initiation is not warranted for previously well-nourished, mild-to-moderately stressed adult patients who are not critically ill. When oral intake is inadequate, it is reasonable to delay the initiation of EN for 5 to 7 days in these patients.[7] In the mild-to-moderately stressed adult patient who is moderately to severely malnourished, most clinicians would initiate EN sooner.

ENTERAL ACCESS

Advances in enteral access techniques have contributed to the expanded use of EN for conditions in which PN had previously been used. In particular, improved methods of achieving jejunal access for feeding have allowed the use of EN during the early postoperative and postinjury period when gastric motility is typically impaired. As outlined in Table 166-3, various factors influence the selection of enteral access site and device, including anticipated duration of use and whether to feed into the stomach or small bowel. Figure 166-2 illustrates the predominant enteral access options.

FIGURE 166-2

Access sites for tube feeding.

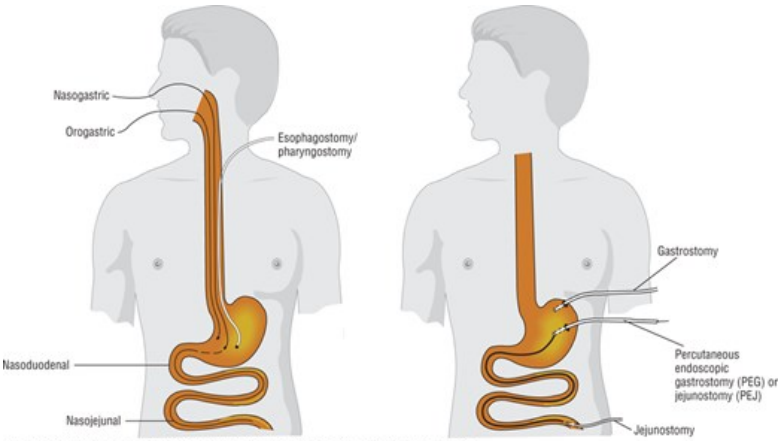


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TABLE 166-3

Options and Considerations in the Selection of Enteral Access

Access	EN Duration/Patient Characteristics	Tube Placement Options	Advantages	Disadvantages
Nasogastric or orogastric	• Short-term • Intact gag reflex • Normal gastric emptying	Manually at bedside	• Ease of placement • Allows for all methods of administration • Inexpensive • Multiple commercially available tubes and sizes	• Potential tube displacement • Potential increased aspiration risk
Nasojejunal	• Short-term • Impaired gastric motility or emptying • High risk of GER or aspiration	• Manually at bedside • Fluoroscopically • Endoscopically	• Potential reduced aspiration risk • Allows for early postinjury or postoperative feeding • Multiple commercially available tubes and sizes	• Manual transpyloric passage requires greater skill • Potential tube displacement or clogging • Bolus or intermittent feeding not tolerated
Gastrostomy	• Long-term • Normal gastric emptying	• Surgically • Endoscopically • Radiologically • Laparoscopically	• Allows for all methods of administration • Low-profile buttons available • Large-bore tubes less likely to clog • Multiple commercially available tubes and sizes	• Attendant risks associated with each type of procedure • Potential increased aspiration risk • Risk of stoma site complications
Jejunostomy	• Long-term • Impaired gastric motility or gastric emptying • High risk of GER or aspiration	• Surgically • Endoscopically • Radiologically • Laparoscopically	• Allows for early postinjury or postoperative feeding • Potential reduced aspiration risk • Multiple commercially available tubes and sizes • Low-profile buttons available	• Attendant risks associated with each type of procedure • Bolus or intermittent feeding not tolerated • Risk of stoma site complications

EN, enteral nutrition; GER, gastroesophageal reflux

Short-Term Access

Short-term enteral access is easier to initiate, less invasive, and less costly than the establishment of long-term access.[21] The most frequently used routes for short-term enteral access are established by inserting a tube through the nose or mouth and passing the tip into the stomach (nasogastric [NG], orogastric [OG]), or jejunum (nasojejunal [NJ], orojejunal [OJ]). In general, these tubes are used in the hospitalized patient when the anticipated

tube feeding duration is less than 4 to 6 weeks. The orogastric route is generally reserved for patients in whom the nasopharyngeal area is inaccessible. Because these routes do not require surgical intervention, they are the least invasive options. The most common technique for placement is blind passage at the bedside by trained medical personnel. Several techniques have been described in the literature to help facilitate bedside placement, and greater skill is required to advance the tip of the feeding tube beyond the pylorus and into the small bowel.[12] Metoclopramide, a prokinetic agent, has been used with variable success to aid passage of the tube beyond the pylorus. A bedside electromagnetic tube placement device has also been used to guide tip position into the small bowel by attracting a metal tip on the end of the tube.[22,23] Alternatively, a variety of endoscopic and fluoroscopic techniques have been described to insert tubes into the small bowel.[12,21] Radiographic confirmation of appropriate tip placement should be obtained prior to use for all bedside placed feeding tubes.[12,24]

NG tubes vary in diameter and stiffness. Large-bore (greater than or equal to 14F) rigid NG tubes are used primarily to decompress the stomach (eg, removal of gas and fluid in the setting of an ileus or obstruction) but can also be used for feeding. There is a low incidence of clogging with these tubes, and they provide a reliable way to measure gastric residual volumes (GRVs). The major disadvantages associated with the use of these tubes are patient discomfort and the risk of irritation or trauma to the gastric mucosa. Small-bore nasal tubes designed solely for feeding are available in varying lengths (12-60 inches [30-152 cm]) and diameters (3.5F-12F) to accommodate both pediatric (including neonates) and adult patients. The tip of the tube can be placed into the stomach or into the duodenum or jejunum (also referred to as transpyloric placement). These tubes consist of a lightweight, pliable silicone or polyurethane material that is designed for patient comfort. A disadvantage of small-bore tubes is that they more easily occlude, often as a result of improper medication administration or flushing technique. The feeding tube is frequently held in place only by a piece of tape on the nose or face; therefore, it can be inadvertently dislodged relatively easily. Nasal bridles have been used with variable results to secure the nasoenteric tube in place.[12] A bridle involves passing a piece of thin tubing or suture into one nostril, then around the bony portion of the nose, and out the other nostril, and finally tying the tubing around the feeding tube.

4 In general, gastric feeding is the least expensive and the least labor-intensive method for enteral feeding; however, feeding into the stomach is not always tolerated. Patients with impaired gastric motility may be predisposed to aspiration and pneumonia when fed into the stomach. Many critically ill, injured, and postoperative patients exhibit delayed gastric emptying, which limits their ability to tolerate gastric feeding. In addition, patients with diabetic gastroparesis or patients with severe gastroesophageal reflux disease or intractable vomiting are at a higher risk for aspiration of gastric contents, which can result in pneumonia. In these patients, placing the tip of the tube into the duodenum or jejunum may be used as a method to decrease aspiration risk.[12] Transpyloric feeding has been associated with a lower rate of vomiting and ventilator-associated pneumonia when compared to NG feeding. However, the difference in aspiration and aspiration pneumonia risk associated with gastric and small bowel feeding is inconclusive.[9] In general, small bowel feeding may be beneficial in patients who do not tolerate gastric feeding and offers an alternative option for EN prior to resorting to PN.[9-11]

Long-Term Access

Feeding tubes used for short-term enteral access are usually not optimal for long-term use because of patient discomfort, complications, and mechanical failures that develop over time. Long-term access should generally be considered when the need for EN is anticipated to be longer than 4 to 6 weeks. Many techniques can be used to establish long-term enteral access, including laparotomy, laparoscopy, endoscopic and image guidance (eg, fluoroscopy and ultrasound).[12] The ability to perform the various techniques is somewhat dependent on the expertise and facilities available within each institution. Long-term enteral access options include gastrostomy and jejunostomy tubes.

A gastrostomy is the most common type of long-term enteral access. It eliminates the nasal irritation and discomfort associated with nasoenteric feeding tubes and inadvertent removal is uncommon. In addition, because feeding gastrostomies use large-bore tubes, clogging is less of a problem. The most commonly placed is the percutaneous endoscopic gastrostomy (PEG). The technique is minimally invasive and can be performed safely and cost-effectively in an endoscopy suite or at the bedside using conscious sedation and local anesthesia in adult patients. Gastrostomy tubes are available in various sizes (12F-28F; 0.8-5 cm shaft lengths) and materials (eg, silicone and polyurethane) and have different retention mechanisms. Since smaller-diameter tubes are prone to more frequent occlusion and dysfunction, the largest diameter size possible is preferred. For patient convenience, comfort, and cosmetic appearance, a low-profile skin-level gastrostomy device may be used. It is typically placed as an exchange tube for a preexisting gastrostomy or jejunostomy once the tract has matured but can also be used at the time of initial tube placement. This “gastric button” consists of a short, silicone, self-retaining conduit with either a mushroom-type or a balloon-type tip at the internal end and a one-way valve and small flange at the skin surface. Because this averts the external tube presence, it tends to be preferred in children or ambulatory adults who are receiving

intermittent feedings. The exit site of all gastrostomies requires general stoma care to prevent inflammation and infection. Routine replacement of the gastrostomy tube at defined intervals (usually 3-6 months) is a standard of practice of many clinicians to prevent failure of the retention mechanism that can occur over time.[12]

In patients with a functional bowel but impaired gastric motility, pancreatitis, or who otherwise do not tolerate gastric feeding and require long-term enteral access, a jejunostomy may be an appropriate option.[21] Various endoscopic and fluoroscopic techniques are available for direct jejunostomy placement. A surgically placed jejunostomy may also be an option. For patients who require small bowel feeding with simultaneous gastric decompression, a gastrojejunal (GJ) tube may be placed utilizing various endoscopic, fluoroscopic, and surgical techniques.[21] Because jejunostomies use smaller-bore tubes, occlusion occurs more commonly than with gastrostomy tubes. GJ tubes are often replaced every 3 to 6 months to prevent occlusion.

