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Complications of Enteral Nutrition

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CONTENTS

Objectives

Understand the risk factors, signs and symptoms, and management of gastrointestinal (GI) complications, including nausea and vomiting, abdominal distention, malabsorption, diarrhea, and constipation.

Consider the risk for complications related to pulmonary aspiration of enteral formulations and the methods to detect and prevent aspiration-related problems.

Compare the metabolic complications associated with enteral nutrition (EN) vs parenteral nutrition (PN).

Review strategies to identify and prevent dehydration in patients receiving EN.

Test Your Knowledge Questions

1. Which of the following actions is most appropriate for enhancing gastric emptying during the administration EN?

A. Keep the bed in Trendelenburg position.
B. Decrease the rate of a continuous feeding infusion, or change from bolus to continuous feeding.
C. Switch to an enteral formulation with a higher fat content.
D. Switch to an enteral formulation with a higher protein content.

2. Which of the following is the most appropriate initial action for the management of tube feeding–associated diarrhea?
A. Change to an enteral formulation with fiber.
B. Review the patient's medication administration record to determine whether hyperosmolar agents are being administered.
C. Change to a peptide-based enteral formulation.
D. Use an antimotility agent.

3. Which of the following methods is not recommended to minimize contamination of enteral feeding formula?
A. Washing hands and donning clean gloves before preparing enteral formula.
B. Immediate use of enteral formula from a newly opened container.
C. Infusing reconstituted powdered formulas or formulas with added modular components in 1 bag for up to 8 hours.
D. Changing an "open" feeding container every 24 hours.

Test Your Knowledge Answers

1) The correct answer is B. Factors that delay gastric emptying include large boluses of fluid given at one time, increased rate of formula infusion, increased fat content of the solution, and infusion of solutions colder than room temperature. Elevation of the head of the bed (HOB) and turning of the patient slightly to the right side allows gravity to help drain the stomach; however, such positions are often difficult to achieve in the hospital environment.
2) The correct answer is B. If clinically significant diarrhea develops during EN, the most appropriate initial action is to evaluate whether hyperosmolar medications that could result in liquid stooling are being administered. If none are in use, testing for the presence of Clostridium difficile; if those results are negative, the addition of fiber from a formulation that contains fiber or supplemental fiber may be beneficial. Adding an antimotility agent or changing to a peptide-based formula should be considered if diarrhea continues despite these initial interventions. PN should be initiated only if the other treatment modalities fail.

3) The correct answer is C. A formula prepared from reconstituted powder or with added modular components should be infused for no more than 4 hours. Infusion times greater than 4 hours are associated with formula contamination. The use of good handwashing technique and clean gloves and immediately using a newly opened formula container will minimize contamination. Changing an "open" feeding container every 24 hours will minimize bacterial growth that can contaminate formula.

Background

Enteral tube feeding is the preferred feeding modality when the GI tract is functional and the patient is unable or unwilling to consume an adequate oral diet. The enteral route is promoted as an efficacious and cost-effective method of providing nutrients to patients (see Chapter 10). However, enteral tube feeding is not without its challenges. The administration of EN may be complicated by disease, illness, or trauma; treatment side effects; and iatrogenic conditions. Distinguishing the potential causes of a complication is essential to preventing or managing it. GI, pulmonary aspiration, and metabolic complications that can contribute to a patient's morbidity and mortality are reviewed in this chapter. Chapter 12 reviews complications specific to enteral feeding devices, and Chapter 18 discusses drug-nutrient interactions.

Clinicians must thoroughly evaluate patients before EN is initiated to identify and, when feasible, avoid or minimize potential problems. Ongoing monitoring and reassessment should be a standard component of follow-up care.

Gastrointestinal Complications

Nausea and Vomiting

Nausea and/or vomiting occur in 7% to 26% of critically ill patients who receive EN support.1–3 Vomiting, especially in minimally responsive patients, is believed to increase the risk of pulmonary aspiration, pneumonia, and sepsis. Multiple etiologies exist for nausea and vomiting with EN. Delayed gastric emptying is the most commonly identified problem.4–6 Potential causes of slowed emptying include the following:

- Diabetic gastropathy
- Hypotension
- Sepsis
- Stress
- Anesthesia and surgery
- Infiltrative gastric neoplasms
- Various autoimmune diseases
- Surgical vagotomy
- Pancreaticoduodenectomy

- Opiate analgesic medications (morphine sulfate, codeine, fentanyl)
- Anticholinergics (chlordiazepoxide hydrochloride and clidinium bromide)
- Excessively rapid infusion of formula
- Infusion of a very cold solution or one containing a large amount of fat or fiber

If delayed gastric emptying is suspected, appropriate interventions include reducing or discontinuing all narcotic medications, switching to a low-fiber, low-fat, and/or isotonic formula, administering the feeding solution at room temperature, temporarily reducing the rate of infusion by 20 to 25 mL/h, changing the infusion method from bolus to continuous, and/or administering a prokinetic agent such as metoclopramide or erythromycin.5,6,10–12 Once tolerance is achieved, the rate or volume will typically be gradually increased every 6 to 24 hours until nutrition goals are met.5,6 If nausea or vomiting occurs as the rate of administration or bolus volume of the EN increases, the rate or volume should be reduced to the greatest tolerated amount, with an attempt to increase the rate again after symptoms abate. If these efforts to increase the rate/volume of EN fail, small bowel access (eg, nasojejunal tube or transgastric jejunostomy tube) should be considered.

Abdominal distention in a patient with nausea indicates a need to monitor the abdomen closely—before the next bolus tube feeding or every 4 hours for continuous feeding. As discussed in greater detail later in the chapter, gastric residual volume (GRV) is often used to assess EN tolerance. However, elevated GRVs alone do not correlate with intolerance.14 Furthermore, in a prospective, randomized trial, checking GRVs did not decrease the incidence of ventilator-associated pneumonia (VAP) in critically ill patients,15 and the Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN) do not recommend routine checks of GRVs in critically ill patients.14

If GRVs are low but nausea persists, patients may benefit from antiemetic medications. Clinicians should also monitor stool frequency in patients who complain of nausea. Obstipation or fecal impaction may lead to distention and nausea, particularly in institutionalized patients or those with chronic critical illness. Distention and vomiting may be caused by diarrheal illness such as Clostridium difficile colitis.

Abdominal Distention

Abdominal and gastric distension are common reasons why EN is interrupted.1,2 Distention and its associated symptoms of bloating and cramping may be caused by GI ileus, obstruction, obstipation, ascites, or diarrheal illness. Additionally, excessively rapid formula administration or infusion of very cold formula may contribute to abdominal distention. Use of fiber-containing formulas can cause abdominal distention because fiber ferments and produces gas in the gut. Theoretically, the role of fiber in slowing gastric emptying may also be a factor.

Abdominal distention is diagnosed by visual inspection and palpation as well as from patient reports. Attempts have been made to define distention objectively (eg, an increase of abdominal girth of more than 8 to 10 cm),16 but careful clinical evaluation remains the most practical means of assessment. If an ileus or bowel obstruction is suspected based on physical examination and symptoms, it may be confirmed by a flat and upright abdominal x-ray. However, upright films are often impractical in hospitalized patients and these “plain” films may be nondiagnostic. Therefore, cross-sectional imaging

(eg, computed tomography) may be needed to confirm the diagnosis. Nevertheless, plain radiology remains the appropriate screening method if ileus or obstruction are suspected.

Another simple method of assessing distention, particularly when the position of the feeding tube is in question, is to inject a small amount of contrast material through the feeding tube and observe intestinal anatomy and motility on a follow-up, single x-ray or under fluoroscopy. This technique can often provide a clear picture of the clinical situation. If intestinal appearance and function are normal, EN may be continued despite the distention. Feedings may need to be discontinued, however, if motility is poor, the bowel is markedly dilated, or the patient's discomfort too severe.

Maldigestion/Malabsorption

Maldigestion refers to impaired breakdown of nutrients into absorbable forms (eg, lactose intolerance). Clinical manifestations of maldigestion include bloating, abdominal distention, and diarrhea.

Maldigestion may result in significant malabsorption, defined as defective mucosal uptake and transport of nutrients (fat, carbohydrate, protein, vitamins, electrolytes, minerals, or water) from the small intestine. Clinical manifestations of malabsorption include unexplained weight loss; steatorrhea; diarrhea; and signs of vitamin, mineral, or essential macronutrient deficiency, such as anemia, tetany, bone pain, pathologic fractures, bleeding, dermatitis, neuropathy, and glossitis.

