Special Report

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Enteral Nutrition Practice Recommendations

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TABLE OF CONTENTS

GLOSSARY OF TERMS

Beyond-Use Date: The date established by healthcare professionals from the published literature or manufacturer-specific recommendations beyond which the pharmacy-prepared or patient-specific product should not be used.[1] These products include the closed enteral feeding systems that do not require pharmacy preparation, but for which

the manufacturer's expiration date is no longer valid once the product is spiked.

Clinical Guidelines: Systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances.[2]

Closed Enteral System: A closed enteral container or bag, pre-filled with sterile, liquid formula by the manufacturer, and considered ready to administer.[3]

Computerized Prescriber Order Entry (CPOE): A prescription ordering system in which the prescriber enters orders directly into a computer system whether or not aided by decision support.[1]

Distilled Water: Water that has been vaporized and recondensed but is not necessarily free of dissolved or suspended matter; used when water purity is not necessary.

Drug-Nutrient Interaction: An event that results from a physical, chemical, physiologic, or pathophysiologic relationship between a drug and nutrient(s), nutrient status, or food in general, which is clinically significant if drug response is altered or nutrition status is compromised. [4]

Enteral Access Devices: Tubes placed directly into the gastrointestinal tract for the delivery of nutrients and/or drugs.[1]

Enteral Misconnection: An enteral misconnection is an inadvertent connection between an enteral feeding system and a non-enteral system such as a vascular access device, peritoneal dialysis catheter, tracheostomy, medical gas tubing, etc.[5]

Enteral Nutrition (EN): Nutrition provided through the gastrointestinal tract via a tube, catheter, or stoma that delivers nutrients distal to the oral cavity. [1]

Expiration Date: The date established from scientific studies to meet U.S. Food and Drug Administration (FDA) regulatory requirements for commercially-manufactured products beyond which the product should not be used.[1]

Fore Milk: Human breast milk that is typically lower in fat, available at the beginning of a feeding.

Hang Time: The length of time an enteral formula is considered safe for delivery to the patient beginning with the time the formula or human breast milk (HBM) has either been reconstituted, warmed, decanted, or has had the original package seal broken.

Hind Milk: Human breast milk which has a higher fat content than the fore milk.

Medical Food: A medical food as defined in section 5(b) of the Orphan Drug Act is a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutrition requirements, based on recognized scientific principles, are established by medical evaluation.[6]

Modular Enteral Feeding: Feeding formulas created by combinations of separate nutrient sources or by modification of existing formulas. [1]

Open Enteral System: An enteral system in which the clinician/patient/caregiver is required to decant formula into the enteral container or bag.

Purified Water: Sterile, solute-free, non-pyrogenic water that is free of any chemical or microbial contaminants; used for preparing or reconstituting commercial products, rinsing equipment and utensils; is required to produce *sterile water for irrigation* and *sterile water for injection*.[1]

Sentinel Event: An unexpected occurrence involving death or serious physical or psychological injury or the risk thereof. Serious injury specifically includes loss of limb or function. The phrase "or the risk thereof" includes any process variation for which a recurrence would carry a significant chance of a serious adverse outcome.[7]

Tap Water: Municipal or locally-available potable water that meets the Environmental Protection Agency's (EPA) National Primary Drinking Water regulations (40 CFR Part 141-143)[8] and is consistent with World Health Organization (WHO) guidelines for water safety.[9]

Transitional Feeding: Progression from one mode of feeding to another while continuously administering estimated nutrient requirements.

References

1. American Society for Parenteral and Enteral Nutrition Board of Directors and Standards Committee: Teitelbaum D, Guenter P, Howell WH, Kochevar ME, Roth J, Seidner DL. Definition of terms, style, and conventions used in A.S.P.E.N. guidelines and standards. *Nutr Clin Pract.* 2005;20:281-285.
2. Institute of Medicine, Field MJ, Lohr KN, eds. *Clinical Practice Guidelines: Directions for a New Program.* Washington, DC: National Academy Press, 1990.
3. Hsu TC, Chen NR, Sullivan MM, et al. Effect of high ambient temperature on contamination and physical stability of one-liter ready-to-hang enteral delivery systems. *Nutrition.* 2000;16:165-167.
4. Santos CA, Boullata JI. An approach to evaluating drug-nutrient interactions. *Pharmacotherapy.* 2005;25(12):1789-1800.
5. Guenter P, Hicks RW, Simmons D, et al. Enteral feeding misconnections: a consortium position statement. *Jt Comm J Qual Patient Saf.* 2008;34:285-292.
6. U.S. Department of Health and Human Services Food and Drug Administration Center for Food Safety and Applied Nutrition. Frequently Asked Questions About Medical Foods May 2007. Available at: http://www.cfsan.fda.gov/~dms/medfguid.html. Accessed April 4, 2008.
7. Joint Commission on Accreditation of Healthcare Organizations. Sentinel Event Policy and Procedures. Revised: July 2007. Available at: http://www.jointcommission.org/SentinelEvents/PolicyandProcedures/. Accessed October 15, 2008.
8. Environmental Protection Agency. *National Primary Drinking Water Regulations.* 40 CFR § 141-142, 2002.
9. World Health Organization. *Guidelines for drinking-water quality.* Geneva, Switzerland:WHO, 2004.