There are ethical implications regarding the determination of appropriate candidates for long-term feeding tube placement.[12,25-27] Because a gastrostomy is relatively easy to place and many patients, families, and clinicians overestimate the benefits of EN, it is prone to inappropriate use. In certain patient populations, such as those with advanced dementia or other near end-of-life conditions, the placement of a gastrostomy is not recommended. Artificial nutrition and hydration (ANH) do not promote the healing of pressure ulcers, increase patient comfort or functional status, or prolong survival when compared to hand feeding in patients with advanced dementia.[25] From a clinical standpoint, ANH does not increase a patient's comfort or improve the nutrition parameters of most terminally ill individuals and can result in medical complications.[25] Survival rates are not improved in older adults with advanced dementia who receive tube feedings, and it is associated with substantial burden, including agitation, greater use of physical and chemical restraints, recurrent aspiration, and tube-related complications.[26,27] Evaluation by a multidisciplinary team is warranted for all patients near the end of life to establish whether the benefit of EN outweighs the risks of feeding tube placement.[25-27]

ADMINISTRATION METHODS

EN may be administered by continuous, cyclic (continuous rate over a portion of the day), intermittent (infused over 20-60 minutes), or bolus (generally given in 5-10 minutes) methods and may be accomplished by syringe, gravity, or pump-controlled techniques. The delivery method depends on the location of the tip of the feeding tube, the patient's clinical condition and intestinal function, and the patient's tolerance to the tube feeding.

Continuous

Pump-assisted continuous administration of EN is generally the method of choice for most hospitalized patients, especially when initiating therapy. They may be candidates for transitioning to intermittent or bolus feeding for long-term use as their medical condition stabilizes, as described below. However, when EN is to be delivered into the small intestine, the continuous method is always preferred because it is associated with enhanced tolerance. The rapid delivery of feeding into the small intestine may contribute to abdominal distension, cramping, hyperperistalsis, and diarrhea. Therefore, conversion to intermittent or bolus administration is not recommended for those with jejunostomies.

The delivery system for continuous administration generally includes a feeding set with an attached reservoir bag or spike set that connects to a feeding container. The feeding set is attached to a pump and then connected to the patient's enteral access tube with an adaptor. Continuous administration may increase nursing time because routine checks are needed, but this disadvantage is usually offset by the improved tolerance. For adults, target EN administration rates generally range from 50 to 125 mL/hr, although this varies considerably based on the EN formula and specific needs of the patient. The primary disadvantage to this method of administration is the cost and inconvenience associated with the pump and administration sets. In the home care setting, battery-operated ambulatory enteral pumps that fit into a backpack with the feeding bag are available to allow the patient greater mobility.

Cyclic

A patient who is not eating well during the day because of complaints of fullness and lack of appetite or who is not able to consume enough calories during the day to meet increased needs (eg, trauma and burns) may benefit from cyclic EN, in which the enteral feeding is administered by pump during part of the day—this typically occurs at night. In addition, nocturnal EN administration will free the patient from the pump during the day and allow for greater mobility. This increased mobility may be particularly useful for the home patient or patient requiring therapy for physical rehabilitation during the day. This method may be used in patients with either gastric or small bowel access.

Bolus

The bolus administration of EN is commonly used for patients in the home or long-term care setting who have a gastrostomy. This administration technique involves the delivery of the enteral feeding formulation over 5 to 10 minutes. Essentially, the only equipment needed is a syringe to instill the feeding volume into the tube. Depending on the patient's nutritional requirements, a feeding volume of 240 to 500 mL is generally used and repeated four to six times daily. From a convenience standpoint, it is generally preferable to adjust the bolus volume in increments of the feeding formulation container size (usually 240-250 mL). Bolus delivery is not appropriate for patients with duodenal or jejunal access, as it may result in cramping, nausea, vomiting, aspiration, and diarrhea. Bolus administration should also be avoided in patients with delayed gastric emptying and in patients who are at high risk of aspiration.

Intermittent

The intermittent method is used in patients with a gastric feeding tube who may be experiencing intolerance to bolus administration over 5 to 10 minutes. In this scenario, the prescribed volume is administered over a longer duration, generally 20 to 60 minutes every 4 to 6 hours. For this method, the desired volume of feeding formulation is emptied into a reservoir bag or container with attached tubing and administered by an enteral pump or via gravity drip using a roller clamp. The bolus and intermittent methods of administration are more consistent physiologically with normal eating patterns compared to the continuous method.

INITIATION AND ADVANCEMENT PROTOCOL

Guidelines for the initiation and advancement of enteral feeding formulations vary greatly and are primarily tailored to patient tolerance. The typical recommendation for continuous EN administration for adults is to start at 20 to 50 mL/hr and advance by 10 to 25 mL/hr every 4 to 8 hours until the desired goal is achieved. For intermittent administration, the typical recommendation is to start with 120 mL every 4 hours and advance by 30 to 60 mL every 8 to 12 hours.[7] Schedules for progression of tube feeding from initial to target rates are important and may influence tolerance. If the protocol is too conservative, it may take an excessively long period of time to reach nutrient goals. The development of an EN protocol within an institution that outlines initiation and advancement criteria is recommended to optimize achievement of nutrient goals.[9,11] Due to frequent interruptions of EN, some institutions have implemented volume-based feeding protocols to improve success in meeting targeted goals. Such a protocol shifts the focus from an hourly rate target goal to a 24-hour volume goal and provides guidance on how to adjust the rate of administration when EN is interrupted for reasons unrelated to GI tolerance such as surgeries or procedures.[28,29]

The optimal dose of EN in critically ill adult patients is a subject of debate. The intentional use of permissive underfeeding (50%-80% of goal) or trophic EN (10-20 mL/hr) in critically ill adult patients requiring short ICU lengths of stay may result in improved GI tolerance and similar short-term outcomes when compared to full feeding.[9] However, the strategy of intentional underfeeding may not be appropriate for patients at high nutrition risk as defined by validated scores accounting for nutrition status, disease severity, preexisting malnutrition, and co-morbidities. Patients who are severely malnourished or at high nutrition risk should have their EN advanced toward their energy goal over 24 to 48 hours while monitoring for refeeding syndrome. This is due to an association with lower mortality in critically ill patients at high nutrition risk who receive adequate nutrition.[9,30]

WATER FLUSHES

All feeding tubes require routine flushing with water before and after administration of EN and medications.[24] Flushing may be done manually with a syringe or via the tube feeding pump. Feeding tubes should be flushed immediately before and after bolus or intermittent feedings and at standard intervals (eg, a minimum of 30 mL every 4 hours) with continuous feedings. Safe drinking water is an appropriate flushing source for most patients. Purified water is the preferred flushing source for immunocompromised or critically ill patients. Any fluid needs unmet by the tube feeding formula itself can be achieved via tube feeding water flushes.[24]

ENTERAL FEEDING FORMULATION SELECTION

Historically, enteral formulas were designed primarily to provide essential nutrients. Over the years, enhancements have been made to meet specific

patient needs and improve tolerance. For example, nutrient composition has been enhanced by changing the content of the amino acids (eg, glutamine and arginine), increasing the omega-3 polyunsaturated fatty acid content, and adding ribonucleic acid (RNA) to enhance immune function and improve therapeutic outcomes. These specific nutrients have been called pharmaconutrients or immunonutrients because of the intent to use them to modify the activity of the immune system and improve clinical outcomes.[31] Enteral feeding formulations are categorized by the Food and Drug Administration (FDA) as medical foods.[32] They are considered components of supportive care and are simply regulated to ensure sanitary manufacture. Unfortunately, they are not subject to rules governing health claims, and the promotion of medical foods for therapeutic intent is not regulated by the FDA.[32]

The macronutrient content of enteral formulas (namely, protein, carbohydrate, and fat) varies in nutrient complexity (Table 166-4). Nutrient complexity refers to the amount of hydrolysis and digestion a substrate requires prior to intestinal absorption. Polymeric or intact substrates are of similar molecular form as the foods we eat. Enteral formulas that contain partially hydrolyzed or elemental substrates are characterized as elemental or defined-formula diets. The caloric contribution of each of the macronutrients is as follows: carbohydrates, 4 kcal/g (17 kJ/g); protein, 4 kcal/g (17 kJ/g); and fat, 9 kcal/g (38 kJ/g).

TABLE 166-4

Enteral Formula Nutrient Complexity

Nutrient	Polymeric or Intact	Partially Hydrolyzed or Elemental
Carbohydrate	• Starches • Fruit, vegetable, cereal solids • Glucose polymers • Corn syrup solids • Polysaccharides	• Oligosaccharides • Maltodextrins • Disaccharides • Maltose, sucrose, lactose • Monosaccharides • Glucose • Galactose
Fat	• Long-chain triglycerides • Polyunsaturated fatty acids • Corn oil • Safflower oil • Soybean oil • Canola oil • Marine oils	• Medium-chain triglycerides • Coconut oil • Palm kernel oil • Free fatty acids • Linoleic
Protein	• Whole • Egg, milk, wheat, whey • Isolates • Caseinate salts • Lactalbumin	• Oligopeptides • Dipeptides • Tripeptides • L-Amino acids

Protein Composition

The essential amino acid content of the protein source determines the quality of the protein, and most commercially available enteral feeding formulations contain proteins of high quality. The form of the protein source in enteral formulas will determine the amount of digestion that is required for absorption. Polymeric or intact protein sources require digestion to smaller peptides and free amino acids before absorption. Protein

sources, such as meat, milk, eggs, and caseinates, require digestion by hydrochloric acid, specific protein enzymes, and pancreatic proteases. Enteral formulations may also contain protein sources that are partially hydrolyzed to peptides or L-amino acids. As the molecular form of protein is reduced in size, the osmotic load of the enteral formulation is increased. Many commercially available enteral feeding formulations contain combinations of intact and partially hydrolyzed protein sources. Most enteral formulations are gluten-free.

Conditionally Essential Amino Acids

Glutamine and arginine are generally considered nonessential amino acids. However, during periods of high physiologic stress, the need for these nutrients may be increased beyond the body's synthetic ability; consequently, these amino acids are characterized as conditionally essential. Because they are usually present in low amounts in most enteral feeding formulations, formulations targeted for the critically ill may be supplemented with glutamine and/or arginine.