Methods used to screen for malabsorption include the following (listed in order of complexity):

- Gross and microscopic examination of the stool
- Qualitative determination of fat and protein content of a random stool collection
- Measurement of serum carotene concentration
- Measurement of serum citrulline levels
- Measurement of d-xylose absorption
- Radiologic examination of intestinal transit time and motility

When laboratory data, history, and/or radiologic examination suggest maldigestion or malabsorption, diagnosis can involve the following:

- Intake-output balance (stool collections for quantitative fecal fat assessment)
- Tests for the maldigestion/malabsorption of specific nutrients, such as lactose tolerance test, Schilling test to screen for abnormal absorption of vitamin B12, essential fatty acid profile for lipid malabsorption, and various radioisotopic tests to identify iron, calcium, amino acid, folic acid, pyridoxine, and vitamin D malabsorption
- Endoscopic small bowel biopsy, which is helpful in diagnosing mucosal disorders such as celiac disease, tropical sprue, and Whipple disease (see Chapter 26 for additional information on the diagnosis of celiac disease)

Causes of maldigestion/malabsorption include gluten-sensitive enteropathy, Crohn's disease, diverticular disease, radiation enteritis, enteric fistulas, human immunodeficiency virus, pancreatic insufficiency, short-gut syndrome, small intestinal bacterial overgrowth (SIBO), and numerous other syndromes. Although it is common practice to use predigested enteral products when malabsorption is suspected, only weak data support their use to prevent intolerance18 or overcome malabsorption/maldigestion during enteral feeding (see Chapter 11). Selected patients with severe malabsorption that is unresponsive to medical therapy or supplementation may require PN.6,17,19

Diarrhea

Diarrhea is the most commonly reported GI side effect in patients receiving EN.20 No definition of diarrhea is universally accepted.21 However, a clinically useful definition is any abnormal volume or consistency of stool. Normal stool water content is 250 to 500 mL/d. Diarrhea has also been defined as greater than 500 mL stool output every 24 hours or more than 3 stools per day for at least 2 consecutive days.22,23 Stool volume can be measured by placing a collection device in the toilet or by using a bedpan; in incontinent patients, it can be measured via a fecal management system or by placing a pad under the patient and weighing it after each stool (assuming 1 g equals 1 mL of stool).

Etiologies

Common causes of diarrhea in patients receiving EN include medications, primary GI disease, and bacterial infection. Characteristics of the formula (osmolality, fat content) and specific components in the formula (eg, lactose) are less likely to cause diarrhea.24,25

Drug-Induced Diarrhea

The hypertonicity of some drugs—such as electrolyte supplements (potassium, phosphorus, magnesium) and medications delivered in liquid form that contain magnesium or sorbitol in the vehicle—may cause diarrhea. As little as 10 to 20 g of sorbitol can lead to GI side effects, including diarrhea.6,26–29 Table 13-1 outlines the sorbitol content of selected liquid medications.25

TABLE 13-1 Sorbitol Content of Selected Medications

Generic Name	Trade Name	% Sorbitol[a]
Acetaminophen elixir	Tylenol	35.0
Amantadine	Symmetrel	72.0
Cimetidine	Tagamet	46.1
Doxycycline	Vibramycin	70.0
Furosemide	Lasix	35.0
Guaifenesin and codeine	Robitussin AC	35.0
Hydroxyzine	Vistaril	116.0
Indomethacin	Indocin	35.0
Isoniazid[b]	—	70.0
Metoclopramide	Reglan	28.0–42.0
Nortriptyline	Aventyl	64.0
Pseudoephedrine and triprolidine	Actifed	49.0

[a]Weight per volume.

[b]Generic version.

Adapted with permission from reference 25: McCarthy MS, Fabling JC, Bell DE. Drug-nutrient interactions. In: Shikora SA, Martindale RG, Schwaitzberg SD, eds. Nutrition Considerations in the Intensive Care Unit: Science, Rationale and Practice. Dubuque, IA: Kendall-Hunt; 2002:153. Copyright 2002 American Society for Parenteral and Enteral Nutrition.

Drugs with direct effects on the gut, such as antibiotics, proton pump inhibitors, and prokinetic medications, can also cause diarrhea (see Table 13-2).30 Antibiotic-associated diarrhea (AAD) is a common medication effect, occurring in up to 25% of patients treated with antibiotics, and C. difficile colitis affects 10% to 20% of all patients who develop AAD.31

TABLE 13-2 Medications Associated with Increased Incidence of Diarrhea

- Ampicillin
- Bisacodyl
- Caffeine
- Clindamycin
- Colchicine
- Digoxin
- Erythromycin
- Hydralazine
- Lactulose
- Magnesium-containing preparations
- Metoclopramide
- Methotrexate
- Neomycin
- Penicillamine
- Procainamide
- Quinidine
- Theophylline

Reprinted from reference 30: Ratnaike RN, Jones TE. Mechanisms of drug-induced diarrhea in the elderly. Drugs Aging. 1998;13(3):245–253. Reprinted with permission of Springer.

The osmotic load of some medications may make diarrhea inevitable. Any drug in a liquid vehicle given via a small bowel feeding tube should be diluted to avoid a hypertonic-induced, dumping-like syndrome. Most drugs and electrolytes (eg, potassium) should be mixed with a minimum of 30 to 60 mL of water per 10-mEq dose to avoid direct irritation of the gut.

Gastrointestinal Diseases

Many primary diseases of the intestine, including inflammatory bowel disease, short bowel syndrome, gluten-sensitive enteropathy, and acquired immunodeficiency syndrome, may result in malabsorption or secretory diarrhea (see Table 13-3).32 Recognition and treatment of these diseases can minimize diarrhea. In some disease states, PN may be required. In others, use of specialized enteral products are proposed to facilitate absorption.

TABLE 13-3 Conditions Associated with Secretory Diarrhea

- Infection with enterotoxic organisms such as Clostridium difficile
- Abuse of stimulant laxatives
- Intestinal resection
- Inflammatory bowel disease
- Bile acid malabsorption
- Fatty acid malabsorption
- Chronic infections
- Celiac sprue
- Small intestinal lymphoma
- Villous adenoma of the rectum
- Zollinger–Ellison syndrome
- Collagen vascular diseases
- Congenital defects
- Malignant carcinoid syndrome

Source: Reprinted with permission from reference 32: Fine KD, Krejs GJ, Fordtran JS. Diarrhea. In: Sleisenger MH, Fordtran JS, eds. Gastrointestinal Disease: Pathophysiology, Diagnosis, Management. 5th ed. Philadelphia, PA: Saunders; 1995:1043. Copyright Elsevier.

Infusion of Hyperosmolar Feeding Solutions

Hyperosmolar EN products rarely cause clinically significant diarrhea unless they are infused at a very high rate or administered by bolus into the small bowel. The highest osmolality of a tube feed is around 750 mOsm/L, which is about 2.5 times greater than normal serum. In contrast, electrolyte supplements have osmolalities in the range of 5000 to 7500 mOsm/L and are far more likely to cause osmotic diarrhea. If the clinician suspects that the hyperosmolality of an enteral formula is causing diarrhea, changing to an isotonic formula may be beneficial. Diluting the formula with water, a measure that was once common for patients with diarrhea, may result in suboptimal nutrient provision, and formula dilution has not been shown to improve tolerance.33,34 In addition, this practice is discouraged because it contaminates formula.

Specific Components of Enteral Formulas

Polymeric enteral formulas with intact protein are recommended for initial use in most individuals starting EN (see Chapter 11).35 Older studies comparing intact protein with peptide-based formulas did not find the latter to be better tolerated.36,37 In a recent, randomized pilot trial comparing a peptide-based formula with a polymeric formula in critically ill patients, the number of days of adverse GI events, including diarrhea, was significantly reduced with the peptide-based formula, but the incidence of diarrhea itself was not significantly different between the 2 groups.18

Most formulas are lactose free, but diarrhea related to lactose intolerance may be observed during the transition from EN to an oral diet. Some patients are lactase deficient prior to the onset of illness, and others develop a transient lactase deficiency during their illness. A lactose-restricted diet may help reduce diarrhea in patients with lactase deficiency.

Management Strategies

A systematic approach can be effective in the management of diarrhea (Practice Scenario 13-1). A 2007 observational study confirmed improvement in diarrhea incidence following the use of a defined diarrhea protocol. Figure 13-1 provides an algorithm for treatment of diarrhea in tube-fed patients.41 If clinically significant diarrhea develops during EN, clinicians should consider the following options:

- Medical assessment of the patient to rule out infectious or inflammatory causes, fecal impaction, diarrheagenic medications, and so on
- Use of an antidiarrheal agent (loperamide, diphenoxylate, paregoric, or octreotide) once C. difficile infection has been ruled out or is being treated
- Changing the formula type (eg, from an intact protein product to a peptide-based formula)
- Addition of soluble fiber or insoluble fiber to the medication regimen and/or changing to an enteral formula with added fiber, except in unstable critically ill patients14
- Continuation of EN as tolerated and initiation of PN to complete delivery of macro- and micronutrients if intolerance or malabsorption is severe and prolonged

Practice Scenario 13-1

Question: How does a nutrition support clinician select an enteral formula for a tube-fed patient who experiences diarrhea?

Scenario: Isotonic, fiber-free, nasogastric enteral feeding was initiated in a 78-year-old man following surgical intervention for a perforated duodenal ulcer, for which he was receiving a proton pump inhibitor. His postoperative course was complicated by hospital-acquired pneumonia requiring ventilator support and the use of antibiotic therapy. Enteral nutrition (EN) was initiated and advanced over a 72-hour period. At first, the patient demonstrated good tolerance to the EN with a slightly distended abdomen; hypoactive to active bowel sounds were heard; and he had 1 to 2 semiloose stools

per day. However, after 5 days of feeding, he developed 4 to 5 watery stools per day and a fecal management system was required.

Intervention: The nutrition support clinician reviewed the patient's medication profile and determined that he was not receiving hypertonic or sorbitol-based medications and a prokinetic agent was not in use. The clinician recommended obtaining a stool culture to assess for the presence of Clostridium difficile and the use of an enteral formula high in soluble fiber to assist in controlling the patient's diarrhea.