PREFACE

A.S.P.E.N. established the Enteral Nutrition Practice Recommendations Task Force to examine the available

literature related to the ordering, preparation, delivery, and monitoring of enteral nutrition and to establish evidence-based practice guidelines. It was recognized from the onset that there was either an absence of research or the research was of limited strength to support many aspects surrounding the practice of administering enteral nutrition. Therefore, in addition to the existing literature, a consensus of expert opinion based on current knowledge and best practices was used to formulate these practice recommendations. The strength of each practice recommendation was graded using a method consistent with the 2002 A.S.P.E.N. Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients.[1] The grading system was based on a modified version of the method used by the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services.[2] After review of the literature cited, the authors used the AHRQ criteria to classify the strength of the evidence supporting each recommendation statement. The evidence supporting each statement is classified as follows:

A   There is good research-based evidence to support the guideline (prospective, randomized trials).
B   There is fair research-based evidence to support the guideline (well-designed studies without randomization).
C   The guideline is based on expert opinion and editorial consensus.

This document was reviewed and approved by the A.S.P.E.N. Board of Directors following review by internal and external content experts and the A.S.P.E.N. Clinical Practice Committee. This document will be reviewed and updated at least every 5 years.

References

1. A.S.P.E.N. Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *JPEN J Parenter Enteral Nutr.* 2002;26 (Suppl):1SA-138SA. Errata 2002;26:144.
2. Pocock SJ, Elbourne DR: Randomized trials or observational tribulations? *New Engl J Med.* 2000;342:1907–1909.

I. INTRODUCTION

Enteral nutrition (EN) in this document refers to the delivery of enteral products, including human breast milk (HBM), delivered through an enteral access device into a functioning gastrointestinal (GI) tract. Consideration is made of patients throughout the lifecycle and throughout all practice settings. The principal indication for EN is a functional GI tract with sufficient length and absorptive capacity and the inability to take nutrients through the oral route either totally or in part. Specific indications for the use of EN are described in the Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients.[1]

While the process of administering EN may appear less complex compared with parenteral nutrition (PN), serious harm and death can result due to potential adverse events occurring throughout the process of ordering, administering, and monitoring. There have been multiple reports of adverse events related to EN. These events include reports of enteral misconnections,[2] enteral access device misplacements[3] and displacements, metabolic abnormalities, mechanical tube complications, bronchopulmonary aspiration, GI intolerance related to formula contamination, and drug-nutrient interactions.[4] Reports such as these and the need to promote optimal practices for EN ordering, preparation, delivery, and monitoring have prompted A.S.P.E.N. to develop this document. Therefore, the intention of the Enteral Nutrition Practice Recommendations Task Force was to investigate and compile practice guidelines and to disseminate these recommendations to clinicians, administrators, educators, and researchers involved in the provision of EN. This document is not intended to serve as a complete reference guide to the administration and management of EN.

Patient safety is a national and international priority in all areas of healthcare. The goal of this document— to identify safety issues related to EN— is in keeping with this purpose. The challenge is to identify evidence-based and strong consensus practices and communicate the information to the healthcare community, patients, and their caregivers. The Joint Commission has been recognized for their well-established patient safety activities in all healthcare settings through its National Patient Safety Goals (NPSG).[5] These goals promote proactive improvements in patient safety, whether based on empirical evidence or best practices. A Sentinel Event Alert released through the Joint Commission in April 2006 identified tubing misconnections as a persistent and potentially deadly occurrence, which is often under-reported.[6] Reports in the media and from organizations such as the Emergency Care Research Institute (ECRI), the U.S. Food and Drug Administration (FDA), the Institute for Safe Medication Practices (ISMP), and United States Pharmacopeia (USP) indicate that misconnection errors, including enteral misconnections, occur with significant frequency and can lead to deadly consequences.

Promoting patient safety in the enterally fed patient is dependent on continuous surveillance and recognition of potential areas of patient harm and medical errors. Identifying areas for potential human error, administrative and organizational conditions that are conducive to error,

and the patient's own tolerance to EN need to be recognized by the healthcare practitioner, and clinical and organizational changes implemented, if EN complications are to be decreased. This applies to all populations across the entire healthcare continuum. The administration of EN is a multidisciplinary process. Policies and procedures for patients fed enterally in the hospital and at alternate sites may not be entirely evidence-based. Compounded with the complexities of modern healthcare and decreasing staff both at the bedside and at the nutrition support level, risk of complications associated with the delivery of EN may increase.