Glutamine serves as a key fuel for rapidly dividing cells, including enterocytes, endothelial cells, lymphocytes, and fibroblasts. The primary site of glutamine production is skeletal muscle. During critical illness, skeletal muscle catabolism provides an increased glutamine supply, but this may not be enough to meet the high rate of glutamine used by cells of the immune system and other cells involved in recovery and repair. Glutamine depletion may develop, particularly during prolonged periods of metabolic stress. Favorable outcomes have been documented in subtypes of critically ill patients when enteral formulations have been supplemented with glutamine.[9] Immune-modulating EN formulas containing glutamine are specifically recommended in patients with traumatic brain injury due to their association with decreased infections.[9] However, high dose glutamine supplementation in critically ill patients with shock and multisystem organ failure should be avoided.[9,33]

Arginine has been added to some immune-modulating enteral formulations in concentrations that range from 4.5 to 14 g/L. Immune-modulating EN formulas containing arginine in combination with fish oil in perioperative patients in the surgical ICU is associated with decreased infections and decreased length of stay.[9] However, arginine supplementation remains controversial, especially in patients with sepsis.[31] Many of arginine's physiologic effects are mediated by its conversion to nitric oxide, which, in turn, modulates immune function, inflammation, and vasodilation. Some of these effects may be potentially harmful in the patient with sepsis, especially when higher arginine intakes are used.[9] Unfortunately, the effects of individual immunonutrients have not been extensively evaluated.

Carbohydrate Composition

The carbohydrate component of enteral feeding formulations usually provides the major source of calories. Polymeric or intact enteral formulations contain starches and numerous types of glucose polymers, which require digestion to monosaccharides prior to intestinal absorption (see Fig. 166-1). As the extent of hydrolysis of carbohydrates increases within an enteral formulation, the osmolality of the formulation increases. Simple sugars, such as glucose and galactose, contribute significantly to the osmolality of enteral formulations. Consequently, polymeric entities, rather than elemental sugars, are preferred. Glucose polymers provide a useful carbohydrate source that is tolerated by most individuals (see Table 166-4). The polymers are large chains that provide minimal osmotic load, yet are absorbed easily in the intestine. The one shortcoming of glucose polymers and oligosaccharides is that they are not as sweet as simple glucose and thus may decrease the palatability of orally consumed products. Finally, almost all commercially available enteral feeding formulations used in adults and older children are lactose-free because disaccharidase production within the gut lumen is reduced during illness and periods of prolonged bowel rest and because lactose intolerance is relatively common in the general adult population.

Fat and Fatty Acid Composition

Fat is an important constituent in the diet because it provides a concentrated calorie source and serves as a carrier for fat-soluble vitamins. Sufficient linoleic acid is required to prevent essential fatty acid deficiency and should approximate at least 1% to 3% of total daily calories. The most common fat sources in enteral feeding formulations are vegetable oils (soy or corn) that are rich in polyunsaturated fatty acids. The fat concentration varies between less than 2% and 45% of total calories. High dietary fat content is associated with delayed gastric emptying. Enteral feeding formulations can also contain fat in the form of MCTs derived from palm kernel or coconut oils. Because MCTs do not contain linoleic acid, enteral formulations that contain MCTs will also have a source of long-chain triglycerides to provide essential fatty acids. Potential advantages of MCTs compared to long-chain triglycerides are that they are more water soluble, undergo rapid hydrolysis, require no pancreatic lipase or bile salts for absorption, and do not require carnitine for transport into the mitochondria, where they are converted to energy. They also do not require chylomicron formation for small

bowel enterocyte absorption and are not transported via the lymphatic system.

The source of long-chain fat within some enteral formulations has been modified from omega-6 to omega-3 fatty acids in an effort to modulate the inflammatory response in critically ill patients.[9] The omega-6 fatty acids are high in linoleic acid and are derived from vegetable oil, whereas the omega-3 fatty acids, derived from cold-water fish oils, are high in linolenic acid. Omega-6 fatty acids serve as precursors to certain arachidonic acid-derived cytokines that are potent inflammatory mediators and also decrease cell-mediated immune response, whereas omega-3 fatty acids are precursors for eicosapentanoic acid-derived cytokines which are less inflammatory. It has been proposed that if the dietary proportion of omega-3 fatty acids is increased and omega-6 fatty acids is decreased, less inflammation and immunosuppression may occur during metabolic stress. However, use of enteral formulas containing omega-3 fatty acids in patients with acute respiratory distress syndromes (ARDS) and acute lung injury (ALI) has fallen out of favor, specifically in the medical ICU population with ARDS or ALI. Thus, immune-modulating formulas containing fish oil (in combination with arginine) are reserved for patients requiring EN in the perioperative setting in the surgical ICU.[9]

Fiber Content

Fiber, in both soluble and insoluble forms, is added to several enteral feeding formulations in amounts ranging from 5.9 to 24 g/L. Fiber supplementation is common in clinical practice, primarily because fiber-free enteral formulations are implicated as a contributing factor to both diarrhea and constipation. Soluble fiber stimulates the growth of "healthy" bacteria such as *Bifidobacterium* and *Lactobacillus* species. It undergoes bacterial degradation within the colon to produce short-chain fatty acids, which in turn provide an energy source for colonocytes and trophic effects on the colonic mucosa by promoting sodium and water absorption. Insoluble fiber is undigested and may help decrease GI transit time by increasing fecal weight. Fiber may play an integral role in regulating bowel function with minimal associated risk.[34] Fiber supplementation may be beneficial when long-term EN is required or in patients who experience diarrhea or constipation while receiving a fiber-free enteral formulation. Supplementation with a fermentable soluble fiber is recommended for routine use in all medical and surgical ICU patients who are on a fiber-free EN formula, particularly in the setting of diarrhea, due to possible benefits in maintaining a healthy gut microbiome. Both insoluble and soluble fiber should be avoided in critically ill patients who are at risk for bowel ischemia or severe dysmotility due to potential for bowel obstruction in surgical and trauma ICU patients.[9]

Osmolality and Renal Solute Load

The unit of measure of osmolality is milliosmoles per kilogram (mOsm/kg) or millimoles per kilogram (mmol/kg); iso-osmolar is considered to be approximately 300 mOsm/kg (mmol/kg). Osmolality and renal solute load can affect tolerance to enteral feeding formulations. The osmolality of a given enteral formulation is a function of the size and quantity of ionic and molecular particles, primarily related to the protein, carbohydrate, electrolyte, and mineral content within a given volume. Enteral formulations with greater amounts of partially hydrolyzed or elemental substrates have a higher osmolality than formulations containing polymeric or intact substrates. Therefore, formulations that contain sucrose or glucose, dipeptides and tripeptides, and amino acids are generally hyperosmolar. Increased caloric density also increases the osmolality of an enteral formulation. In general, the osmolality of commercially available enteral feeding formulations ranges from 280 to 875 mOsm/kg (mmol/kg).[32]

Symptoms of gastric retention, diarrhea, abdominal distension, nausea, and vomiting have been attributed to enteral formulations with a high osmolality based on the assumption that higher osmolality draws water into the gut lumen. However, clinical evidence to support this relationship between osmolality and GI tolerance is lacking. The practice of diluting hyperosmolar formulations does not enhance tolerance and is not recommended due to the increased risk of microbial contamination.[17,24] Factors, such as concurrent antibiotic therapy, method of enteral feeding administration, and the formulation's composition, are likely to play a greater role in GI tolerance than the osmolality.

The renal solute load is determined by the protein, sodium, potassium, and chloride content of the enteral formulation. Formulations that contain a greater solute load increase the obligatory water loss via the kidney. It is estimated that 40 to 60 mL of water is the minimal amount necessary to excrete 1 g of nitrogen. Those receiving high-protein enteral formulations unable to ingest or tolerate supplemental water may be at risk for developing dehydration.

CLASSIFICATION OF ENTERAL FEEDING FORMULATIONS

5 Most patients' nutritional needs can be met using a standard enteral feeding formulation; however, certain disease states or clinical conditions may warrant the use of a specialty feeding formulation. Development of an evidence-based, enteral formulary should focus on clinically significant

characteristics of available formulations and avoid duplication. Categorizing enteral feeding formulations according to therapeutic class is necessary for developing a formulary system for adults (Table 166-5).

TABLE 166-5

Adult Enteral Feeding Formulation Classification System

Category	Features	Indications
Standard polymeric	• Isotonic • 1-1.2 kcal/mL (4.2-5 kJ/mL) • NPC:N 125:1-150:1 • May contain fiber	• Designed to meet the needs of the majority of patients • Patients with functional GI tract • Not suitable for oral use
High protein	• NPC:N <125:1 • May contain fiber	• Patients with protein requirements >1.5 g/kg/day, such as trauma patients and those with burns, pressure sores, or wounds • Patients receiving propofol
High caloric density	• 1.5-2 kcal/mL (6.3-8.4 kJ/mL) • Lower electrolyte content per calorie • Hypertonic	Patients requiring fluid and/or electrolyte restriction, such as kidney insufficiency
Elemental	• High proportion of free amino acids • Low in fat	• Patients who require low fat • Use has generally been replaced by peptide-based formulations
Peptide-based	• Contains dipeptides and tripeptides • Contains MCTs	• Indications/benefits not clearly established • Trial may be warranted in patients who do not tolerate intact protein due to malabsorption
Disease-specific		
Kidney	• Caloric dense • Protein content varies • Low electrolyte content	Alternative to high caloric density formulations, but generally more expensive
Liver	Increased branched-chain and decreased aromatic amino acids	Patients with hepatic encephalopathy
Lung	• High fat, low carbohydrate • Anti-inflammatory lipid profile and antioxidants	Patients with ARDS and severe ALI
Diabetes mellitus	High fat, low carbohydrate	Alternative to standard, fiber-containing formulation in patients with uncontrolled hyperglycemia

Immune-modulating	Supplemented with glutamine, arginine, nucleotides, and/or omega-3 fatty acids	• Patients undergoing major elective GI surgery, trauma, burns, head and neck cancer, and critically ill patients on mechanical ventilation • Use with caution in patients with sepsis • Select nutrients may be beneficial or harmful in subgroups of critically ill patients
Oral supplement	• Sweetened for taste • Hypertonic	Patients who require supplementation to an oral diet

ALI, acute lung injury; ARDS, acute respiratory distress syndrome; MCT, medium-chain triglyceride; NPC, N, nonprotein calorie-to-nitrogen ratio.

Standard Polymeric

A large number of commercially available enteral feeding formulations fall into the standard polymeric formulation category. These formulations are approximately isotonic (300 mOsm/L), provide 1 to 1.2 kcal/mL (4.2-5 kJ/mL), and are composed of intact nutrients in a nutritionally balanced mix of carbohydrates, fat, and protein. They may contain dietary fiber. The nonprotein calorie-to-nitrogen ratio of these products is approximately 125:1 to 150:1. This ratio is a useful parameter for assessing protein density in relation to calories provided (see Chapter 164). Certain feeding formulations in this category may be promoted as high nitrogen but actually fall within standard protein amounts. To maintain isotonicity, many products within this category are not sweetened, making them unpalatable and generally suited only for tube feeding; however, flavored products are available for oral supplementation. The nutrient requirements of the majority of adults receiving EN can generally be met using feeding formulations in this category.