Answer: The inclusion of a gelatinous soluble fiber (eg, psyllium) in the EN regimen is one approach to manage diarrhea.

Rationale: Diarrhea in patients receiving EN can have many causes. A review of this patient's medication record does not identify any motility agents, sorbitol-based drugs, or hypertonic medications, but antibiotics and/or the proton pump inhibitor may be contributing factors.

Several management strategies can be employed to help control the patient's diarrhea. One is to add fiber to his EN regimen. Multiple small studies have demonstrated that the addition of soluble fiber to EN improves diarrhea,38,39 and adding fiber to EN is the recommended standard of care.14 However, the beneficial effect has been small, and a meta-analysis that aggregated data from 400 subjects found no difference in diarrhea in patients receiving EN with fiber vs EN without fiber.40 Interestingly, hospital length of stay was reduced in supplemented patients in this analysis, but no difference in mortality was seen.40 The addition of fiber can be achieved by using a fiber-containing enteral formula or by using a fiber modular supplement. A fiber-containing formula is usually preferable because modular fiber supplements can clog feeding tubes.

Testing for the presence of C. difficile in the stool is recommended in any patient deemed at risk for C. difficile infection. If the C. difficile results are negative, and offending medications cannot be stopped, the initiation of antidiarrheal agents is appropriate. Changing the enteral formula to a peptide-based formulation may be an option if other interventions are ineffective, but these formulas are costlier than intact-nutrient formulas. The addition of fiber to the EN regimen or changing the formulation should never be the primary intervention or the end of the evaluation or intervention for diarrhea.

Small Intestinal Bacterial Overgrowth

Bacterial overgrowth in the GI tract can cause severe enteritis with marked diarrhea, abdominal cramps and pain, hypoalbuminemia, protein catabolism, cachexia, fever, and even sepsis. Increasingly, SIBO is seen in patients after Roux-en-Y gastric bypass surgery.42 SIBO is difficult to diagnose definitively, especially in patients with blind intestinal limbs, such as those who have undergone Roux-en-Y bypass. Techniques such as hydrogen breath testing may provide false-negative results in these patients, necessitating empiric treatment. In patients who have altered GI anatomy or have been treated with prolonged antibiotic therapy, SIBO should be considered in the differential diagnosis if they present with bloating, abdominal pain, and/or otherwise unexplained catabolism/hypoalbuminemia. Prolonged use of broad-spectrum antibiotics increases the incidence of SIBO.43,44 Treatment is often empiric and

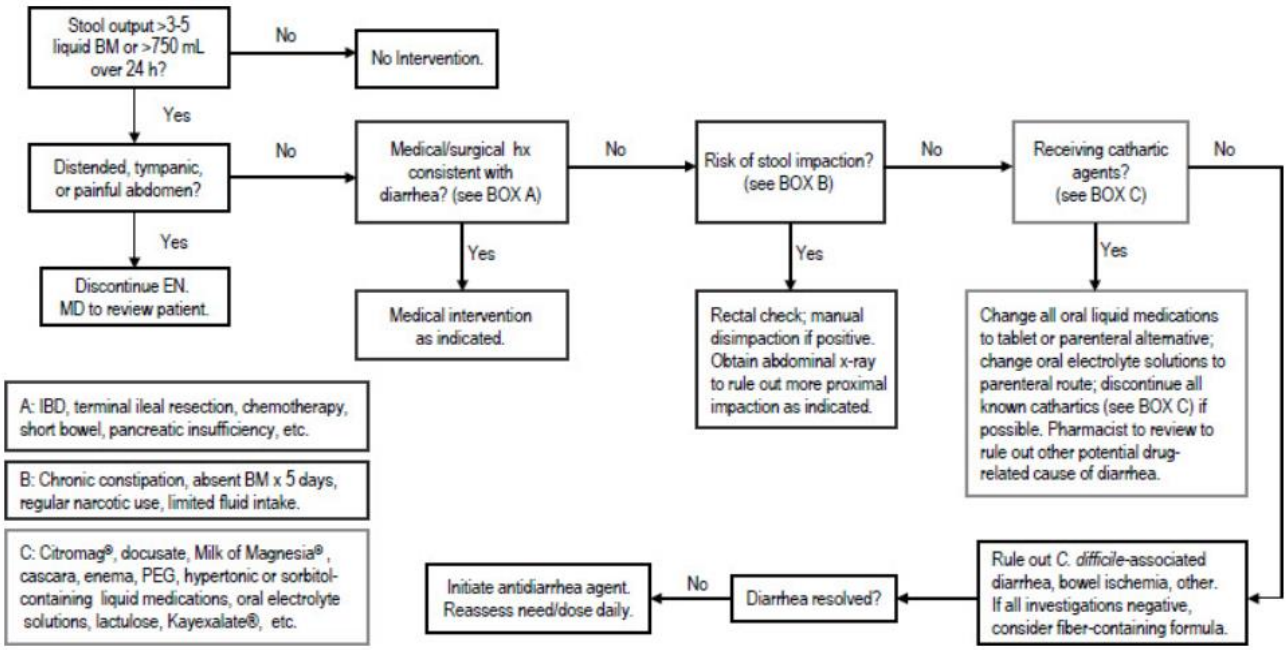
includes antibiotics. Nonabsorbable antibiotics are the treatment of choice, but systemic antibiotics are often necessary when the overgrowth is suspected to be in a nonalimentary bowel limb because the oral medication will not pass through the effected segment of bowel. Refer to Chapter 26 for additional discussion of SIBO.

Complications Related to Formula Contamination

Whenever enterally fed patients have diarrhea, abdominal upset, or fever, the contamination of enteral formula and the enteral delivery system should be considered as a potential cause of the problem. Contamination of enteral formulas can lead to diarrhea, abdominal distention, pneumonia, infectious enterocolitis, bacteremia, septicemia, and death.45–47 Neonates, critically ill and immune-suppressed patients, and those with a compromised gastric acid microbial barrier may be at greater risk for morbidity and mortality related to formula contamination.

Enteral feeding formula can become contaminated with microorganisms during formula storage, preparation, or administration. Enteral formulas that require minimal handling with sterile technique, such as those supplied in "closed-system" containers or sterile formulas that are carefully transferred to a feeding receptacle, have a lower incidence of microbial contamination compared with those that require reconstitution, mixing, or dilution (see Chapter 11). This difference translates to a small reduction in the incidence of diarrhea with formulas that require minimal handling, but no other clinical benefit has been demonstrated.48

FIGURE 13-1 Algorithm for Management of Diarrhea



BM, bowel movements; C. difficile, Clostridium difficile; EN, enteral nutrition; hx, history; IBD, inflammatory bowel disease; MD, Doctor of Medicine; PEG, percutaneous endoscopic gastrostomy.

Source: Adapted from reference 41: Greenwood J. Critical Care Nutrition at the Clinical Evaluation Research Unit. Study tools: management of diarrhea algorithm. 2010. www.criticalcarenutrition.com/docs/tools/Diarrhea.pdf. Accessed June 4, 2017. Reproduced with permission from Critical Care Nutrition: www.criticalcarenutrition.com.

Enteral "open" delivery systems provide liquid formula delivered via syringe or poured into a bag and delivered to the patient by gravity drip or pump. Formulas poured into feeding bags directly from cans, screw-top plastic bottles, and Brik Paks, have hang times from 4 to 12 hours; specific hang times depend on the feeding protocol at the facility and the manufacturer's recommendations. Reconstituted powdered formulas or formulas with added modular components delivered by gravity drip or pump should hang no more than 4 hours at room temperature. Enteral "closed" delivery systems use prefilled, sterile bottles or non-air-dependent containers that are accessed with a spike or screw-top tubing. These are administered by pump infusion and allow for longer hang times of 24 to 48 hours.

Formulas provided in liquid form undergo heat sterilization, whereas powdered formulas are not required to be sterile and may contain contaminants. To minimize the risk for contamination, powdered formulas should ideally be reconstituted with sterile water.49 Preparation and administration of any type of formula must always involve trained personnel using good handwashing, clean gloves, and aseptic technique in a clean environment.

Formulas should be used immediately after being opened, or after reconstitution with sterile water, with strict adherence to the manufacturer-recommended hang times for room-temperature formula. If formula is leftover after the intended volume is poured into the feeding system, the excess should be refrigerated immediately and stored according to the manufacturer's recommendations, typically a maximum of 24 to 48 hours.

For example, if the formula rate is 25 mL/h and the formula hang time is 8 hours, a maximum of 200 mL of formula can be poured into the feeding bag and administered at room temperature during that 8-hour period; any formula leftover after the feeding bag is filled should be immediately refrigerated for future use.

Use of a blender to add carbohydrate and protein modular additives to formula carries a high risk for contamination during the mixing process and should be avoided.50 The lids of cans should be cleansed with isopropyl alcohol and allowed to dry before pouring the formula into the delivery receptacle.51 Feeding bags do not need to be rinsed with water before additional formula is added, but formula should not be added until the previous formula has infused. The feeding bag itself should be changed every 24 hours.52

Lyman and colleagues investigated the risk for formula contamination and associated complications in pediatric patients who received sterile, undiluted formula provided from cans into enteral feeding bags over 12-hour hang times.53 Aseptic technique and clean gloves were used; the cans and the hub of the tubing were cleansed with alcohol wipes; and touch contamination was avoided. No bacterial contamination was found in 90% of formula cultures, and acceptable, very low-level bacterial contamination was identified in 5% of cultures. The 5% of patients who were exposed to unacceptable

bacterial contamination of formula did not show any clinical signs of bacterial gastroenteritis (increased stool output, fever, or clinical deterioration).