References

1. A.S.P.E.N. Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *JPEN J Parenter Enteral Nutr.* 2002;26(Suppl):1SA-138SA. Errata 2002;26:144.
2. Guenter P, Hicks RW, Simmons D, et al. Enteral feeding misconnections: a consortium position statement. *Jt Comm J Qual Patient Saf.* 2008;34:285-292.
3. Bankhead RR, Fang JC. Enteral access devices. In: Gottschlich MM, ed. *The A.S.P.E.N. Nutrition Support Core Curriculum: A Case-Based Approach—The Adult Patient.* Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2007: 233-245.
4. Malone AM, Seres DS, Lord L. Complications of enteral nutrition. In: Gottschlich MM, ed. *The A.S.P.E.N. Nutrition Support Core Curriculum: A Case-Based Approach—The Adult Patient.* Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2007: 246-263.
5. The Joint Commission. National Patient Safety Goals. 2007. http://www.jointcommission.org/PatientSafetyNationalPatientSafety Goals/. Accessed April 4, 2008.
6. The Joint Commission Sentinel Event Alert. *Tubing Misconnections— A Persistent and Potentially Deadly Occurrence.* 2006. http://www. jointcommission.org/SentinelEvents/SentinelEventAlert/sea_36. htm. Accessed October 15, 2008.

II. ORDERING AND LABELING OF ENTERAL NUTRITION

A. Formulary Selection Process

The first commercially produced enteral formulas were made available for use in the 1940s. The numbers of these products have expanded to include common standardized and blenderized formulas, disease-specific products, modular components, and powdered formulas, often used in infants and toddlers. Because of this increase in available products, the clinician must rely on nutrition and physical assessment, consideration of metabolic abnormalities, evaluation of GI function, overall medical condition, and expected outcomes for each individual patient to determine product selection. This systematic comparison of the patient's condition and nutrient needs with the specific properties of the available nutritional formulas can be used to identify the enteral formula that will most closely meet the individual's requirements. The simple practice of correlating a medical diagnosis with a specifically marketed formula can result in the administration of inappropriate nutrition support and an increased cost of nutrient provision.[1] A potential safety issue may arise if an enteral formulary is limited to products based on an institutional contract in that they might not be appropriate for the patient population or setting.

Historically, dietetic/nutrition departments have been responsible for procuring, preparing, and distributing EN formula in hospital settings. In one study published in 1989, more than 75% of the hospitals had developed enteral formularies. The documented reasons were cost containment, decreased product duplication, staff education, and inventory management.[2] Another method to control costs is participation in a group purchasing organization. These groups offer significant savings opportunities for major patient care and diagnostic equipment purchases. The value of group purchasing allows healthcare facilities to control costs while providing the best patient care. Typically, an established commitment level is set for institutional compliance and results in benefits for the purchase of products and services at lower costs.[3-4] A clause should allow purchase of a noncompeting product outside of the contract without penalty if it better meets the patients' needs.

Practice Recommendations

1. Facilities should establish a formulary of available EN formulas specific to the institution. (C)
2. A specific EN formulary should be established based on patient population and estimated nutrient needs rather than specific diagnosis. (C)
3. When the facility participates in corporate buying groups for the purchase of EN products, a clinician with expertise in nutrition support should be involved in the selection process of available formulas that best meets the patient's nutrient requirements. (C)

References

1. Fussell ST. Enteral formulations. In: Materese LE, Gottschlich MM. *Contemporary Nutrition Support Practice.* 2nd Ed. Philadelphia, PA: Saunders;2004: 188-200.
2. Coffey LM, Carey M. Evaluating an enteral nutrition formulary. *J Am Diet Assoc.* 1989;89:64-68.
3. Anderson A, Baker G, Carmody M, et al. Partnering to improve the supply chain. *Mater Manag Health Care.* 2006;15(2):42-51.
4. Smith CR. Determining when integrated delivery systems should belong to GPOs. *Healthc Financ Manage.* 1998;52:38-41.

B. Elements of the Order

Many problems associated with EN orders result in inadequate delivery of formula to patients in critical care settings. These problems are attributed to under-ordering, frequent cessation of the administration, and slow advancement of the EN to goal rate.[1,2] Standard protocols[2,3] and an algorithm[4] have been implemented to address these problems. One group developed a protocol that standardized ordering, nursing procedures, rate advancement and limited administration interruptions. Use of the protocol improved delivery of goal volumes, although there was physician resistance to using a standard order form.[2] A Canadian group was also able to improve delivery of the required formula volume using a protocol.[3] A feeding algorithm was developed to increase the likelihood of meeting nutrition requirements. The algorithm also resulted in an increased utilization of EN (rather than PN) and in the number of patients who met EN administraton goals.[4]

Patient-specific EN orders should include 4 elements: 1) patient demographics, 2) formula type, 3) delivery site/device, and 4) administration method and rate. For examples, see Figures 1 and 2 (Adult and Pediatric order forms). Orders can be written as a single order representing a specific prescription, or they can be part of a larger protocol that directs advancement of EN from initiation to a goal rate or volume that represents a nutritionally adequate endpoint. The inclusion of transitional orders will direct weaning from EN, and ancillary orders may address various patient care issues. Orders may be handwritten in the medical record or entered through a Computerized Prescriber Order Entry system (CPOE).

Patient Demographics: The order should clearly state the patient's name, date of birth, weight, location, and medical record number (MRN).