High Protein

Enteral feeding formulations with a nonprotein calorie-to-nitrogen ratio less than 125:1 can be categorized as high protein. The lower the ratio, the higher the protein density in relation to calories provided. In patients with high protein requirements, it is generally unacceptable to use a feeding formulation with standard protein amounts because the volume necessary to meet protein requirements will result in excessive calorie intake. Patients who may be candidates for a high-protein feeding formulation are critically ill patients and those with pressure sores, surgical wounds, and high output enterocutaneous fistulas. In general, adult patients with estimated protein requirements exceeding 1.5 g/kg/day may benefit from a high-protein formulation. High-protein formulations may also be beneficial in mechanically ventilated patients who are receiving propofol for sedation. The vehicle for propofol is a soybean fat emulsion that contains 1.1 kcal/mL (4.6 kJ/mL). At therapeutic dosages, propofol intake can contribute to caloric intake, and a high protein formulation may be beneficial in allowing for the provision of protein requirements while minimizing overfeeding.

High Caloric Density

High caloric density formulations are concentrated to provide less fluid and electrolyte intake in comparison to a standard polymeric formulation. They provide approximately 1.5 to 2 kcal/mL (6.3-8.4 kJ/mL) and similar calorie and protein intake can be achieved as a standard polymeric formulation, using less volume. High caloric density formulations are often necessary for patients who require fluid and/or electrolyte restriction, such as those with heart, kidney, liver, or respiratory failure. Although specialty enteral formulations targeted for acute kidney injury and chronic kidney disease are available, many patients with kidney failure can be managed using a product in this category.

Elemental/Peptide-Based

Formulations in this category contain protein and/or fat components that are hydrolyzed into smaller, predigested forms. Traditionally, enteral formulations in this category were referred to as elemental and contained a high proportion of protein in the form of free amino acids and a low amount of fat. Many of these formulations have been reformulated to provide a portion of the protein in the form of dipeptides and tripeptides and fewer free amino acids because dipeptides and tripeptides are more readily absorbed than an equivalent intake of free amino acids.[35] These peptide-based formulations may be beneficial in patients with impaired digestion or absorption. Peptide-based formulations are generally higher in fat than the more elemental formulations and use MCTs in varying proportions as the fat source.

Evidence to support the use of elemental or peptide-based formulations is limited, and their routine use is generally not recommended. Patients who do not tolerate standard, intact nutrient formulations as a result of malabsorption or short bowel syndrome might be candidates for a trial of a peptide-based formulation. In addition, elemental or peptide-based products that have higher percentages of MCTs and small amounts of long-chain triglycerides may be beneficial for patients with severe pancreatic insufficiency, such as chronic pancreatitis and cystic fibrosis; severe abnormalities of the intestinal mucosa, such as untreated celiac disease; biliary tract disease, such as biliary atresia or severe cholestasis; or chylothorax or chylous ascites.

Disease-Specific

Enteral feeding formulations have also been designed to meet unique nutrient requirements and manage metabolic abnormalities associated with specific disease states. Specialized enteral feeding formulations are marketed for use in adult patients with kidney and liver failure; lung disease, including ARDS; diabetes mellitus; wound healing; and metabolic stress (see Table 166-5).

Specialized enteral formulations designed to modulate the inflammatory response in adult patients with severe metabolic stress have been referred to as immune-modulating formulations or immunonutrition. These formulations are supplemented with nutrients such as glutamine, arginine, antioxidants, nucleotides, and omega-3 polyunsaturated fatty acids, because of their potential role in regulating immune function. However, nutrition guidelines recommend against the routine use of immune-modulating enteral formulations in the medical ICU population due to the lack of benefit and potential harm. These formulas should be reserved for patients in the surgical ICU and in patients with traumatic brain injury where beneficial effects have been demonstrated.[9,36,37]

Diabetes-specific formulas are lower in carbohydrate and higher in fat and fiber compared to standard formulas.[38] They contain slowly digestible carbohydrates and their primary fat sources are omega-3 fatty acids and monounsaturated fatty acids. The rationale for this combination of ingredients is to slow gastric emptying and improve glycemic control. Use of diabetes-specific formulas in hospitalized patients may lead to an improvement in glycemic control and a decrease in total insulin requirements, but to date the supporting evidence is limited. Therefore, in hospitalized patients with diabetes mellitus or stress-induced hyperglycemia, a standard enteral formula in combination with pharmacologic management of hyperglycemia is appropriate.[38]

Enteral formulas with lower protein, higher amounts of branched-chain amino acids (BCAAs) (leucine, valine, and isoleucine), and lower amounts of aromatic amino acids (AAAs) have been marketed for use in patients with hepatic encephalopathy. However, these formulations may result in under-dosing protein in a population with a high prevalence of malnutrition. Additionally, they do not improve outcomes in patients with hepatic encephalopathy and are therefore not recommended for routine use in this patient population.[32]

Oral Supplements

In general, oral supplements are not intended for tube feeding but are taken by mouth to enhance an oral diet. They are sweetened to improve taste and therefore are hypertonic (~450-700 mOsm/kg [mmol/kg]), but osmolality is rarely a problem in the patient with a functioning GI tract. However, in the tube-fed patient, a sweetened product is unnecessary and may contribute to GI intolerance, particularly diarrhea. Powder supplements that are mixed with milk should be avoided in lactose-intolerant patients. In addition to liquid supplements, puddings, gelatins, bars, and milkshake-like supplements are available.

Modular Products

A module is a powder or liquid form of a single nutrient (eg, protein, carbohydrate, fat, and dietary fiber) that is used to supplement nutrition intake when the diet or commercially available enteral formulation does not fully meet a patient's needs.[32] Alternatively, formulations available in powder or concentrate can be mixed with less water than needed for the standard dilution to deliver more nutrients in less volume. The mixing process required for modular components increases the potential for bacterial contamination and incorrect preparation. Contamination is a particular concern with the use of blenders and reconstitution of powders.[24] Modular products used to supplement tube feedings should not be mixed with the EN formula but administered separately via a feeding tube similar to the process required for medication administration.

Rehydration

Oral rehydration formulations are useful in maintaining hydration or treating dehydration in patients with high GI output (eg, frequent vomiting, diarrhea, ostomy output). Such formulations are available commercially in powder or liquid form or can be extemporaneously compounded. They can be administered orally or given via a feeding tube. The glucose content of oral rehydration solutions is essential to the absorption of sodium, because it stimulates active transport systems, which, in turn, stimulate passive glucose-coupled sodium and water uptake for rehydration. Therefore, oral or enteral administration of rehydration solutions may decrease fecal water loss and generate a positive fluid and electrolyte balance.[39]

FORMULARY AND DELIVERY SYSTEM CONSIDERATIONS

For an institution's enteral formulary, generally no more than one product per category is necessary, and it may be possible to omit certain categories based on the specific patient population cared for within a given institution. Additional selection criteria include container size and type, liquid or powder form, shelf life, ease of use, and cost.

Most enteral products are available as ready-to-use, prepackaged liquids, but a few are available in the powdered state and require reconstitution prior to use. Advantages of ready-to-use liquid formulations are convenience and reduced susceptibility to microbiologic contamination. One disadvantage is that more storage space may be required. The ease or convenience of a ready-to-use liquid is especially important for self-care patients, those with disabilities, and those who have difficulty reading or following printed instructions. Ready-to-use liquid enteral formulations are generally available in ready-to-hang rigid plastic containers or bags (*closed systems*), cans, or bottles. Bolus administration of EN is usually achieved using formulas available in cans or bottles. However, when formula from a can/bottle is used for continuous or cyclic administration, it must first be poured into a feeding bag and attached to an administration set to allow for administration via a pump. This "open system" has a higher risk of microbial contamination than the ready-to-hang containers. The use of a powder formula is also considered an open delivery system.

Contamination of enteral feeding formulations is a potential cause of diarrhea.[7,24] Contamination is caused by a lack of attention to proper handling techniques, inadequate cleaning and disinfection of preparation equipment, and the use of nonsterile or contaminated tube-feeding additives. Unlike liquid formulations, powdered products are not guaranteed by the manufacturer to be sterile because it is not possible to sterilize the powder without destruction of some of its components. Closed-system containers supply a ready-to-hang, prefilled, sterile supply of formula in volumes of 1 to 1.5 L. Most but not all enteral formulations intended for use in adults are available in the closed-administration system. The closed-administration system also offers the advantage of not requiring refrigeration and allowing hang times of 24 to 48 hours, whereas the conventional open-delivery system necessitates hang times of generally 4 to 8 hours.[24]

New enteral connectors are being integrated into the EN marketplace to prevent enteral misconnections and improve patient safety. An enteral misconnection occurs when a component of the enteral feeding system is inadvertently connected to a non-enteral site, such as a tracheostomy tube, peritoneal dialysis catheter, or other medical device or intravenous (IV) tubing. Misconnections are commonly attributed to the use of universal connectors that allow for misconnections between incompatible systems. Due to potential serious patient harm, including death, an international standard (ISO 80369) has been developed to guide the redesign of all small-bore connectors and the new enteral connectors, referred to as the ENFit™ system.[40] The ENFit™ connector provides a unique connection that is not compatible with any other device and has been specifically designed for all nutrition sources, enteral administration sets, enteral syringes, and all feeding tubes.[40] Thus, filling and administration instructions for syringes used to deliver medications via feeding tubes should differ from oral syringes with the implementation of the ENFit™ system. Information about these processes and other resources is available at the Global Enteral Device Supplier Association (GEDSA) Website (www.stayconnected.org).[41]

COMPLICATIONS AND MONITORING

The majority of complications associated with EN are metabolic, GI, or mechanical. The early detection and management of potential complications is necessary to allow for the safe and successful use of EN. In addition, measures to avoid complications should be incorporated into the management of all patients receiving EN (Table 166-6).