The risk of contamination is reduced with the “closed” delivery system because the formula is less exposed to contact with anything nonsterile.54,55 However, prefilled containers require the attachment of tubing, so touch contamination is still a risk. Contamination is reduced with delivery systems that have recessed spike sets and recessed nutrient container seals.56,57 These features prevent inadvertent touching of the parts of the closed delivery system that come into contact with the formula. Tubing used with “closed” delivery systems, such as spike sets, should be replaced every 24 hours to lower the incidence of diarrhea.48

Enteral formulas may also become contaminated in a retrograde manner if the patient’s endogenous microorganisms (from stomach, throat, lungs) reproduce within the feeding tube and then migrate into the enteral delivery system.58 These microorganisms may then proliferate within the feeding formula and be reinfused to the patient in greater numbers. Most enteral delivery tubing systems contain a drip chamber that minimizes the occurrence of this problem during formula delivery.59,60 However, if formula infusions are interrupted, the stagnant period could allow microorganisms to proliferate.

The procedure of checking for GRV pulls potentially pathogenic microorganisms up the feeding tube and can lead to a contaminated feeding tube hub and contaminated gloves.61 The exposure of a patient’s body fluids in this manner is labeled a “dirty” procedure. In a “clean” procedure, the individual checking GRV will remove gloves, thoroughly wash hands (or use a hand sanitizer), and put on clean gloves before administering the enteral formula. Research on the benefits and risks of GRV assessment is discussed in greater detail later in this chapter.

The Y-ports of enteral delivery systems are used to deliver medications and water flushes to minimize disconnection of the enteral formula. Mathus-Vliegen and colleagues took cultures in enteral feeding systems and identified bacterial contamination of more than 100 CFU/mL in 48.1% of the “closed” delivery systems at the Y-port vs a 2.4% contamination rate in the formula containers.58 The investigators determined that the contamination was caused by either administration of medications through the Y-port or retrograde movement of microorganisms from the feeding tube to the delivery system. Although this study looked at the results of cultures and not clinical outcomes of patients, Mathus-Vliegen et al recommended that tube feedings not be allowed to remain within the delivery system without the infusion process occurring and that delivery sets be changed frequently.

Lopez valves are 3-way stopcocks that are frequently attached to enteral feeding tubes that do not contain a clamp, such as nasogastric, balloon gastrostomy, balloon gastrojejunostomy, and jejunostomy tubes. These 3-way valves swivel to block or allow fluid passage. An in vitro investigation showed the development of a bacterial biofilm in Lopez valves within 3 days when the valves were attached to enteral bags delivering a continuous drip, polymeric formula inoculated with Pseudomonas aeruginosa on Day 1.62 The bag and tubing were changed every 24 hours, and sterile formula was used on Days 2 and 3. Biofilms are resistant to antibiotics and the patient’s own immune response and can cause acute

or chronic infections. The authors of this study suggest changing Lopez valves at intervals of 3 days or less and perhaps at each tubing change.

An investigation of hospitalized patients showed that the incidences C. difficile infection and C. difficile–associated diarrhea were significantly higher in tube-fed patients compared with non-tube-fed patients, and risk was greatest for those receiving postpyloric tube feeding. The investigators recommended testing for C. difficile while investigating other etiologies for diarrhea in tube-fed patients.45 Alterations in the fecal microbiota were found to occur in patients receiving enteral tube feedings who developed diarrhea.63 The patients who developed diarrhea had significantly higher concentrations of clostridia and lower concentrations and proportions of bifidobacteria, which may be involved in the pathogenesis of the diarrhea.

The implementation of enteral quality control programs and institutional protocols can reduce enteral formula contamination to acceptable levels.49,64 An enteral quality control program should define the process for receiving, distributing, storing, preparing, handling, and administering enteral formula, and identify who is responsible for each task. The formula container should be visually inspected for damage, and the expiration date should be noted. Proper handwashing or application of a hand sanitizer should be performed before the feeding administration set and formula are handled. If clinicians wear gloves to perform other patient care needs, they must put on clean gloves before handling formula and enteral devices. A clean area, such as a clean towel or underpad, should be set up beneath the feeding tube connection. Flip-top cans should be wiped with isopropyl alcohol and allowed to dry. Once opened, the formula should be inspected for altered formula characteristics such as formula separation, thickening, clumping, or curdling. If a powdered formula or modular component requires reconstitution or dilution, sterile water should be used. Aseptic technique should be used in preparing the formula, when pouring formula into a receptacle or spiking the formula container, and when connecting the administration set or syringe to the feeding tube. Recommendations for formula hang times at room temperature, refrigeration times, and timing for feeding set changes should be followed. “Closed” EN delivery systems should be used whenever feasible. If an “open” delivery system is used, new formula should not be added to remaining formula in the feeding bag. The addition of a 3-way stopcock increases contamination risk; therefore, the manufacturer’s recommendations should be followed for cleaning and routine replacement schedules should be established. Disconnections within the enteral delivery system should be minimized. When they are necessary, the distal end of the delivery system should be covered with a clean cap, and long periods of formula stagnation should be avoided. All related equipment, such as flush syringes and their containers, must be kept as clean and dry as possible, and enteral equipment should be stored away from potential sources of contamination, such as dirty wounds, fistula, or ostomy dressings and supplies. It is also important to educate patients and their caregivers on the ways to minimize contamination risk with tube feeding delivery.

Constipation, Impaction, and Intestinal Bezoar

Constipation is difficult to define because normal defecation patterns range from 4 stools each day to 1 stool every 4 or 5 days. With EN, the variation in defecation patterns increases depending on the residue and extent of absorption of an enteral feeding product. The best clinical definition of constipation is the

accumulation of excess waste in the colon, often up to the transverse colon or even the cecum. A rectal examination and plain abdominal x-ray are often effective for diagnosis and can differentiate constipation from small bowel obstruction or ileus. With uncomplicated constipation, small bowel dilatation is rarely found.

Common causes of constipation include dehydration and either inadequate or excessive fiber in the diet.7,20,65 To avoid dehydration, patients receiving EN require adequate fluid (see discussion of dehydration later in this chapter). Hydration may be problematic when a concentrated formula is needed for fluid restriction. If a patient has constipation and the usual hydration volume is contraindicated, the addition of a stool softener (docusate sodium or docusate calcium, or various emollients) and a laxative or cleansing enema may be considered. Chronic use of stimulants (eg, senna) often results in tachyphylaxis and is not indicated. Frequent rectal exams and abdominal radiographs may be required in patients with serious constipation.

Fiber helps propel waste through the colon, and inadequate fiber intake can result in infrequent bowel movements with significant buildup of waste in the colon. If fiber is added to the enteral regimen, administering a minimum of 1 mL of fluid per kcal enterally may help prevent solidification of waste in the colon and constipation. Patients often need additional fluid to facilitate regular stool output and minimize the chance of impaction. Inadequate physical activity can also contribute to constipation. Patients should ambulate whenever possible. Shorter-chain fibers are recommended for prevention of constipation in hemodynamically stable patients.14

A variant of constipation is impaction, a firm collection of stool in the distal colon (sigmoid colon or rectum). Liquid stool will seep around an impaction, occasionally at high volume. If impaction is near to the rectum, it can be diagnosed and may be treated by rectal examination. Impaction higher up in the sigmoid colon cannot be easily detected by examination, and a high level of clinical suspicion should be maintained in patients at risk. Impaction should be considered in patients, particularly older adults and patients who are bed-bound, when stool volumes have been small and then become liquid. Impaction may be the cause of confusion and agitation in older adults.66 Enemas, cathartics (sorbitol, lactulose), and even endoscopy may be required to treat severe impaction.

Finally, case reports67 have described rare but life-threatening complications caused by intestinal bezoar associated with tube feeds that contain fiber. These bezoars may present insidiously as obstruction or bowel perforation, have been reported most often in severely ill patients for whom hypomotility is more likely, and can be, in the experience of one of the authors, fatal. SCCM/ASPEN guidelines recommend that fiber be avoided in patients who are not hemodynamically stable,14 but the risk factors are not well understood.

Intestinal Ischemia

Intestinal ischemia has several etiologies and is rarely nutrition related; however, in case reports of ischemia in conjunction with EN,68 nonocclusive bowel necrosis (NOBN) has been associated with a high degree of morbidity and possibly with death. Neonates, critically ill and immune-suppressed patients, and patients with a compromised gastric acid microbial barrier may be at greater risk for NOBN.