Formula: The formula should be clearly identified in the order either by a generic name or by the specific product depending on institutional policy. For example: Osmolite® (Abbott Laboratories. Abbott Park, IL) which contains 1 calorie per mL can be generically identified as "isotonic" or "standard"; TwoCal® HN (Abbott Laboratories) which contains 2 calories per mL can be generically identified as "calorie dense"; Peptamen® 1.5 (Nestle Nutrition, Vevey, Switzerland), a partially hydrolyzed formula, can be generically identified as "semi-elemental" or "peptide-based." Formula orders may also include the administration of modular products used to enhance the protein, carbohydrate, fat, or fiber content of the enteral regimen. In the adult population, these products are usually administered directly to the patient via the enteral access device in prescribed amounts and frequency with specific administration guidelines, but

are most often not added to the enteral formula. In the neonatal and pediatric population, fluid tolerance limits are a concern, therefore the base formula is often augmented with a modular macronutrient. When this type of manipulation to infant formula is prescribed, the base formula, the modular product, and the base and final concentration of formula per 100 calories are all considered.[5,6] If this is done in the home, it is important to teach the parents or caregivers the proper method to prepare a formula with additives.

Delivery site/device: The route and access site for formula administration should be clearly identified in order to prevent wrong-site administration. Enteral misconnections (see later section on the same) have been reported in the literature.[7] Identification of the site (eg, jejunal port of gastrojejunostomy tube) also decreases the chance of inadvertent use of the site for another therapeutic entity.

Administration method and rate: Bolus, gravity, or continuous method: volume or rate of administration, and timing of formula delivery within a specified period of time (24 hours or cyclic) should be clearly set forth in an EN order.

Additional Orders: Orders that differ from the standard formula rate, route, and volume prescriptions. These can include:

Advancement orders: These orders direct the progression of an EN regimen from initiation through to an endpoint or goal formula volume over a specified time period. Increases in formula volume or rate of administration to achieve a goal should be clearly written. These advancement orders also need to be coordinated with decreases in parenteral nutrition.

Transitional orders: The incremental decreases in formula volume over a period of time to accommodate for an increasing oral intake.

Ancillary orders: Routine or ancillary orders will depend on both the population and setting. These orders are based on institutional policies for care of the enterally fed patient, such as orders for flushing the enteral access device, head of bed (HOB) elevation, and monitoring laboratory parameters.

C. Enteral Nutrition Order Forms

The EN Order Form contains the four elements that should be part of an EN order plus suggestions for ancillary and transitional orders. The examples seen in Figures 1 and 2 should be adapted to meet the need of each individual institution and can be paper- or computer-based. Many institutional settings utilize CPOE systems, which should provide clinical decision support and address each of the elements in the figure (eg, a separate

Figure 1. Adult Enteral Nutrition Order Form

Patient Name: _____ Medical Record No: _____ DOB:_____
Room Number: _____ Dosing Weight: _____

FORMULA   [select one]

[ ] Standard   [ ] Standard/Fiber
[ ] Protein-rich   [ ] Reduced-calorie
[ ] Calorie-rich   [ ] Peptide-based
[ ] Low Electrolytes   [ ] Substrate-enriched
[ ] Modular Product: Pro:_____ ____CHO:_____Fat:_____
[ ] Other:_____

DELIVERY SITE   [select a route and an access]

Route: Access:
[ ] Gastric   [ ] Nasogastric   [ ] Oralgastric   [ ] Gastrostomy
[ ] Post-pyloric   [ ] Nasoduodenal [ ] Oralduodenal
                     [ ] Nasojejunal   [ ] Oraljejunal   [ ] Jejunostomy

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METHOD OF ADMINISTRATION   [select a method and then a rate]

Method: Rate:
[ ] Pump-assisted   [ ] Initial ____ mL/h
                              [ ] Advance by ____ mL/h every ____ h to goal of ____ mL/h

[ ] Gravity-assisted   [ ] Initial ____ mL bolus over ____ min ____ times daily
     (30-60 min)   [ ] Advance by ____ mL each day to a goal of _____ mL
                                  feeding over ____ min ____ times daily

[ ] Bolus (Syringe)   [ ] Initial ____ mL bolus over ____ min ____ times daily
     (10-20 min)   [ ] Advance by ____ mL each day to a goal of _____mL
                                  feeding over ____ min ____ times daily

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OTHER ORDERS   [based on institutional protocol]
(For example)
[ ] Flush the feeding tube with ____ mL of water every ____ h our
[ ] Keep head of bed elevated to 30°-45°

MONITORING   [based on institutional protocol]
(For example)
[ ] Check GRV every _____ hour(s)
        If GRV greater than____ mL → hold administration for ____ hour(s)and re-check
        If GRV greater than 500 mL → hold administration indefinitely (will require a new order to
        re-start feedings)
[ ] Confirm HOB elevation to 30°-45°
[ ] Observe for abdominal distension, firmness or discomfort every ____ hour(s)
[ ] Tube site care and assessment every _____hour(s)
[ ] Intake and Output every _____hour(s)
[ ] Weigh once daily
[ ] Labs:

Prescriber: Date: Time:_____

CHO, carbohydrate; DOB, date of birth; GRV, gastric residual volume; HOB, head-of-bed; Pro, protein.