TABLE 166-6

Suggested Monitoring for Adult Patients on Enteral Nutrition

Parameter	During Initiation of EN Therapy	During Stable EN Therapy
Vital signs	Every 4-6 hours	As needed with suspected change (ie, fever)
Clinical assessment		
Weight	Daily	Weekly
Total intake/output	Daily	As needed with suspected change in intake/output
Tube-feeding intake	Daily	Daily
Enterostomy tube site assessment	Daily	Daily
GI tolerance		
Stool frequency/volume	Daily	Daily
Abdomen assessment	Daily	Daily
Nausea or vomiting	Daily	Daily
Tube placement	Prior to starting, then ongoing	Ongoing
Laboratory		
Electrolytes, blood urea nitrogen/serum creatinine, glucose	Daily until stable, then 2-3 times/week	Every 1-3 months
Calcium, magnesium, phosphorus	Daily until stable, then 2-3 times/week	Every 1-3 months
Liver function tests	Weekly	Every 1-3 months
Trace elements, vitamins	If deficiency/toxicity suspected	If deficiency/toxicity suspected

EN, enteral nutrition.

Metabolic Complications

Metabolic complications associated with EN are similar to those associated with PN, but the incidence tends to be lower.[17] Critically ill patients, especially those with underlying organ dysfunction, are at the risk of developing complications related to hydration and electrolyte imbalance and altered glucose control. Patients who present with a history of minimal dietary intake for an extended period of time and have experienced significant weight loss are at risk of developing refeeding syndrome, which can be evidenced by hypophosphatemia, hypokalemia, hypomagnesemia, thiamine deficiency, and sodium retention.[42] The frequency of clinical and laboratory assessment to monitor hydration, electrolytes, organ function, and glucose adequately for a patient who is critically ill or at risk of developing refeeding syndrome is greater than for a stable hospitalized patient or patients residing in rehabilitation units or at home (see Table 166-6). Patients receiving long-term EN at home may require laboratory monitoring only every 2 to 3 months, depending on their clinical status. It is also important to evaluate the actual water and micronutrient content provided by the enteral formulation, especially in critically ill patients. Supplemental fluid, electrolytes, and minerals may be required in some patients. Conversely, for patients who have fluid retention or elevated serum electrolytes, the enteral formulation may need to be changed to one that is more concentrated or provides less of a particular nutrient, if available.

Gastrointestinal Complications

6 The GI complications associated with tube feeding include nausea, vomiting, abdominal distension, cramping, aspiration, diarrhea, and constipation. GRV refers to the volume of contents in the stomach and is measured by using a syringe and aspirating from a large-bore NG or gastrostomy tube. Historically, GRV has been used to identify patients at risk of vomiting, aspiration, and/or ventilator-associated pneumonia. However, when GRV alone is used to assess tolerance to EN, it can lead to unnecessary holding of EN and prevent patients from meeting their EN goal.[43] Further, introducing stomach acid into feeding tubes may contribute to clogging. Current guidelines recommend against the use of GRV as part of routine monitoring for ICU patients receiving EN.[9,44] However, some argue that GRV monitoring remains a useful tool in patients at high risk for EN intolerance, and it continues to be used in some practice settings.[44] For ICUs that continue to utilize GRV, avoid holding EN in response to any GRV less than 500 mL in the absence of other symptoms suggesting intolerance (eg, nausea, abdominal pain, distension).[9]

If symptoms of intolerance are present, and GRVs are greater than 500 mL, a decrease in the tube feeding rate or discontinuation may be warranted. Unless GRVs are excessive (greater than 500 mL in adults), they are generally reinstilled through the tube to minimize nutrient, fluid, and electrolyte losses. In patients at high risk for aspiration, clinicians should implement other measures to reduce aspiration risk, including elevating the head of the patient's bed to a 30° to 45° angle, advancement of the feeding tube into the small bowel, and initiation of a prokinetic agent such as metoclopramide or erythromycin.[17,24] Other potential interventions include minimizing the use of narcotics, sedatives, or other agents that may slow gastric emptying and correcting underlying fluid and electrolyte imbalances that can impair GI motility.[24] Aspiration pneumonia is considered the most serious complication associated with tube feeding. Although aspiration is a fairly common event for critically ill patients receiving tube feeding, progression to aspiration pneumonia is difficult to predict. Risk factors for aspiration include a previous aspiration episode, decreased consciousness, neuromuscular disease, structural airway or GI tract abnormalities, endotracheal intubation, vomiting, persistently high GRVs, and prolonged supine positioning.[44] Historically, blue food coloring had been added to enteral formulations in an attempt to detect aspiration. However, because of its low sensitivity for detection and association with several serious adverse medication reactions, including death associated with mitochondrial toxicity, the addition of blue food dye to enteral formulations is not advised. There are no reliable methods available to detect aspiration in enterally fed patients.[9]

Diarrhea is the most common GI complication in patients receiving EN, but the actual incidence is unclear due to the lack of a standard definition and the large number of contributing factors.[7,17] When monitoring for diarrhea, stool frequency, consistency, and volume should be evaluated, and previous bowel habits should be considered. Diarrhea has been defined as more than three liquid stools daily or a stool volume of more than 250 to 500 mL/day for at least 2 consecutive days.[17] Therefore, the intermittent occurrence of one or two loose stools does not constitute diarrhea or require intervention.

7 Diarrhea in patients receiving tube feeding may be caused by a number of factors, and the management should be directed at identifying and correcting the most likely cause(s).[17] Tube feeding-related factors that may contribute to diarrhea include too rapid delivery or advancement of formula, intolerance to the formula composition, administration of large volumes of feeding into the small bowel, and formula contamination. Thus, measures to prevent or manage diarrhea-related directly to the tube feeding should address these potential causes.[17] If diarrhea occurs when using a fiber-free formulation, a fiber-containing formulation or supplement may be considered in hemodynamically stable patients. If using a high-fat formulation, it may be beneficial to switch to a formulation lower in fat or having a higher proportion of the fat supplied as MCTs; although, a high MCT

concentration has also been associated with diarrhea. Finally, it is important to assess the risk of bacterial contamination of the formula and take steps to minimize any potential risk factors. If infectious etiologies have been excluded, severe diarrhea may require pharmacologic treatment with loperamide, diphenoxylate/atropine, or opioids (see Chapter 54).

Medication therapy, particularly the use of broad-spectrum antibiotics, is a common cause of diarrhea that is unrelated to tube feeding. Sorbitol, used as a sweetening agent in many liquid formulations to enhance palatability, is an osmotic laxative that can cause diarrhea. In addition, many medications available in a liquid form are hyperosmolar, which may contribute to diarrhea, especially when these medications are not diluted properly before administration. Because many patients receiving tube feeding also receive medications in a liquid form, all medications should be evaluated for their potential contribution. Malabsorption, secondary to the underlying disease state or condition, may also cause diarrhea. Infectious causes, such as antibiotic-induced bacterial overgrowth by *Clostridioides difficile* or other intestinal flora, need to be considered when diarrhea develops. Certain probiotic strains may have a role in the prevention and treatment of infectious and antibiotic-associated diarrhea.[45] However, the value of adding probiotics to patients on EN in the ICU setting is unclear. The makeup of intestinal flora becomes disrupted in response to antimicrobial treatment and stress response of ICU patients. The use of probiotics has been associated with the reduction of ventilator-associated pneumonia, antibiotic-associated diarrhea, and overall infections in critically ill patients.[5,9] However, the existing evidence is limited. Further, the use of probiotics concomitantly with fiber and jejunal feeding in patients with severe acute pancreatitis increases risk of mortality. Therefore, the use of studied probiotic strains should be considered only for select ICU patient populations such as trauma, pancreatectomy, and liver transplantation.[9]

Mechanical Complications

Mechanical complications of EN are those associated with the feeding tube, including tube occlusion or malposition, and inadvertent nasopulmonary intubation. Feeding tube occlusion usually results from improper medication administration and/or flushing. Kinking of the tube may also cause occlusion. Adult feeding tubes should be flushed with at least 15 to 30 mL of water before and after administering any medication. If more than one medication is scheduled for a given time, each should be administered separately, and the tube should be flushed with 5 to 15 mL of water between medications.[24,46] The frequency of flushing should be at least every 8 hours during continuous feeding and before and after each intermittent feeding. If tube occlusion occurs, the tube should be irrigated with warm water. Other fluids such as carbonated beverages and cranberry juice have been used to irrigate occluded tubes but are likely not any more effective than warm water. Because the acid in these liquids may actually precipitate with protein in the enteral formula and lead to new or worsening of occlusions, this practice should be avoided.[24] Pancreatic enzymes mixed with sodium bicarbonate may be used to reestablish patency in this situation.[46] Declogging devices that are specifically designed to unclog feeding tubes are available. They have been designed to either mechanically break through or remove the occlusion or provide an applicator and syringe prefilled with pancreatic enzymes and various powders targeted to restore patency.[7,46]

Inadvertent nasoenteric tube removal or displacement has been reported in approximately 40% of patients receiving EN.[47] An agitated or confused patient may pull at the feeding tube and cause its removal or malposition. Measures to decrease agitation and confusion should be attempted. Securing the tube with tape may be helpful, as well as marking the tube with permanent ink at the exit site to assess for position change. A nasal bridle that uses a magnetic retrieval system has proven to be a simple and effective method for securing nasoenteric feeding tubes and preventing accidental removal.[48]

When a feeding tube is inserted nasally or orally, there is a risk that the tube may inadvertently enter the tracheobronchial tree. The risk may be higher in patients who have an impaired cough or gag reflex and when a stylet is used for tube insertion. Proper positioning of the tube should always be confirmed by radiography prior to feeding initiation and routinely reassessed to avoid inadvertent administration of enteral formula into the lung.[24]

Other Complications

Infectious complications of feeding tube placement include sinusitis (with nasoenteric placement), exit site-related infections (eg, cellulitis, subcutaneous abscess, necrotizing fasciitis), and intraabdominal infections (eg, peritonitis, abscess). Leaking and bleeding around the exit site can also occur.[12] Formation of excessive granulation tissue around the exit site is often the cause of leaking and bleeding and can be managed by applying silver nitrate and topical corticosteroids.[49]

NUTRITION CARE PLAN

A nutrition care plan that incorporates nutrition assessment and therapy goals should be developed for all patients who require EN (see Chapter 164). Desired outcomes of EN are to promote an adequate nutritional state while minimizing any associated metabolic complications. The EN goals are individualized and based on meeting estimated fluid, calorie, protein, and micronutrient requirements. The desired end point should be included in the care plan. The end point may be resolution of a disease or condition that impairs ability to eat, such as in a critically ill patient who is expected to transition back to an oral diet. EN may be considered a lifelong therapy for those with a permanent impairment that restricts or limits eating, such as gastroparesis.