Underlying factors possibly associated with NOBN include the use of jejunal feedings, hyperosmolar formulas, and feeding in the presence of hypotension, as well as disordered peristalsis. Typical signs of enteral feeding intolerance, including abdominal distention and nausea and vomiting, are common with NOBN, but the symptoms are nonspecific and may be observed in enterally fed patients in the intensive care unit (ICU) without NOBN. NOBN may present later in the patient's clinical course rather than shortly after enteral feeding initiation. In a review of NOBN among surgical patients, the mean day of diagnosis after EN initiation was Day 6 with a range from Day 4 to Day 18.69

Although it is difficult to predict who may develop NOBN in conjunction with enteral feedings, precautionary measures may be preventive. Delaying EN until the patient is fluid-resuscitated is likely of greatest importance. According to a review of case series reports of patients who developed NOBN, all reports cited the presence of hypotension and/or hypovolemia as precipitating factors.68 Other considerations may include the initial use of an isotonic and fiber-free enteral formula. Ongoing monitoring of EN is essential because acute changes in abdominal assessment can prompt early recognition and treatment of NOBN. A patient who previously demonstrated enteral feeding tolerance and then develops abdominal distention, abdominal pain, and an acute change in nasogastric tube output should be fully evaluated.

Pulmonary Aspiration Complications

Pulmonary aspiration is defined as the inhalation of material into the airway. This problem is of concern in all patients, and its occurrence in those receiving EN has received considerable attention. The assumption is that patients could develop pneumonia if they inhale gastric contents and/or the tube feeding formula into the airway. However, while there is a strong association between tube feeding and pneumonia, and a stronger association between tube feeding and aspiration, causal relationships have not been established. In fact, pulmonary aspiration can be asymptomatic (silent aspiration), and aspiration of saliva is a normal phenomenon during sleep. In a 2-day study of 10 normal volunteers, half aspirated overnight.70 In contrast, the incidence of pneumonia is low. In a report on US veterans, for example, the incidence of community-acquired pneumonia was 4.4 cases of pneumonia per 1000 patient years.71 Thus, aspiration seems to be a poor surrogate for pneumonia risk, given the disparity between the apparent incidence of aspiration and low incidence of pneumonia. On the other hand, it is incontrovertible that inhalation of significant volumes of vomitus is highly likely to be deleterious.

Chemical pneumonitis and/or pneumonia can result from pulmonary aspiration of significant volumes of enteral formula; however, aspiration of very small amounts of fluid alone is likely insufficient to cause pneumonia. The progression from aspiration to aspiration pneumonia is hard to predict and may depend on the quantity and acidity of the formula in addition to the particulates and contaminants in the formula. Age, immune status, and comorbidities also are likely to strongly influence the development of aspiration pneumonia.

When the quantity and acidity of the formula overwhelm either the patient's natural defense mechanisms or the patient's altered pulmonary defense mechanisms, pneumonia is more likely to occur. Acute symptoms of clinically significant aspiration include dyspnea, wheezing, frothy or purulent

sputum, hypoxia, cyanosis, anxiety, and agitation. Patients can also have a fever, tachycardia, tachypnea, rhonchi and rales, leukocytosis, leukopenia, and a new or progressing infiltrate on chest film. When pneumonia develops in ventilated patients, it is labeled VAP. Aspiration and VAP are also discussed in Chapter 25.

Incidence and Risk Factors

Pulmonary aspiration of tube feeding formula is one of the most feared complications of EN support because it can lead to acute pulmonary pathology. Aspiration pneumonia may account for 5% to 15% of pneumonia in hospitalized patients,72 but diagnostic criteria vary, and proving that aspiration was the cause of pneumonia is nearly impossible. In addition to pneumonia, potential complications of aspiration include pneumonitis, atelectasis, empyema, bronchitis, acute lung injury, and acute respiratory distress syndrome. However, relating pathologic respiratory developments to the aspiration of tube feeding formula is difficult because pulmonary aspiration can also occur when a patient inhales oropharyngeal and gastric secretions.

Reported incidence of aspiration in tube-fed patients varies and depends on the patient population studied and the technique and criteria used to identify aspiration. Investigations using advanced aspiration detection techniques have reported the presence of gastric contents in the tracheal secretions of 22% to 31% of critically ill, tube-fed patients.73,74 These studies identified aspiration of gastric contents by detecting either pepsin (a major enzyme in gastric fluid) or yellow microscopic beads (added to tube feeding formula) in tracheal aspirates. When pepsin-positive secretions were used, Metheny et al identified low HOB elevation, vomiting, gastric tube feedings (as opposed to small bowel feedings), low Glasgow coma score, and GI reflux disease as risk factors for aspiration.74 Patients with a higher number of pepsin-positive secretions and those with paralytic agents and high sedation levels were at higher risk for pneumonia, but a causal relationship was not proven. Additional risk factors associated with an increased incidence of aspiration include a malpositioned feeding tube, transportation within the hospital, and inadequate nursing staff.75,76

Detection

No reliable method to detect pulmonary aspiration of tube feeding formula is currently available for routine clinical use. Radiographic findings are generally nonspecific and insensitive. However, after an episode of emesis and regurgitation of tube feeding formula, aspiration of feeding formula or vomitus can be presumed if a patient develops dyspnea, cyanosis, and agitation and there is evidence of a new infiltrate on chest film. Patients with dysphagia may aspirate saliva and develop aspiration pneumonia independent of the presence of gastric contents. Regardless of the underlying cause, aspiration is a medical urgency. Emergency measures may include sitting the patient upright, orotracheal suctioning, oxygen, and antibiotics.

Methods historically used to detect pulmonary aspiration of formula include tinting enteral formula with blue dye or checking tracheal secretions with glucose oxidase strips. These methods are unsatisfactory because they are neither sensitive nor specific.74 Numerous problems surround the practice of tinting formulas. The dose of food coloring has never been standardized, and concerns about bacterial

contamination, allergic reactions, and false-positive guaiac testing have been raised. More importantly, a Public Health Advisory issued by the US Food and Drug Administration on September 29, 2003, reported blue discoloration of body parts and fluids followed by refractory hypotension, metabolic acidosis, and death in patients receiving tube feedings containing Food Drug and Cosmetic Blue No. 1 dye.77 Based on this report and the method's lack of sensitivity, specificity, or standardization, the practice of tinting enteral formulas should be abandoned.

Glucose oxidase strips can be used to detect a high glucose level in tracheal aspirates, which might indicate that the aspirates contain feeding formula. However, high tracheal concentrations of glucose can also be found in aspirates of nonfed patients and those with elevated blood glucose levels, as well as in aspirates that contain some blood.78,79 A study using an animal model demonstrated a correlation between pepsin levels in tracheal aspirates and aspiration pneumonia, with a sensitivity of 90% and a specificity of 100%; however, this assay is not available for routine clinical use.80

Risk Assessment

Gastric Residual Volume

Because elevated GRVs can predict vomiting or reflux, clinicians have used GRV to determine the risk for aspiration. To measure GRV, the clinician withdraws or suctions fluid intermittently from enteral access devices with a syringe or by gravity drainage. Then, in the hope of preventing aspiration, tube feedings may be held when the GRV is determined to be too high. However, interpretation of GRVs is highly subjective and the accuracy of GRV measurements can be influenced by many factors, including the diameter and position of the tube tip, the number and location of the tube's openings, the patient's position altering the level of stomach fluid, and the skill of the clinician.

Studies of the value of GRV measurement have reached conflicting conclusions. For example, Metheny and colleagues reported that frequent aspirators (ie, patients with greater than 40% pepsin-positive secretions) had a significantly higher incidence of GRVs of at least 200 mL times 2 or 250 mL times 1.81 These investigators noted that aspiration can occur without high GRVs, but that it occurs more frequently when GRVs are high. Based on her research findings, Metheny encourages facilities to keep GRV checks in nursing protocols.82 Conversely, McClave and associates found no correlation between GRVs greater than 200 mL or greater than 400 mL and aspiration in critically ill, mechanically ventilated patients receiving gastric tube feedings by either a nasogastric feeding tube or gastrostomy tube.83 These investigators identified aspiration by the addition of yellow microscopic beads to the tube feeding formula and use of calorimetric fluoroscopy for detection in the tracheal aspirate, and they noted less aspiration with the gastrostomy tube feedings compared with the nasogastric tube feedings.

Other investigations have evaluated not obtaining GRV at all, holding gastric tube feedings for varying levels of GRV, re-instilling vs discarding of GRV and the frequency of GRV checks in relation to the incidence of VAP and non–ventilator pneumonia, rates of emesis/regurgitation, and the achievement of tube feeding volume goals in critically ill patients. Selected findings from such studies are reviewed here.

A “before and after” study at 1 hospital compared the effects of obtaining vs not obtaining GRVs in 205 critically ill, ventilated, medical patients who had an aggressive, nasogastric, continuous tube feeding schedule initiated within 48 hours of admission with the intent to reach goal feedings within 24 hours.1 In the “before” group, GRVs were obtained every 6 hours and re-instilled if they were 250 mL or less. If the GRV were greater than 250 mL or emesis occurred, the tube feeding was decreased to the previous rate and intravenous (IV) erythromycin was initiated. In the “after” group, no GRVs were obtained and the protocol to lower the tube feeding rate and initiate IV erythromycin was used for emesis only. All patients had the HOB elevated 45°. The median daily volume of enteral feeding was significantly higher in the “after” group (1489 kcal/d vs 1381 kcal/d), and there were no differences in incidence of emesis (approximately 25% in each group) or VAP rates (19.6% in “before” group vs 18.4% in “after” group).