Figure 2.   Pediatric Enteral Nutrition Order Form

Patient Name: _____   **Medical Record No:** _____   **DOB:**_____ **Room Number:**_____   **Dosing Weight:**_____
FORMULA: _____   **at concentration:**   _____ **kcal/30mL** **Additional Nutritional Additive:** _____ **Final concentration:** _____ **kcal/30mL** **Other additives/medications:** _____
DELIVERY SITE **Oral: PO ad lib or**   _____ **mL** **Feeding tube:** **Nasogastric___ Gastrostomy____ Nasojejunal____ Gastrojejunal_____ Jejunostomy__**
METHOD OF ADMINISTRATION: **[select a method and then a rate]**

METHOD OF ADMINISTRATION: **[select a method and then a rate]**

Method	Rate
[ ] Pump-assisted	[ ] Initial ___ mL/h [ ] Advance by ___ mL/h every ___ hour(s) to goal of ___ mL/h
[ ] Gravity-assisted (30-60 min)	[ ] Initial ___ mL bolus over ___ min ___ time(s) daily [ ] Advance by ___ mL each day to a goal of ___ mL feeding over ___ min ___ time(s) daily
[ ] Bolus (Syringe) (10-20 min)	[ ] Initial ___ mL bolus over ___ min ___ time(s) daily [ ] Advance by ___ mL each day to a goal of ___ mL bolus over ___ min ___ time(s) daily
[ ] Oral	Offer PO every _____ minute(s), then give remaining via tube

OTHER ORDERS   **[based on institutional protocol]**
(For example)
[ ]   Flush the feeding tube with ___ mL of water every ___ hour(s)
[ ]   Keep head of bed elevated to 30°-45°

MONITORING   **[based on institutional protocol]**
(For example)
[ ]   Observe for abdominal distension every ___ hour(s)
[ ]   Tube site care and assessment every _____hour(s)
[ ]   Intake and Output every _____hour(s)
[ ]   Weigh daily
[ ]   Labs:

Prescriber: **Date:**   **Time:_____**

DOB, date of birth; PO ad lib, by mouth at will.

screen for each element; for example, if a post-pyloric enteral access device order is selected then the intermittent administration delivery screen(s) would not be an option). These systems should be designed with detailed order sets that promote safety by using drop-down menus within each element of an EN order, including required fields. Such menus may facilitate standardized advancement of initial administrations to goal volumes, uniform enteral access device flushing volumes and methods, and population-specific ancillary orders.

Practice Recommendations

1. Standardized order forms (paper or CPOE) should be developed and designed for adult and pediatric EN regimens to aid prescribers in meeting each patient's nutrition needs and to improve order clarity. (C)
2. EN orders should include 4 elements: 1) patient identifiers, 2) the formula, 3) the enteral access delivery site/device, and 4) the administration method and rate. (C)
3. Order protocols may also incorporate feeding advancement, transitional orders, and implementation of ancillary orders.(C)
4. The use of generic terms to describe EN formulas is encouraged. (C)
5. Avoid the use of dangerous abbreviations or inappropriate numerical expressions. (C)
6. All elements of the EN order must be completed when EN is modified or re-ordered. (C)

References

1. McClave SA, Sexton LK, Spain DA, et al. Enteral tube feeding in the intensive care unit: factors impeding adequate delivery. *Crit Care Med.* 1999;27:1252-1256.
2. Spain DA, McClave SA, Sexton LK, et al. Infusion protocol improves delivery of enteral tube feeding in the critical care unit. *JPEN J Parenter Enteral Nutr.* 1999;23:288-292.
3. Mackenzie SL, Zygun DA, Whitmore BL, Doig CJ, Hameed SM. Implementation of a nutrition support protocol increases the proportion of mechanically ventilated patients reaching enteral nutrition targets in the adult intensive care unit. *JPEN J Parenter Enteral Nutr.* 2005;29:74-80.
4. Woien H, Bjork IT. Nutrition of the critically ill patient and effects of implementing a nutritional support algorithm in ICU. *J Clin Nurs.* 2006;15:168-177.
5. Klein CJ. Nutrient requirements for preterm infant formulas. *J Nutr.* 2002;132(6 Suppl 1):1395S-1577S.
6. Raiten DJ. Assessment of nutrient requirements for formulas. *LSRO Report.* 1998;128(11S):2059S-2094S.
7. Guenter P, Hicks RW, Simmons D, et al. Enteral feeding misconnections: a consortium position statement. *Jt Comm J Qual Patient Saf.* 2008;34:285-292.

D. Labeling of Enteral Nutrition

To avoid misinterpretation, a label should be affixed to all EN formula administration containers (bags, bottles, syringes used in syringe pumps). The label should reflect the four elements of the order form and therefore contain the following: patient demographics, formula type, enteral access delivery site/access, administration method, individuals responsible for preparing and hanging the formula, and time and date formula is prepared and hung.[1,2] See Figures 3 through 6 for examples which may also include nutrient information if the label is computer generated. Furthermore, the labels for all EN formula containers, bags, or syringes should be standardized. All EN labels in any healthcare environment shall express clearly and accurately what the patient is receiving at any time. Having standard components on a label decreases potential confusion when a patient is transferred to a different unit within a facility, or when a new staff member takes over a patient's care (see Table 1).[3] Clear labeling that the container is "Not for IV Use" helps decrease the risk for an enteral misconnection. Proper labeling also allows for a final check of that enteral formula against the prescriber's order.[1] Care should be taken in developing a label that is clear and concise and of a size that fits neatly on the container.