Assessing the outcome of EN requires monitoring objective measures of body composition, protein and energy balance, and muscle function and wound healing. In addition to optimizing nutrition, the goal of EN is to reduce disease-related morbidity and mortality. Measures of disease-related morbidity include length of hospital stay, infectious complications, and the patient's functional status and sense of well-being. A target weight should be established for each patient and energy content from the EN regimen adjusted as needed to safely achieve or maintain the target weight. Adult patients should generally gain or lose no more than 1 to 2 pounds (~0.45-0.9 kg) per week. EN may be used to supplement an oral diet when oral intake is inadequate and should be modified as needed based on changes in tolerance.

MEDICATION DELIVERY VIA FEEDING TUBE

Using enteral feeding tubes to deliver medications is a common practice and offers an alternative for patients unable to take medications by the oral route. However, in addition to tube occlusion, effects on medication bioavailability and other potential interactions need to be considered when using this route. Medications have been given as a concomitant bolus administration via the feeding tube or admixed with the enteral feeding formulation.

Concomitant Medication Administration

Concomitant administration of medications with enteral feedings can be extremely complicated and potentially deleterious. Depending on the indication for enteral nutrition (eg, inadequate oral intake), oral administration may still be the most appropriate route for medication administration.[24] Therefore, if it is feasible and appropriate, oral medications should be continued to be delivered orally whenever possible. If medication must be delivered through a feeding tube, then larger bore feeding tubes (eg, nasogastric or gastrostomy tubes) are preferred over small bore tubes. Delivering medications directly into the stomach allows for the normal process of drug dissolution. Medication delivery directly into the small bowel, however, may result in alterations in drug dissolution because the stomach is bypassed. In addition, therapeutic effects designed to occur within the stomach, such as with antacids and sucralfate, may not be achieved. Because many medications are best absorbed in the fasting state, care should be taken to ensure proper timing of drug administration relative to EN administration when clinically appropriate. Patients on bolus gastric feeding must receive these medications appropriately spaced between feedings, and patients on continuous feeding may require feeding interruptions for drug administration.

Selecting the proper medication dosage form for coadministration with the tube feeding is another important consideration. If crushing a given solid dosage form results in changes to medication absorption, then it should be avoided. Medications in sublingual form, sustained-release capsules or tablets, and enteric-coated tablets should not be crushed and therefore should not be administered via enteral feeding tubes.[24,46] Solid dosage forms that are appropriate to crush should be prepared as a fine powder and mixed with 15 to 30 mL of purified water or other appropriate solvents before administering through the tube. In addition, many capsules may be opened and the contents administered in the same manner. Pellets contained inside microencapsulated dosage forms should generally not be crushed. It may be acceptable to administer intact pellets through larger bore feeding tubes, provided that the pellets are small enough and drug absorption is not compromised.[50] To avoid the need to crush a solid dosage form, liquid dosage forms are commonly preferred for administration through feeding tubes. However, the risk of GI intolerance should be considered because of the hyperosmolality of many liquid formulations and possible sorbitol content.[46,51] Although the use of a liquid dosage preparation may be more convenient than a solid dosage form, it may not be the best choice if GI intolerance is an issue.

Admixture of Medications with Enteral Feeding

Mixing liquid medications with certain enteral feeding formulations is associated with several types of physical incompatibilities, including granulation, gel formation, separation, and precipitation.[46,51] Not only can these physical incompatibilities inhibit drug absorption, but gel formation may clog small-bore feeding tubes. Physical incompatibility with medications is more common in formulations that contain intact protein than in those with

hydrolyzed protein. Also, medication and enteral formula incompatibilities are more common with the use of acidic pharmaceutical syrups. The most prudent recommendation is to avoid the routine admixture whenever possible, especially for nonaqueous preparations and syrups. In the clinical setting, exceptions do exist, such as adding sodium or magnesium to enteral formulas to assist in maintaining or repleting electrolytes. However, this practice has fallen out of favor, and a closed EN delivery system should be used whenever possible to minimize the risk of contamination.[24]

Drug-Nutrient Interactions

9 The most significant drug-nutrient interactions that can occur during continuous enteral feeding are those in which the drug's bioavailability is reduced, and the desired pharmacologic effect is not achieved (Table 166-7).[52] One of the well-documented interactions is between phenytoin and enteral feeding. Phenytoin serum concentrations may decrease by 50% to 75% when phenytoin is given concomitantly with EN, possibly as a result of the binding of phenytoin to calcium caseinates or protein hydrolysates in the enteral formulation. Management options include holding EN for 1 to 2 hours before and after drug administration in addition to flushing the tube with water before and after medication delivery. The dosing of phenytoin should be divided into two doses per day rather than three divided doses to minimize interruption of EN. If EN cannot be held around the administration of phenytoin suspension per tube, then patients will typically require higher than normal phenytoin doses.[46] The patient's clinical response and phenytoin serum concentrations should be monitored to assure that the desired therapeutic effects are achieved.

TABLE 166-7

Select Medications with Special Considerations for Enteral Feeding Tube Administration

Drug	Interaction	Comments
Phenytoin	• Reduced bioavailability in the presence of tube feedings • Possible phenytoin binding to calcium caseinates or protein hydrolysates in enteral feeding	• To minimize interaction, holding tube feedings 1-2 hours before and after phenytoin has been suggested • Adjust tube-feeding rate to account for time held for phenytoin administration • Monitor phenytoin serum concentration and clinical response closely • Consider switching to IV phenytoin or an alternative treatment option if unable to reach therapeutic serum concentration
• Fluoroquinolones • Tetracyclines	Potential for reduced bioavailability because of complexation of drug with divalent and trivalent cations found in enteral feeding	• Consider holding tube feeding 1 hour before and after administration • Avoid jejunal administration of ciprofloxacin • Monitor clinical response
Warfarin	Decreased absorption of warfarin because of enteral feeding; therapeutic effect antagonized by vitamin K in enteral formulations	• Adjust warfarin dose based on INR • Anticipate need to increase warfarin dose when enteral feedings are started and decrease dose when enteral feedings are stopped • Consider holding tube feeding 1 hour before and after administration
• Omeprazole • Lansoprazole	Administration via feeding tube complicated by acid-labile medication within delayed-release, base-labile granules	• Granules become sticky when moistened with water and may occlude small-bore tubes • Granules should be mixed with acidic liquid when given via a gastric feeding tube • An oral liquid suspension can be extemporaneously prepared for administration via a feeding tube

INR, International normalized ratio.

Decreased bioavailability of certain antibiotics, particularly quinolones, has been documented when coadministered with enteral feeding due to complexation with multivalent cations such as calcium, magnesium, and iron contained in the feeding.[46,50] Although the practice of holding tube feeding for 30 minutes before and 30 minutes after quinolone administration has been recommended, it does not improve drug absorption. Another option is to increase the quinolone dose when given concurrently with EN. Oral ciprofloxacin is absorbed primarily in the duodenum and early jejunum. Ciprofloxacin bioavailability is significantly decreased when given via a jejunostomy tube due to bypassing the site of absorption, so this practice should be avoided.[46]

Warfarin resistance has been documented during enteral feeding, possibly as a consequence of decreased absorption, binding to protein in EN, or the antagonist effects of vitamin K in the feeding formulation. Before 1980, it was thought that the content of vitamin K (up to 1,330 µg/1,000 kcal [or 317 µg/1,000 kJ] of enteral feeding formula) was contributing to the pharmacologic interaction with warfarin. Subsequently, the vitamin K content within

formulas intended for use in adults was reduced to less than 200 µg/1,000 kcal (or 48 µg/1,000 kJ). However, warfarin resistance continues to be reported in patients on EN. Holding EN for one hour before and after warfarin administration along with close monitoring of the International Normalized Ratio is warranted to ensure therapeutic drug concentrations are maintained.[53] Conversely, when EN is discontinued, a reduction in warfarin dosage may be required.

Decreased absorption of levothyroxine has been described in patients receiving continuous EN.[50,54] This is thought to be due to the binding of the medication to the tube feeding formula and/or the binding of thyroid hormones to enteral nutrition during enterohepatic recirculation. Several recommendations have been described, including holding tube feedings for 1 hour before and after medication administration and increasing the dose of levothyroxine while continuous tube feedings are required. Thyroid function tests should be monitored closely (eg, every 7 days) during this time.[54]

CONCLUSION

Identifying appropriate candidates for EN and designing a personalized EN regimen and monitoring plan is a complex process that is often under-appreciated. The successful use of EN can minimize the need for PN in patients unable to meet nutrient requirements with an oral diet. Ultimately, no disease process can improve with prolonged starvation and malnutrition. The American Society for Parenteral and Enteral Nutrition (ASPEN) has identified safety issues related to the administration and management of EN and created practice recommendations based on evidence-based research and expert opinion. These guidelines address the provision and assessment of nutrition support therapy, including EN for adult critically ill patients.[9,24] A multidisciplinary team approach, either as a formal nutrition support service or as a team of caregivers within the practice setting, is recommended to optimize patient outcomes.

ABBREVIATIONS

ALI	acute lung injury
ASPEN	American Society for Parenteral and Enteral Nutrition
ANH	artificial nutrition and hydration
ARDS	acute respiratory distress syndrome
EN	enteral nutrition
FDA	Food and Drug Administration
GALT	gut-associated lymphoid tissue
GI	gastrointestinal
GJ	gastrojejunal
GRV	gastric residual volume
ICU	intensive care unit
IV	intravenous
IgA	immunoglobulin A
MCT	medium-chain triglyceride
NG	nasogastric
NJ	nasojejunal
NPO	nothing by mouth
OG	orogastric
OJ	orojejunal
PEG	percutaneous endoscopic gastrostomy
PN	parenteral nutrition
RNA	ribonucleic acid

REFERENCES

1. Colaizzo-Anas T. Nutrient intake, digestion, absorption, and excretion. In: Mueller CM, ed. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:3–25.

2. Abumrad NA, Nassir F, Marcus A. Digestion and absorption of dietary fat, carbohydrate, and protein. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management*. 10th ed. Philadelphia, PA: Saunders Elsevier; 2016:1736–1764.

3. Hise M, Brown JC. Lipids. In: Mueller CM, ed. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:71–95.

4. Dotan I, Mayer L. Mucosal immunology and inflammation. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management*. 10th ed. Philadelphia, PA: Saunders Elsevier; 2016:16–27.