A more recent, prospective multicenter study also compared the effects of obtaining vs not obtaining GRVs. In this trial, 449 critically ill, ventilator-dependent patients (over 90% in the medical ICU) receiving nasogastric tube feedings were randomly assigned to GRV checks every 6 hours (control group) and no GRV checks (intervention group).15 Tube feedings were initiated at goal rates within 36 hours after intubation. HOB was elevated 30° to 45°, and oral care with chlorhexidine was given every 6 to 8 hours. Up to 250 mL GRV was re-instilled in the control group. Intolerance was defined as GRV greater than 250 mL and/or vomiting in the control group and vomiting alone in the intervention group. There was significantly more vomiting in the intervention group (41.8% vs 26.5% of patients over the study period), perhaps because the control group received more erythromycin. Notably, VAP occurrence was similar in both groups (15.8% in control group vs 16.7% in intervention group). The proportion of patients that received 100% of their energy goal was reportedly higher in the intervention group, but the amounts of enteral formula lost through vomiting or residual discard were not measured and it is likely that energy intake was overestimated.

The prospective REGANE study investigated the consequences of using a higher GRV as the point at which tube feeding is held. The investigators randomly assigned 329 critically ill, ventilated patients (80% medical patients) receiving nasogastric tube feedings in multiple ICUs to holding feedings for 6 hours after a GRV equal to or greater than 200 mL (control group) vs a GRV equal to or greater than 500 mL (study group).84 It was not reported whether any of the GRV was re-instilled. All patients had the HOB elevated 30° to 45° and received metoclopramide every 8 hours for the first 3 days of feedings. VAP rates were similar for both groups (27.3% in control group vs 28% in study group). The percentage of prescribed formula received was significantly higher in the study group but only for the first week (88.20% vs 84.48%). Some patients received PN to help meet nutrient needs.

A single-institution investigation of 122 surgical and medical ICU patients receiving nasogastric tube feedings studied the effects of re-instilling GRV vs discarding it. Participants were randomly assigned to the “return” or “discard” (control) group.85 GRV checks were obtained every 6 hours, and the “return” group had up to 250 mL GRV re-instilled with the remaining volume discarded. GRV was completely discarded in the control group. All patients had the HOB elevated 30° to 45°, were on continuous tube feeding schedules, and received 40 mg omeprazole daily; some patients also received PN. Feedings were held if patients had GRV greater than 500 mL, experienced vomiting, had diarrhea for more than 48 hours, and underwent radiologic or surgical procedures. The “return” group had a significantly lower

incidence of subsequent high GRV. The authors suggested that the re-instilling of the GRV may have an impact on gastric function by maintaining GRV at "closer physiological levels."85 (The stomach empties intermittently, and a certain volume of fluid needs to be reached to promote gastric contractions and emptying.86 The volume required to facilitate this process varies among individuals and is unknown.) The frequency of hyperglycemia in the "return" group was significantly higher.85 No differences were found in obstruction of the nasally placed feeding tubes, intolerance episodes (nausea, vomiting, diarrhea and abdominal distention), discomfort episodes, or hypokalemic episodes. The authors reported no difference in enteral feeding delays (defined as >20% difference between feeding prescribed and amount administered per day), with the administered feeding averaging 89% of prescribed in the control group and 93% of prescribed in the intervention group, but the study did not account for feeding lost via discarded GRV. The authors stated that there was no difference in pulmonary aspiration between groups based on blood glucose levels in tracheal aspirates;85 however, this method does not measure formula content, and it is therefore not useful for detection of tube feeding formula aspiration.87 This study suggests that re-instilling up to 250 mL GRV poses no additional risk for increased accumulation of gastric fluid levels or GI intolerance, but it did not address the incidence of pulmonary aspiration between groups.85

A single-institution, randomized controlled trial studied the frequency of GRV checks in 357 medical and surgical critically ill patients (98% on mechanical ventilation) receiving tube feedings by a nasogastric tube or a nasoenteric tube (with a concurrent nasogastric tube).88 Tube feedings were administered by a continuous drip, and target feeding goals were to be achieved within Day 1 of ICU admission; some patients in the study received PN. All participants had GRV checks every 4 hours initially. The intervention group progressed to GRV checks every 8 hours once they tolerated the goal feeding volume for at least 4 hours (ie, GRV was less than the volume of the previous 2 hours' feeding). GRV checks continued every 4 hours in the control group. Up to 300 mL of GRV was re-instilled, and the remaining volume was discarded as per the facility's usual practice. If the GRV were greater than the volume of the previous 2 hours' feeding, prokinetics were considered and, in the intervention group, the frequency of GRV checks reverted, at least temporarily, to every 4 hours. Despite the aggressive early EN protocol, the percentage of subjects who received at least 80% of prescribed feeding volume was only 48% in the control group and 50% in the intervention group. The mean number of daily GRV checks was 5.4 for the control group and 3.4 for the intervention group. Incidence of regurgitation was significantly higher in the intervention group (3.6% vs 2.1%), but the incidence of pneumonia did not significantly differ between groups (14.1% in control group vs 13.2% in intervention group). Because regurgitation was increased in the intervention group, the investigators did not advocate decreasing the frequency of GRV checks.88

One review of GRV monitoring has addressed the evidence for and against monitoring.89 It noted, with some important caveats, that recent prospective, randomized trials of critically ill, ventilator patients showed no benefit from adjusting EN based on GRV checks. Surgical and trauma patients, who are at higher risk for aspiration pneumonia, have not been fully evaluated. The authors also noted that in trials where enteral feedings continued despite elevated GRVs, strict protocols were employed to prevent gastric reflux and aspiration of contaminated oral secretions, including HOB elevation, regular oral

decontamination, and use of prokinetic agents. They also pointed out that with the recent introduction of more aggressive, volume-based or top-down feeding protocols, GRV checks should be considered at least during the initial days of feeding and in patients at risk for enteral feeding intolerance. The review stressed the overall importance of viewing patient characteristics and the EN delivery strategy when designing protocols for the use or abolishment of GRV checks.

Alternate Techniques to Detect Delayed Gastric Emptying

Alternate techniques for detecting gastric emptying delays during enteral feedings are either experimental or of unproven value. Methods such as scintigraphy, the paracetamol absorption test, the carbon-isotope breath test, refractometry, ultrasound, and gastric impedance tend to be time-consuming, are difficult to perform at the bedside, and require standardization and validation in critically ill patients.90

Minimizing Aspiration Risk

Since there is no reliable and standardized bedside method to determine gastric emptying, identifying patients at high risk for aspiration is difficult. However, preventive measures and protocols aimed at risk reduction have been tested with some benefits. For example, raising the HOB 30° to 45° during gastric feedings has been associated with decreased esophageal and pharyngeal reflux of gastric contents and a lowered incidence of aspiration pneumonia.90 A written physician's order set for HOB elevation and the hourly recording of the bed angle on bedside flowsheets have been recommended to improve compliance.91

A protocol including HOB elevation of 30°, GRV checks every 4 hours, and prokinetics for those with elevated GRVs was studied in critically ill, mechanically ventilated patients being fed through nasally inserted feeding tubes.92 The protocol used a decision tree to direct actions depending on amount of GRV obtained. When the GRV was greater than 200 mL, a prokinetic agent was to be given once and then repeated if GRV remained higher than 200 mL. If the GRV was equal to or greater than 200 mL after the prokinetic intervention, the EN delivery method was changed to a small bowel feeding tube. With this protocol in place, the practice of HOB elevation increased from 38% to 88% and the shift of patients to small bowel feeding tubes increased from 39% to 68%. Aspiration incidence decreased from 88% to 39%, and the occurrence of pneumonia decreased from 48% to 19%.

Juve-Udina and colleagues studied the effects of EN protocol use in medical and surgical ICU patients. The protocols included HOB elevation 30° to 45°, continuous tube feeding schedules, use of omeprazole, and the re-instillation of GRVs (up to 250 mL). The protocols also called for holding EN for GRVs greater than 500 mL, vomiting, or diarrhea for more than 48 hours. With these protocols, patients received 93% of prescribed EN, 93% of the GRVs were less than 150 mL, and 2.3% of patients had GRV greater than 250 mL. However, the study did not adequately address the incidence of pulmonary aspiration.85

Guidelines

SCCM/ASPEN 2016 guidelines suggest that GRVs should not be used as part of routine care to monitor ICU patients receiving EN. If ICUs still use GRVs, SCCM/ASPEN further recommend that clinicians avoid holding EN for GRVs less than 500 mL in the absence of other signs of feeding intolerance (quality of evidence: low).14

Guidelines recently published in other nations have not concurred with the SCCM/ASPEN recommendations. The 2013 Canadian critical care nutrition guidelines deem that abandoning GRV checks or using a 500-mL threshold is premature, question the external validity of the current trials, and suggest a GRV threshold of 250 to 500 mL.93 The German Society for Nutritional Medicine (2013) proposes the omission of GRV checks in medical ICU patients as long as the medical team adjusts the enteral infusion as needed, such as when vomiting occurs. It recommends obtaining GRV checks in surgical ICU patients and adjusting the EN delivery rate when GRV reaches 200 mL.94

It may be advisable to follow different protocols for gastrostomy tubes, as opposed to nasal tubes. Gastrostomy tubes are positioned in the anterior abdomen and are unlikely to allow full withdrawal of stomach contents during GRV checks. A GRV of 100 mL or greater with a gastrostomy tube has been suggested as a prudent trigger for careful evaluation of the patient for GI symptoms.83

Prevention Methods

Tube-fed patients should be assessed for signs of tube feeding intolerance (eg, abdominal distention, feeling of fullness, discomfort, nausea, or emesis) at 4-hour intervals,95 and measures should be implemented to reduce aspiration risk. These measures include HOB elevation of at least 30° to 45° or positioning the patient upright in a chair (if such positioning is contraindicated, consider the reverse Trendelenburg position), good oral care twice daily (with chlorhexidine in critically ill patients), continuous tube feeding schedules, use of minimal sedation techniques, and appropriate and timely oropharyngeal suctioning (eg, prior to lowering the HOB, deflating the cuff of endotracheal tubes, or extubation).