Special consideration with the labeling of HBM: Clear and concise labeling of HBM is essential to prevent errors in the delivery of breast milk to the infant. The label of milk stored in the hospital must include the following: contents in container (HBM), infant's name, medical record number, date and time of milk expressed, medications or supplements taken by the mother, whether milk is fresh or frozen, date and time milk was thawed, and expiration date based on whether milk is fresh or frozen.[4] If the mother is separating fore and hind milk, this designation should appear on the label. Unique identifiers may be used to describe other factors such as colostrum, transitional, and mature milk. The HBM label may also include information on fortification and caloric density if additives have been mixed with the milk. Hospitals have developed novel approaches to this process. Unique identifiers, such as bar codes, special colors, or symbols, may be used to further identify the HBM. Hospitals may use computer generated or handwritten labels[4] (see Figures 5 and 6).

Practice Recommendations

1. The labels for EN formula administration containers, bags, or syringes should be standardized. (C)
2. Patient transfer between and within healthcare environments require clinician-to-clinician communication to promote the accurate transfer of the EN prescription. (C)
3. All EN labels in any healthcare environment shall express clearly and accurately what the patient is receiving at any time. (C)
4. The EN label should be compared with the EN order for accuracy and hang time or beyond-use date before administration. (C)
5. Clearly label human breast milk (HBM) with the patient's name and medical record number in order to prevent errors in delivery of HBM to infant. Preprinted labels and/or bar coding systems may help avoid breast milk mixups. (C)

Figure 3.   Standard Enteral Nutrition Label Template (Adult Patient)

Figure 4.   Standard Enteral Nutrition Label Template (Neonatal or Pediatric Patient)

References

1. Perry AG, Potter PA. *Clinical Nursing Skills & Techniques.* 6th ed. St. Louis, MO: Mosby; 2006:1032.
2. Stamps DC. Enteral nutrition. In: Wiegand DJL, Carlson KK, eds. *AACN Procedure Manual for Critical Care.* St. Louis, MO:Elsevier; 2005:1142.
3. Mirtallo J, Canada T, Johnson D, et al; Task Force for the Revision of Safe Practices for Parenteral Nutrition. Safe practices for parenteral nutrition. *JPEN J Parenter Enteral Nutr* 2004;28: S39–S70. Errata 2006;30:177.
4. Robbins ST, Beker LT, eds. *Infant Feedings: Guidelines for Preparation of Formula and Breastmilk in Health Care Facilities.* Chicago, IL: American Dietetic Association, 2004.

III. ENTERAL FORMULA (MEDICAL FOOD) AND INFANT FORMULA REGULATION

A. Background

Enteral formulas, including adult and pediatric formulas, are classified by the U.S. Food and Drug Administration (FDA) under the heading of medical foods. Currently, the FDA defines medical foods as "a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation."[1] Infant formulas, used in bottle-feeding and in enteral (tube) feeding when required, are regulated by the FDA. This is not the case with medical foods. Manufacturers have sought to take advantage of the relatively unregulated status of medical foods to develop and market products under the classification of medical food, although the regulations, or lack thereof, are so confusing that even potential manufacturers confuse the legal differences between medical foods, infant formulas, and parenteral products which are classified and regulated as drugs by the FDA.[2,3] Thus, the public (patients) and healthcare professionals must give special attention to the veracity (accuracy, credibility) of enteral formula manufacturers on the labeled content and health claims attributed to formulas.

B. Medical Foods

Medical foods have been defined, but they are not regulated as either conventional food or as drugs. In fact, they are essentially without regulation other than those that apply to Good Manufacturing Practices for conventional foods. These require vendors to ensure clean manufacturing facilities, inclusion of required ingredients, and provision of appropriate concentrations of ingredients in processed foods. Vendors also fall under regulations that ensure the sterility of low-acid thermally processed foods.[4] But they are exempt from regulations on labeling (including *Nutrition Facts*) and health claims that apply to conventional foods as well as regulations that apply to drugs. The current legal definition of medical foods provided above dates to the Orphan Drug Act of 1988. In addition to defining medical foods, the Act introduced a subcategory called orphan medical foods to be used in the management of "…any disease or condition that occurs so infrequently in the United States that there is no reasonable expectation that a medical food for such a disease or condition will be developed without assistance."[1] This is similar to the provision that applied to drugs in the original Orphans Drug Act of 1973, to ease normally required development costs for those drugs (orphan drugs) not anticipated to return development costs due to minimal need for rare diseases. However, there are no developmental regulations for medical foods that would require the creation of an orphan category.[5]

C. Infant formulas

Infant formulas were distinguished from foods (and medical foods) for special dietary use in 1980. In 1979, two infant formulas designed to be low in sodium chloride caused multiple cases of failure to thrive associated with metabolic alkalosis attributed to the formula. This incident incited Congress to pass the Infant Formula Act of 1980, which placed infant formulas in a new category of foods for special dietary use. More recently, the FDA has issued a Health Information Advisory related to Chinese manufactured formulas that may be contaminated with melamine. These formulas are not approved for sale in the U.S. and specialty Asian markets in the U.S. are being investigated for sale of these products manufactured in China.[6] Infant formulas designed for uncommon medical conditions were classified as "exempt" because the nutritional requirements of infants with rare conditions differ from those of healthy infants.[5] Infant formulas are subject to regulations applying to quality control, labeling, nutrient requirements, formula recall, notification (for new products), and exempt products.[7]