5. Manzanares W, Langlois PL, Wischmeyer PE. Restoring the microbiome in critically ill patients: Are probiotics our true friends when we are seriously ill? *JPEN J Parenter Enteral Nutr.* 2017;41(4):530–533. doi: 10.1177/0148607117700572

6. Sanders ME, Merenstein DJ, Reid G, et al. Probiotics and prebiotics in intestinal health and disease: From biology to the clinic. *Nat Rev Gastroenterol Hepatol.* 2019;16(10):605–616. doi: 10.1038/s41575-019-0173-3

7. Kozeniecki M, Fritzshall R. Enteral nutrition for adults in the hospital setting. *Nutr Clin Pract.* 2015;30(5):634–651. doi: 10.1177/0884533615594012

8. Doley J, Phillips W. Overview of enteral nutrition. In: Mueller CM, ed. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:213–225.

9. McClave SA, Taylor BE, Martindale RG. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr.* 2016;40(2):159–211. doi: 10.1177/0148607115621863

10. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr.* 2019;38(1):48–79. doi: 10.1016/j.clnu.2018.08.037

11. Dhaliwal R, Cahill N, Lemieux M, et al. The Canadian critical care nutrition guidelines in 2013: An update on current recommendations and implementation strategies. *Nutr Clin Pract.* 2014;29(1):29–43. doi: 10.1177/0884533613510948

12. Itkin M, DeLegge MH, Fang JC, et al. Multidisciplinary practical guidelines for gastrointestinal access for enteral nutrition and decompression from the Society of Interventional Radiology and American Gastroenterological Association (AGA) Institute, with endorsement by Canadian Interventional Radiological Association (CIRA) and Cardiovascular and Interventional Radiological Society of Europe (CIRSE). *Gastroenterol.* 2011;141(2):742–65. doi: 10.1053/j.gastro.2011.06.001

13. McCleary EJ, Tajchman S. Parenteral nutrition and infection risk in the intensive care unit: A practical guide for the bedside clinician. *Nutr Clin Pract.* 2016;31(4):476–489. doi: 10.1177/0884533616653808

14. Doig GS, Simpson F, Sweetman EA, et al. Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition: A randomized controlled trial. *JAMA.* 2013;309(20):2130–2138. doi: 10.1001/jama.2013.5124

15. Harvey SE, Parrott F, Harrison DA, et al. Trial of the route of early nutritional support in critically ill adults. *N Engl J Med.* 2014;371(18):1673–1684. doi: 10.1056/NEJMoa1409860

16. Reignier J, Boisrame-Helms J, Brisard L, et al. Enteral versus parenteral early nutrition in ventilated adults with shock: A randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). *Lancet*. 2018;391(10116):133–143. doi: 10.1016/S0140-6736(17)32146-3

17. Malone AM, Seres DS, Lord LM. Complications of enteral nutrition. In: Mueller CM, ed. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:265–283.

18. Lal S, Pironi L, Wanten G, et al. Clinical approach to the management of Intestinal Failure Associated Liver Disease (IFALD) in adults: A position paper from the Home Artificial Nutrition and Chronic Intestinal Failure Special Interest Group of ESPEN. *Clin Nutr.* 2018;37(6):1794–1797. doi: 10.1016/j.clnu.2018.07.006

19. Sabino KM, Fuller J, May S, et al. Safety and tolerance of enteral nutrition in the medical and surgical intensive care unit patient receiving vasopressors. *Nutr Clin Pract.* 2021;36(1):192–200. doi: 10.1002/ncp.10548

20. Wischmeyer PE. Enteral nutrition can be given to patients on vasopressors. *Crit Care Med.* 2020;48(1):122–125. doi: 10.1097/CCM.0000000000003965

21. Fang JC, Kinikini M. Enteral access devices. In: Mueller CM, ed. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:251–264.

22. McCutcheon KP, Whittet WL, Kirsten JL, et al. Feeding tube insertion and placement confirmation using electromagnetic guidance: A team review. *JPEN J Parenter Enteral Nutr.* 2018;42(1):247–254. doi: 10.1002/jpen.1015

23. Powers J, Luebbehusen M, Aguirre L, et al. Improved safety and efficacy of small-bore feeding tube confirmation using an electromagnetic placement device. *Nutr Clin Pract.* 2018;33(2):268–273. doi: 10.1002/ncp.10062

24. Boullata JI, Carrera AL, Harvey L, et al. ASPEN safe practices for enteral nutrition therapy. *JPEN J Parenter Enteral Nutr.* 2017;41(1):15–103. doi: 10.1177/0148607116673053

25. Schwartz DB, Barrocas A, Annetta MG, et al. Ethical aspects of artificially administered nutrition and hydration: An ASPEN position paper. *Nutr Clin Pract.* 2021;36(2):254–267. doi: 10.1002/ncp.10633

26. American Geriatrics Society Ethics Committee and Clinical Practice and Models of Care Committee. American Geriatrics Society feeding tubes in advanced dementia position statement. *J Am Geriatr Soc.* 2014;62(8):1590–1593. doi: 10.1111/jgs.12924

27. Schwartz DB, Barrocas A, Wesley JR, et al. Gastrostomy tube placement in patients with advanced dementia or near end of life. *Nutr Clin Pract.* 2014;29(6):829–840. doi: 10.1177/0884533614546890

28. McClave SA, Saad MA, Esterle M, et al. Volume-based feeding in the critically ill patient. *JPEN J Parenter Enteral Nutr.* 2015;39(6):707–712. doi: 10.1177/0148607114540004

29. Taylor B, Brody R, Denmark R, et al. Improving enteral delivery through the adoption of the “Feed Early Enteral Diet Adequately for Maximum Effect (FEED ME)” protocol in a surgical trauma ICU: A quality improvement review. *Nutr Clin Pract.* 2014;29(5):639–648. doi: 10.1177/0884533614539705

30. Rahman A, Hasan RM, Agarwala R, et al. Identifying critically-ill patients who will benefit most from nutritional therapy: Further validation of the “modified NUTRIC” nutritional risk assessment tool. *Clin Nutr.* 2016;35(1):158–162. doi: 10.1016/j.clnu.2015.01.015

31. McCarthy MS, Martindale RG. Immunonutrition in critical illness: What is the role? *Nutr Clin Pract.* 2018;33(3):348–358. doi: 10.1002/ncp.10102

32. Roberts S, Kirsch R. Enteral nutrition formulations. In: Mueller CM, ed. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:227–249.

33. Heyland D, Muscedere J, Wischmeyer PE, et al. A randomized trial of glutamine and antioxidants in critically ill patients. *N Eng J Med.* 2013;368(16):1489–1497. doi: 10.1056/NEJMoa1212722

34. Zaman MK, Chin KF, Rai V, et al. Fiber and prebiotic supplementation in enteral nutrition: A systematic review and meta-analysis. *World J Gastroenterol.* 2015;21(17):5372–5381. doi: 10.3748/wjg.v21.i17.5372

35. Young LS, Kim DW. Protein. In: Mueller CM, ed. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:97–112.

36. van Zanten ARH, Sztark F, Kaisers UX, et al. High-protein enteral nutrition enriched with immune-modulating nutrients vs standard high-protein enteral nutrition and nosocomial infections in the ICU: A randomized clinical trial. *JAMA.* 2014;312(5):514–524. doi: 10.1001/jama.2014.7698

37. Rice TW, Wheeler AP, Thompson BT, et al. Enteral omega-3 fatty acid, gamma-linolenic acid, and antioxidant supplementation in acute lung injury. *JAMA.* 2011;306(14):1574–1581. doi: 10.1001/jama.2011.1435

38. Walker R, Tucker AM, Birtcher KK. Diabetes mellitus. In: Mueller CM, ed. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:675–700.

39. Limketkai BN, Hurt RT, Palmer LB. Short bowel syndrome. In: Mueller CM, ed. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:587–601.

40. Guenter P. New enteral connectors: Raising awareness. *Nutr Clin Pract.* 2014;29(5):612–614. doi: 10.1177/0884533614543330

41. Global Enteral Device Supply Associate (GEDSA). Stay Connected. Available at: www.stayconnected.org. Accessed July 19, 2021.

42. da Silva JSV, Seres DS, Sabino K, Adams SC, et al. ASPEN consensus recommendations for refeeding syndrome. *Nutr Clin Pract.* 2020;35(2):178–195. doi: 10.1002/ncp.10474

43. Marik PE. Enteral nutrition in the critically ill: Myths and misconceptions. *Crit Care Med.* 2014;42(4):962–969. doi: 10.1097/Ccm.0000000000000051

44. Elke G, Felbinger TW, Heyland DK. Gastric residual volume in critically ill patients: A dead marker or still alive? *Nutr Clin Pract.* 2015;30(1):59–71. doi: 10.1177/0884533614562841

45. Guarino A, Guandalini S, Lo Vecchio A. Probiotics for prevention and treatment of diarrhea. *J Clin Gastroenterol.* 2015;49:S37–S45. doi: 10.1097/MCG.0000000000000349

46. Williams NT. Medication administration through enteral feeding tubes. *Am J Health Syst Pharm.* 2008;65(24):2347–2357. doi: 10.2146/ajhp080155

47. Gunn SR, Early BJ, Zenati MS, et al. Use of a nasal bridle prevents accidental nasoenteral feeding tube removal. *JPEN J Parenter Enteral Nutr.* 2009;33(1):50–54. doi: 10.1177/0148607108321704

48. Bechtold ML, Nguyen DL, Palmer LB, et al. Nasal bridles for securing nasoenteric tubes: A meta-analysis. *Nutr Clin Pract.* 2014;29(5):667–671. doi: 10.1177/0884533614536737

49. Warriner L, Spruce P. Managing overgranulation tissue around gastrostomy sites. *Br J Nurs.* 2012;21(5):S14–S16, S8, S20 passim. doi: 10.12968/bjon.2012.21.Sup5.S14

50. Wohlt PD, Zheng L, Gunderson S, et al. Recommendations for the use of medications with continuous enteral nutrition. *Am J Health Syst Pharm.* 2009;66(16):1458–1467. doi: 10.2146/ajhp080632

51. Klang M, McLymont V, Ng N. Osmolality, pH, and compatibility of selected oral liquid medications with an enteral nutrition product. *JPEN J Parenter Enteral Nutr.* 2013;37(5):689–694. doi: 10.1177/0148607112471560