The American Academy of Critical-Care Nurses (AACN) advocates that clinicians check GRV every 4 hours to help determine tolerance to gastric tube feedings while also assessing patients for other signs of GI intolerance, such as nausea, emesis and abdominal distention and discomfort. AACN also recommends residual checks with both gastric or small bowel feeding tubes every 4 hours to help determine changes in tube placement.95 Changes in the volume (and pH, if measurable) of aspirate can indicate movement of a feeding tube between the small bowel, stomach, and esophagus. Tube placement should also be checked by noting any change in the visible tube length or marking at nares/stoma every 4 hours,95 as well as after emesis, coughing episodes, or events during which the tube was tugged. If tube placement is questionable, a radiograph should be obtained. Feeding tube position should be assessed with routine chest and abdominal radiographs. See Chapter 12 for additional discussion of the assessment of enteral tube placement.

Unless the patient is vomiting, GRVs up to 250 mL should be re-instilled to replace fluid, electrolytes, and feeding formula. Prokinetic agents and small bowel feedings should be considered for patients determined to be at high aspiration risk.14 Continued study is required to delineate methods to assess risk of aspiration during tube feeding and to develop strategies to prevent this complication.

Metabolic Complications

EN, by itself, is unlikely to cause metabolic derangements, other than refeeding syndrome, or specific nutritional deficiencies. However, patients receiving EN are likely to have underlying conditions that predispose them to metabolic derangements (see Table 13-4).16,96 The nutrition support regimen may be the sole source of nutrients, fluids, and electrolytes for the patient. Therefore, the nutrition support clinician must be well schooled in the underlying medical issues that may affect formula selection, the fluid and electrolyte prescription, and the response to feeding in previously starved or electrolyte-depleted patients. Nutrition support clinicians must work closely and as part of a team with the primary healthcare providers to set therapeutic goals and monitor the patient's progress.

TABLE 13-4 Metabolic Complications of Enteral Nutrition

Problem	Possible Causes	Prevention or Therapy
Hypertonic dehydration	• Excessive fluid loss • Inadequate fluid intake • Concentrated (energy, protein) formula administered to a patient who cannot express thirst	• Monitor daily fluid I/O. • Monitor body weight daily.[a] • Estimate fluid losses.[b] • Monitor serum electrolytes, urine-specific gravity, BUN, and Cr daily.[c] • Provide enteral or IV fluid as indicated.
Overhydration	• Excessive fluid intake • Rapid refeeding • Catabolism of lean body mass with potassium loss • Refeeding syndrome • Renal, hepatic, or cardiac insufficiency	• Monitor I/O daily. • Assess fluid status daily. • Monitor body weight daily.[a] • Check aldosterone levels, which will be elevated with sodium retention. • Consider use of less-concentrated formula. • Diuretic therapy.
Hypokalemia	• Refeeding syndrome • Catabolic stress • Depleted body cell mass • Effect of ADH and aldosterone • Diuretic therapy • Excessive losses (diarrhea, NGT) • Metabolic alkalosis • Insulin therapy • Dilution	• Supplement potassium to normal before initiation of TF. • Monitor serum potassium daily until stable with patient at goal TF rate. • Supplement potassium and chloride. • Consider supplementation protocol.
Hyperkalemia	• Metabolic acidosis • Poor perfusion (eg, congestive heart failure) • Renal failure • Excessive potassium intake from TF, IV fluid, oral diet	• Correct acidosis, if possible; recheck serum potassium. • Correct serum potassium before initiation of TF, if possible. • Monitor serum potassium daily. • Treat cause of poor perfusion. • Potassium-binding resin, glucose, and/or insulin therapy. • Eliminate potassium from IV fluids; reduce potassium in TF and oral diet.
Hyponatremia	• Dilution, from elevated ADH levels • Hepatic, cardiac, or renal insufficiency • Reduced sodium intake relative to output	• Consider addition of table salt to TF. • Monitor sodium level daily. • Assess fluid status. • Diuretic therapy, if indicated. • Fluid and/or sodium restriction.
Hypernatremia	• Inadequate fluid intake with increased fluid loss (sweating, osmotic diuresis) • Increased sodium intake (IV fluid) • Depletion of total body sodium, extracellular mass, ECF, SIAD	• Monitor daily I/O. • Monitor electrolytes and BUN:Cr daily.[c] • Monitor body weight daily.[a] • Estimate fluid loss.[b] • Replace fluid loss via enteral or parenteral route to replete ECF.

Hypophosphatemia	• Refeeding syndrome • Excessive energy intake • Binding by epinephrine • Sucralfate, antacids • Insulin therapy	• Supplement phosphorus to achieve normal level before initiation of TF. • Monitor serum phosphorus daily and replete as necessary as clinical course changes. • Supplement phosphorus as sodium or potassium form, as clinically indicated, via enteral or parenteral route.
Hyperphosphatemia	• Renal insufficiency	• Phosphate-binder therapy.
Hypercapnia	• Overfeeding energy • Excessive carbohydrate provision in patient with respiratory dysfunction	• Choose TF product with lower phosphorus content. • Measure energy requirement via IC, if possible. • If IC is unavailable, provide maintenance energy needs only until hypercapnia resolves. • Provide appropriate balance of carbohydrate, protein, and fat; consider providing 30%–50% of total energy as fat.
Hypozincemia	• Excessive losses (NGT, protein-losing enteropathy, ostomy, wound)	• Supplement zinc via enteral or parenteral route.
Vitamin K deficiency	• Inadequate vitamin K intake • Prolonged use of low-fat or low–vitamin K formula • Antibiotic use, cirrhosis, malabsorption, pancreatic insufficiency	• Supplement vitamin K. • Consider probiotic agents. • Measure PT and PTT or INR daily until stable.
Thiamin deficiency	• Chronic alcoholism • Advanced age • Long-term malnutrition • Malabsorption • Antacid therapy • Dialysis	• Supplement thiamin for 3–7 days. • Consider addition of folate and multivitamin in cases of alcoholism or chronic disease.
Essential fatty acid deficiency	• Inadequate linoleic acid intake	• Provide ≥4% of energy needs as linoleic acid. • Add modular fat component to TF if needed. • Provide 5 mL safflower oil per day via enteral route.
Hyperglycemia	• Refeeding syndrome • Diabetes mellitus, sepsis, catabolism, trauma, or other disease states or conditions • Insulin resistance • Glucocorticoids • Excessive carbohydrate	• Correct serum glucose levels before initiation of TF, if possible. • Monitor serum glucose every 6 hours, or per protocol. • Treat underlying disease. • Maintain appropriate intervascular volume and hydration. • Provide OHA or insulin therapy as needed to maintain serum glucose as low as possible. • Consider providing 30%–50% of total energy as fat. • Consider use of a product with fiber.
Hypoglycemia	• Abrupt cessation of EN in a patient receiving OHA or insulin	• Monitor serum glucose every 6 hours, or per protocol. • Treat with glucose (IV or via tube) to increase serum level to >100 mg/dL. • Taper TF gradually.

ADH, antidiuretic hormone; BUN, blood urea nitrogen; Cr, creatinine; ECF, extracellular fluid; IC, indirect calorimetry; INR, international normalized ratio; I/O, intake/output; IV, intravenous; NGT, nasogastric tube; OHA, oral hypoglycemic agent; PT, prothrombin time; PTT, partial thromboplastin time; SIAD, syndrome of inappropriate antidiuresis; TF, tube feeding.

[a]Weight change >0.2 kg/d reflects change in ECF volume.

[b]Mild fluid loss = 3% weight decrease; moderate loss = 6% weight decrease; severe loss = 10% weight decrease.

[c]BUN:Cr is usually 1:10 in state of normal hydration.

Source: Data are from references 16 and 96.

Many people assume that patients receiving EN are at less risk for metabolic complications than those receiving PN (see Chapter 17). Certainly, PN carries greater potential for metabolic alterations because the content of individual nutrients can be manipulated in PN solutions and the formulation is administered intravenously. However, with the exception of hyperglycemia studies, few randomized controlled trials have compared the metabolic effects of EN vs PN or EN vs no intervention.97 Therefore, it is unclear whether enteral feedings may cause metabolic alterations or if EN provides any advantage over PN with regard to metabolic complications.

Refeeding Syndrome

The potential for the serious electrolyte deficiencies associated with refeeding syndrome should be anticipated in all malnourished patients, especially those with large electrolyte losses. Patients at increased risk for refeeding syndrome include those with diarrhea, high-output fistulas, or vomiting

(Table 13-5).98 The frequency of refeeding syndrome with EN therapy has not been reported, but the syndrome may be life-threatening if it is uncorrected.