Practice Recommendations

1. The veracity (accuracy, credibility) of adult enteral formula labeling and product claims is dependent on formula vendors. (C)
2. Nutrition support clinicians and consumers are responsible for determining the veracity of adult enteral formulas. (C)
3. The U.S. government regulates the veracity of infant formula labeling and product claims. (C)
4. Interpret enteral formula content/labeling and health claims with caution until such time as more specific regulations are in place. (C)

Figure 5.   Standard Human Breast Milk Label Template (Infant Patient)


```
ENTERAL USE ONLY
Institution and Department Name – Contact Information

Patient Name      _____        Patient ID      _____
Room Number _____

                    Human Breast Milk Contents

                      Fresh or Frozen (circle)

    HBM Fortifier ____cal/oz. and/or _____to make

                    _____ (as per prescriber order)

Prepared by: _____         Date: _____       Time: _____

                         Delivery Site

               Route of Delivery:_____
               Enteral   Access Site:_____

                          Administration
          Method of Administration:  Bolus   Continuous
                Rate of Administration:_____mL/h
          Formula Hung By: _____, NurseDate: ____Time: _____

                  Expiration Date: _____        Time: _____
```

Figure 6.   Human Breast Milk Storage Label


```
Institution and Department Name – Contact Information

Patient Name _____  Patient ID _____
Room _____

Pumped:  Date_____Time_____
                MEDICATIONS TAKEN:



Expiration Date:_____   Time: _____
```

References

1. 21 US Code 360ee(b).
2. Moyer P. "Medical food" available for management of osteoarthritis. *Medscape Medical News*. Feb 21, 2006. www.medscape.com/viewarticle/524011. Accessed April 23, 2007.
3. Brown C. Health claim regulations need not apply to medical foods. *Functional Foods & Nutraceuticals*. May 2003. www.ffnmag.com/NH/ASP/strArticleID/337/strsite/FFNSite/articleDisplay.asp. Accessed April 23, 2007.
4. Serafina JM. Food manufacturing practice and quality control for medical foods. *Food Drug Cosmet Law J*. 1989;44:523-532.
5. Mueller C, Nestle M. Regulation of medical foods: toward a rational policy. *Nutr Clin Pract*. 1995;10:8-15.
6. U.S. Food and Drug Administration. FDA issues health information advisory on infant formula. September 12, 2008. http://www.fda.gov/bbs/topics/NEWS/2008/NEW01883.html. Accessed October 29, 2008.
7. 21 US Code 106, 107.

IV. WATER AND ENTERAL FORMULA SAFETY AND STABILITY

Patient care plans that include EN add a degree of complexity to overall management. Two areas of concern in assuring formula safety include microbial contamination and nutrient stability.

A. *Water Safety*

Water may be required for reconstitution of an EN formula as well as to dilute medications, provide flushes, and maintain patient hydration. The source of water may differ depending on the patient.

   1.   **Types of Water Used in EN:**

      a. Purified Water – sterile, solute-free, non-pyrogenic water that is free of any chemical or

Table 1.   Components of the Formula Label

Labeling of Enteral Formula	Labeling of Incoming Human Breast Milk

• Patient's name and room number
• Medical record ID number
• Formula name and strength of formula, if diluted
• Date and time formula prepared*
• Date and time formula hung*
• Administration route
• Rate of administration expressed as mL/hr over 24 hours if continuous administration
• Administration duration and rates are to be expressed on the label if the EN is cycled or intermittent
• Initials of who prepared, hung, and checked the EN against the order
• Appropriate hang time (expiration date and time)
• Dosing weight if appropriate
• "Not For IV Use"
	• Infant's name and room number
	• Medical record ID number
	• Dosing weight
	• Date and time milk expressed
	• Medication or supplements being taken by the mother
	• Specify whether milk is fresh or frozen
	• Contents in syringe/container (expressed breast milk)
	• If frozen, date and time milk thawed
	• Expiration date (based on whether the milk was fresh or frozen)
	• "Not For IV Use"
	• Fortified Human Breast Milk also includes:
	  o Name of fortifier
	  o Final concentration
	  o Date and time formula prepared
	  o Initials of who prepared, hung, and checked the HBM against the order

*Date-time formula prepared and date-time formula hung may be different so note both.
EN, enteral nutrition; HBM, human breast milk; ID, indentification; IV intravenous.

microbial contaminants; used for preparing or reconstituting commercial products, rinsing equipment and utensils; is required to produce *sterile water for irrigation and sterile water for injection*.[1]

b. Distilled Water – water that has been vaporized and recondensed but is not necessarily free of dis-solved or suspended matter; therefore should not be used for the preparation or administration of medications.

c. Tap Water – municipal or locally-available potable water that meets the Environmental Protection Agency's (EPA) National Primary Drinking Water regulations (40 CFR Part 141-143)[2] and is consistent with World Health Organization (WHO) guidelines for water safety.[3]