52. Chan LN. Drug-nutrient interactions. *JPEN J Parenter Enteral Nutr.* 2013;37(4):450–459. doi: 10.1177/0148607113488799

53. Dickerson RN, Garmon WM, Kuhl DA, et al. Vitamin K-independent warfarin resistance after concurrent administration of warfarin and continuous enteral nutrition. *Pharmacotherapy*. 2008;28(3):308–313. doi: 10.1592/phco.28.3.308

54. Dickerson RN, Maish GO, Minard G, et al. Clinical relevancy of the levothyroxine-continuous enteral nutrition interaction. *Nutr Clin Pract.* 2010;25(6):646–652. doi: 10.1177/0884533610385701

SELF-ASSESSMENT QUESTIONS

1. Enteral administration sets with universal connectors increase the risk of:
   A. Feeding tube occlusions
   B. Tube feeding intolerance
   C. Malpositioning of the feeding tube
   D. Enteral misconnections
2. Which of the following strategies has been recommended to minimize the risk of aspiration in patients receiving enteral nutrition?
   A. Keep the head of the bed elevated to a 30- to 45-degree angle
   B. Add blue food dye to the enteral formula
   C. Change from continuous to bolus administration
   D. Change from standard polymeric to high caloric density formula
3. The end-product of bacterial degradation of fiber within the colon is:
   A. Medium-chain triglycerides
   B. Long-chain triglycerides
   C. Short-chain fatty acids
   D. Omega-3 fatty acids
4. In a patient with gastroparesis who has failed nasogastric feeding and will require long-term enteral nutrition and gastric decompression in the home setting, the *preferred* access choice is:
   A. Nasojejunal
   B. Gastrostomy
   C. Jejunostomy
   D. Gastro-jejunostomy
5. An advantage of the bolus method of enteral nutrition administration compared to the continuous method is that it:
   A. Requires less equipment
   B. Can be used for rapid delivery into the jejunum
   C. Is better tolerated
   D. Can be used with all types of feeding tubes

6. Enteral nutrition should be *avoided* in which of the following patients?

   A. A patient receiving cancer chemotherapy

   B. A patient with >50% total body surface area burn

   C. A patient with bowel ischemia

   D. A patient with acute pancreatitis

7. Which of the following techniques is *most appropriate* for medication administration via a nasogastric feeding tube?

   A. Routinely hold the feeding for one hour before and after administering medications.

   B. Flush the tube with 15 to 30 mL of water before and after administration of each medication

   C. Pellets contained within a microencapsulated dosage form should generally be crushed prior to administration.

   D. If more than one medication is scheduled for the same time, they should be mixed prior to administration.

8. A patient who has a stable INR between 2 and 3 while receiving warfarin with continuous tube feeding is transitioned off of tube feeding to an oral diet. Which of the following INR values is most likely to result after this change?

   A. 1

   B. 1.5

   C. 2.5

   D. 4.5

9. Which of the following is a result of gut barrier dysfunction?

   A. Secretion of immunoglobulins by gut-associated lymphoid tissue (GALT)

   B. Small bowel peristalsis

   C. Bacterial translocation

   D. Secretion of hydrochloric acid by the stomach

10. In an older adult with a history of massive stroke and a hemicolectomy, which of the following is a potential *advantage* of enteral nutrition via a jejunostomy compared with a gastrostomy?

    A. Decreased risk of aspiration

    B. Decreased diarrhea

    C. Decreased infection risk

    D. Decreased cost associated with placement

11. When initiating enteral nutrition in a hospitalized patient with a jejunostomy, which of the following methods is *preferred*?

    A. Continuous infusion at a rate of 120 mL/hr

    B. Continuous infusion at a rate of 20 mL/hr

C. Bolus administration at a dose of 480 mL every 4 hours

D. Intermittent administration at a dose of 480 mL every 4 hours

12. Which of the following is an *advantage* of enteral nutrition compared to parenteral nutrition?

A. Lower risk of aspiration

B. Decreased incidence of gastrointestinal intolerance

C. Lower risk of cholestasis

D. Fewer administration interruptions

13. Which of the following enteral formulas is *most likely* to contribute to the development of diarrhea?

A. Use of a fiber-containing formula

B. Use of a peptide-based formula

C. Use of an MCT-containing, low fat formula

D. Use of a powder formula that requires reconstitution

14. In an adult patient receiving enteral nutrition who experiences a gastric residual volume of 150 mL, which of the following interventions is *preferred*?

A. Hold the feeding

B. Decrease the administration rate

C. Dilute the formulation and continue the same rate

D. No intervention required

15. When should enteral nutrition be initiated in most adult critically ill patients who are mechanically ventilated?

A. Within 6 hours of arrival to the intensive care unit

B. Within 24 to 48 hours of arrival to the intensive care unit

C. After 5 to 7 days of admission to the hospital

D. It depends on the patient's underlying nutritional status

SELF-ASSESSMENT QUESTION-ANSWERS

1. **D.** Enteral misconnections are commonly attributed to the use of universal connectors that allow for inappropriate connections between different delivery systems such as enteral tubing and intravenous tubing. Answers A, B, and C refer to different types of feeding tube complications unrelated to misconnections. See the "Formulary and Delivery System Considerations" section.

2. **A.** One strategy to lower aspiration risk is to elevate the patient's head of the bed to a 30° to 45° angle. Addition of blue food dye to enteral feeding is not recommended due to reports of mitochondrial toxicity from this practice (B is incorrect). Answer C is incorrect because bolus feeding would be more likely to increase aspiration risk. Answer D is incorrect because these are strategies that may affect tolerance to a tube feeding formula is not a standard strategy to reduce aspiration risk. See the"Gastrointestinal Complications" section.

3. **C.** The end-product of bacterial degradation of fiber within the colon is short-chain fatty acids. These fatty acids serve the important role of

providing energy and nourishment for the colonic mucosa. See the "Digestion and Absorption" section.

4. **D.** The enteral tube option that can provide both a route for enteral nutrition and a route for gastric decompression is a gastrojejunostomy tube. This type of tube has two lumens – one that ends in the stomach (for removal of gas and fluid/decompression) and one that ends in the jejunum (for feeding). A, B, and C are incorrect because none of these options provide both a route of decompression and feeding. See the "Long-Term Access" section.

5. **A.** Bolus administration of enteral nutrition (EN) requires less equipment compared to other methods of administration such as continuous or cyclic enteral nutrition, which require a pump. Options B is incorrect because bolus feeding is never appropriate for delivery into the jejunum. C is incorrect because bolus feeds are not typically better tolerated. D is incorrect because bolus feeds are only an option for gastric feeding tubes (not any feeding tube that delivers EN into the small bowel). See the "Administration Methods" section.

6. **C.** Bowel ischemia is considered a contraindication to delivery of enteral nutrition. Answers A, B, and D are incorrect because none of these options are contraindications to EN. See the "Indications for Enteral Nutrition" section.

7. **B.** The feeding tube should be flushed with 15 to 30 mL of water before and after administration of each separate medication. The feeding tube should be flushed with 15 to 30 mL of water before and after administration of each separate medication. Holding EN for 1 hour before and after medication administration is only necessary for medications with known interactions with EN (A is incorrect). Pellets or any extended release dosage forms should not be crushed (C is incorrect). Each medication should be delivered separately and never mixed prior to administration (D is incorrect). See the "Mechanical Complications" and "Medication Delivery via Feeding Tube" sections.

8. **D.** An INR of 4.5 reflects an increase in INR, which corresponds to the transition from continuous EN to an oral diet. Warfarin resistance has been documented during administration with enteral feeding. Therefore, when EN is discontinued, one can expect an increased response to a patient's warfarin dose. Answers A, B, and C are incorrect because these values reflect unchanged or lower INR values. See the "Drug–Nutrient Interactions" section.

9. **C.** Bacterial translocation can occur due to dysfunction of the gut barrier. See the "Gut Host Defense Mechanism" section.

10. **A.** Feeding into the jejunum (eg, small bowel feeding) is a good option for patients at increased aspiration risk such as those with a history of stroke. Answers B, C, and D are incorrect because these options do not correctly describe benefits of jejunal feeding. See the "Enteral Access" section.

11. **B.** Small bowel feeding in hospitalized patients should be initiated at lower rates such as 10 to 30 mL/hr with further advancement to goal as tolerated. Higher volumes associated with bolus or intermittent feedings are not recommended for small bowel feeding (C and D are incorrect). Option A is incorrect because it is too high for an initial rate when EN is first started. See the "Initiation and Advancement Protocol" section.

12. **C.** Enteral nutrition is associated with a lower risk of cholestasis compared to parenteral nutrition because EN stimulates bile flow through the biliary tract. Patients requiring bowel rest and parenteral nutrition are at increased risk for cholestasis due to the lack of bile flow stimulation. Options A, B, and D are incorrect because these are all complications that are more common with EN than parenteral nutrition. See the "Enteral Versus Parenteral Nutrition" section

13. **D.** The process of reconstituting enteral nutrition introduces a higher risk of contamination which is a potential cause of diarrhea. Options A, B, and C are incorrect because these describe alternative EN formulas that may improve diarrhea attributed to EN. See the"Formulary and Delivery System Considerations" section.

14. **D.** Routine monitoring of gastric residual volume (GRV) is not recommended because it can lead to unnecessary hold of EN and potentially even increase the risk for clogging of the feeding tube. However, if GRV is used as a monitoring tool, avoid holding EN in response to any GRV less than 500 mL unless other symptoms of intolerance are present. Therefore, no intervention is required for a single GRV of 150 mL in the absence of other symptoms (D is correct; A, B, C are incorrect). See the"Gastrointestinal Complications" section.

15. **B.** Guidelines for critically ill adults recommend the initiation of enteral nutrition within 24 to 48 hours of arrival to the intensive care unit for most adults. While subsets of patients may benefit for early EN, such as within 6 hours, most ICU patients are still undergoing resuscitation during this time and it may not be feasible or advisable to initiate EN at this point (A is incorrect). EN initiation after 5 to 7 days is appropriate for well-

nourished, non-critically ill patients in the hospital but this is too long to go without EN for critically ill adults (C is incorrect). Current guidelines refer to nutrition status and nutrition risk as important factors for considering how quickly a nutrition regimen is advanced to goal, but this does not play into the recommendation on when EN should be initiated in the ICU (D is incorrect). See the "Timing of Initiation" section.