TABLE 13-5 Risk Factors for Refeeding Syndrome

- Malnutrition
- Inadequate nutrition intake for >2 weeks
- Poorly controlled diabetes
- Cancer, both before and during treatment
- Anorexia nervosa
- Short bowel syndrome
- Inflammatory bowel disease
- Being an older adult living alone
- Low birth weight and premature birth
- Chronic infections (eg, HIV)

Source: Data are from reference 98.

Refeeding syndrome, which has been reviewed extensively elsewhere,99–101 occurs after nutrition formulas are started, but it may also arise in malnourished patients who are resuscitated with standard IV solutions containing dextrose. With refeeding syndrome, decrements in electrolyte levels may occur in a matter of hours and may lead to arrhythmias, respiratory and cardiac failure, aspiration, and death (see Chapter 17). Although refeeding syndrome is typically associated with the use of PN, its incidence in patients receiving EN has been well documented.98,101,102 The nutrition support clinician should examine the patient's chart for previous episodes of hypophosphatemia, hypomagnesemia, or hypokalemia because these abnormalities may suggest multiple, unrecognized electrolyte deficiencies.

Electrolyte deficiencies may occur in the presence of normal serum levels. For potassium, a total body deficit of approximately 80 mEq is required before serum levels drop below normal. All patients should be evaluated for refeeding risk prior to EN initiation, with the assessment including the factors outlined in Table 13-5,49,98 and any electrolyte abnormalities should be corrected.49 ASPEN recommends that EN for patients at risk for refeeding syndrome should provide only 25% of the energy goal on Day 1, with attention to the energy contribution from IV fluids, and then cautiously advanced toward the energy goal over the next 3 to 5 days as dictated by clinical status and/or stable electrolyte levels.49

Hyperglycemia

Hyperglycemia is more commonly associated with PN than EN. The enteral products developed to improve glycemic control are typically higher in fat and contain fiber, both to slow gastric emptying and decrease the glycemic index. These effects may not be desirable in acutely ill patients in whom antropyloric dysfunction (poor gastric emptying, gastroparesis) commonly complicates gastric feeding. Furthermore, absorption of glucose from continuous feeds is more affected by the rate of carbohydrate delivery than the glycemic index, because glycemic index refers to the rate of glucose increase after a bolus. Slow advancement of EN and close collaboration with the medical team should allow for

adequate glucose control with standard feeding products. Glycemic control should be considered a primarily medical issue in the acutely ill patient. Diabetes-specific enteral products may help improve the ease of glycemic control in chronic care, but they have yet to be consistently proven to be of benefit in the acutely ill.103–105 See Chapters 15 and 34 for further discussion of formula selection and glycemic control.

Dehydration

Dehydration is an excessive fluid volume deficit, which may be accompanied by sodium imbalance. It is caused by insufficient fluid intake (orally, by tube, or intravenously) and/or excessive fluid losses, such as from fever, diarrhea, vomiting, significant blood volume loss, chronic illness (eg, diabetes, kidney disease), overuse of diuretics, drainage tube or paracentesis losses, wound seepage, or high nasogastric, fistula, or ostomy outputs.

Dehydration is associated with an increased risk for falls, pressure ulcers, constipation, urinary tract infections, respiratory infections, and medication toxicities. Persistent dehydration can lead to delirium, renal failure, coma, and death.

Hospital-Acquired Dehydration

Hospital patients are at risk for dehydration and its complications. A retrospective investigation compared hospitalized US veterans between 1997 and 2000.106 The overall development of dehydration in this group of patients was 3.5%. Mortality rates at 30 days and 6 months postdischarge were significantly higher (about double) for those patients who developed dehydration during their hospital stay compared with those who did not. For the patients who had volume-depleted dehydration, the mortality rate was 13.8% (vs 6.0% for controls) at 30 days and 29.3% (vs 14.7% for controls) at 6 months.

Risk Factors

Patients who are tube fed are at risk for dehydration. Enteral formulas alone typically do not meet total fluid needs; therefore, patients require additional water flushes. The risk for dehydration is greater in older adults. They have lower water reserves because of the decrease in lean body mass that occurs with aging. Other age-related changes that increase dehydration risk include altered sense of thirst, diminished cognition, dysphagia, dysgeusia, hyposmia, reduced kidney function, impairment of hormonal modulators of sodium and water balance (lowered aldosterone secretion, vasopressin release, and renin activity), and limitations in function.107–109 Younger tube-fed patients with characteristics similar to those described for older adults, patients with chronic disease, and those at risk for adverse drug reactions are also at higher risk for dehydration.

Detection

Clinicians need to assess for multiple signs and symptoms to determine whether a patient is dehydrated. Early signs include dry mouth and eyes, thirst, light-headedness (especially when standing), headache, fatigue, loss of appetite, flushed skin, heat intolerance, and dark urine with a strong odor. Tongue

dryness can be a simple, quick, reliable, cost-effective way to identify dehydration in the older adults, provided that other etiologies of dry mouth, such as diuretic and anticholinergic use, are ruled out.110 Alternatively, moist mucous membranes without tongue furrows can help rule out dehydration.110 Dehydrated patients usually develop orthostatic hypotension (a drop in systolic blood pressure of 20 mm Hg or more on standing) and a rise in pulse rate by at least 10 beats per minute. Signs of progressive dehydration include dysphagia, clumsiness, poor skin turgor (sternum: more than 2 seconds), sunken eyes with dim vision, painful urination, muscle cramps, and delirium.

Laboratory results for dehydrated patients usually show an elevation, relative to predehydration levels, in blood urea nitrogen (BUN), plasma osmolality, and hematocrit, whereas serum sodium levels can be elevated, low, or normal, depending on the etiology of the dehydration. In dehydration, the BUN level usually rises out of proportion to the usual BUN-to-creatinine ratio of 20:1. The BUN:creatinine ratio should be evaluated in the context of the patient's nutrition state and underlying renal function. Patients with low muscle mass have low creatinine concentrations. A rise in creatinine from 0.2 mg/dL to 0.4 mg/dL in a patient with severe loss of muscle mass signals a drop by 50% in glomerular filtration rate. BUN reflects protein intake as well as hydration and renal function. A patient with renal failure and no protein intake may have a normal or even low BUN concentration. A severely cachectic patient with renal failure with a creatinine level significantly lower than 1 mg/dL, a BUN level greater than 100 mg/dL, and a BUN:creatinine ratio greater than 100:1 might still be adequately hydrated.

An elevated urine-specific gravity (greater than 1.028) paired with low urine output usually reflects dehydration. Typical urine-specific gravity measurements are 1.010 to 1.025.111 One report showed that assessment of hydration status by comparing urine color to a standardized color reference chart was comparable to urine-specific gravity and osmolality results.112 When greater precision and accuracy in assessment are not required, clinicians may infer that tube-fed patients who achieve and maintain urine that is pale yellow or straw-colored are not dehydrated.

In hospitalized patients at risk for dehydration, fluid status can be tracked by strict intake and output measurements (including ostomy, fistula, liquid stool, drains, nasogastric tube, paracentesis outputs) and daily weights. The minimum urine output required to remove waste is 30 mL/h or about 700 mL/d. The urine output range for adults is typically 0.5 to 2.0 mL/kg/h,113 and an output of at least 1 mL/kg/h is useful as a guideline for adequate urine output. When evaluating daily weight changes and intake and output volumes, clinicians can assume that 1 kg of weight change equals 1 liter of fluid. If a patient loses weight while total fluid output exceeds total fluid intake by more than 800 to 1000 mL/d (the volume equal to insensible losses from lungs, feces, and skin), dehydration may develop. However, higher urine outputs with concurrent weight loss are expected when fluid overload is resolving.

Prevention

Clinicians need to be attuned to the fluid needs of their tube-fed patients to be sure they are providing maintenance fluid needs and replacing any additional losses. Ongoing assessments are required, and fluid intake should be increased if a patient has a fever, emesis, diarrhea, high fistula and ostomy outputs, or hyperglycemia. For patients with fever, increase fluid intake by 12% per degree Celsius

above 37.8°C.113 If a patient misses a feeding, then the fluid content of that feeding should be replaced. At times, the replacement of large fluid losses cannot be accomplished via the GI tract. The clinician may then need to consider IV fluid therapy.

When a patient is being diuresed, the clinician must be watchful and determine when the patient achieves a euvolemic state and then initiate adequate fluids to prevent dehydration. The presence of edema, indicating total body fluid and salt overload, does not guarantee intravascular volume adequacy. Aggressive diuresis of an acutely ill patient may lead to low vascular volume, which may be difficult to detect but can lead to renal, cardiac, or other organ failure as well as hypoperfusion, and hypotension. Useful signs of intravascular volume depletion in acutely ill patients include an increased heart rate, decreased or more concentrated urine, and an increase in oxygen extraction (an increase in the difference between arterial and venous oxygen concentration). Chapter 7 discusses methods for estimating fluid requirements for patients receiving EN.

Conclusion

All interventions, including EN, involve risks. The potential complications of EN range from uncomfortable GI symptoms to life-threatening problems. Fortunately, careful assessment, use of evidence-based nutrition support protocols, and ongoing monitoring of patients receiving EN can help prevent many complications and spur prompt intervention when complications do occur.