2.   Indications for Use of Water

a. Maintaining Hydration/Flushes

Tap water or bottled water may be adequate for hydration of the otherwise healthy, immunocompetent, orally-fed patient. However, the acute or chronically-ill patient requiring invasive enteral feeding with any presumed alteration to their GI barrier function may be at higher risk from exposure to non-sterile products including water. Nosocomial infections from contaminated tap water sources have been demonstrated in critically ill patients.[4-7] This has also been reported in less acutely ill but immunocompromised patients and is best avoided.[8-11] Terminal filtration of tap water may be useful, but retrograde contamination is still an issue.[12]

b. Diluting Medications

Tap water may not be used in the preparation of dosage forms[1] and is also specifically discouraged if being administered via a post-pyloric enteral access device.[13] Purified (sterile water for irrigation) or saline should be used as the diluent or flushing vehicle in preference to any other fluid including tap water. Depending on the source, the latter may contain contaminants including not only pathogenic micro-organisms but also pesticides, medication residue, and heavy metals.[14,15] The metals and medications may interact with the large surface area of the crushed medication product ingredients and thereby reduce bioavailability. For infants, the recommendation is to flush the enteral access device with sterile water before and after administration of enteral formula and medication.[16]

c. Formula Reconstitution

The water supply may be a source of potential contamination if purified water (sterile water for irrigation) is not used in formula reconstitution. Hard water refers to the higher mineral content of the water (especially calcium, magnesium, and possibly iron). Softened water is water that has been treated with ion exchange to remove excess minerals, with the exception of sodium (< 15 mmol/L) and potassium. Chemically softened water is not appropriate for use in the preparation of infant formula.[16] All water supplied for feeding preparation must meet federal standards for drinking water and be sterile.[16,17] Only chilled, sterile water is recommended for preparing infant formula preparation.[16]

Figure 7. Potential Points for Contamination in the Preparation, Storage, Handling, and Adwministration of Enteral Nutrition
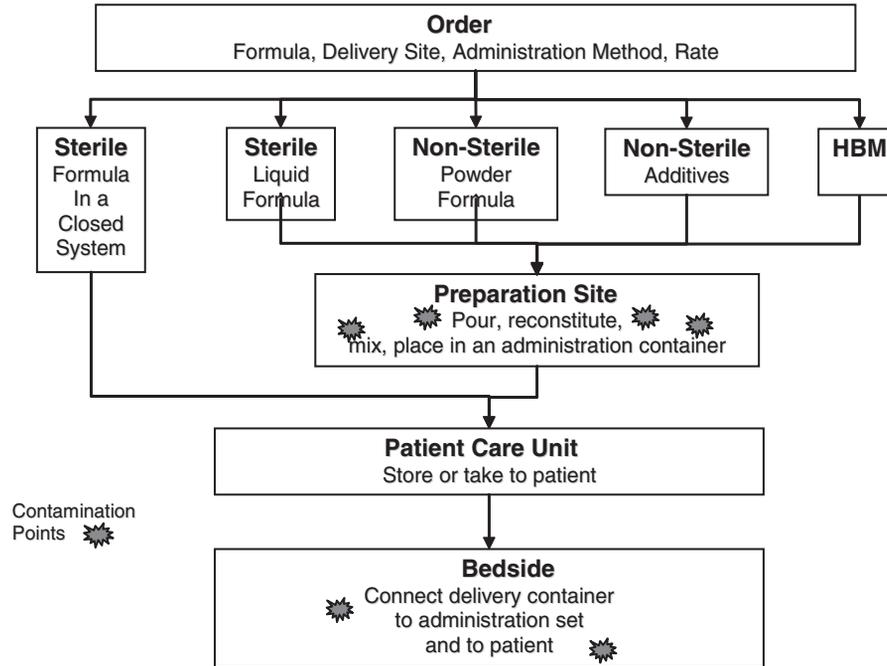
HBM, human breast milk.

B. EN Formula Safety

1. Contamination

Background

Contamination of EN formula with micro-organisms can occur at any point throughout the production, preparation, storage, or administration process (see Figure 7). This can pose a significant risk to the patient—particularly if immunocompromised—at either end of the age spectrum or with an alteration of GI barrier function.

EN products in liquid form are considered an ideal growth medium for potentially pathogenic micro-organisms and therefore undergo heat sterilization at the end of production. Commercially-available EN products manufactured in dry powder form are not required to be sterile and may be contaminated by the end of the production process prior to reaching the market. A study of powdered infant formulas across several European countries revealed *Enterobacter spp.* contamination in 53% of 141 samples.[18] Although these were found in amounts within the accepted maximal limits, once these products are reconstituted with water, especially if at room temperature or in bottle warmers, the organism would be expected to multiply rapidly.[19] The meningitis and subsequent death of an infant was directly linked to the presence of *Enterobacter sakazakii* in a powdered infant formula.[17] Of 49 infants screened at that same

Tennessee site, 10 were found to be infected or colonized with *Enterobacter sakasakii*.[17] Dozens of cases of meningitis and necrotizing enterocolitis related to *Enterobacter sakazakii* in infant formulas and on associated utensils have been published.[20] A limited number of powdered products are also available for use in older children and adults.

Preparation/Storage

Contamination of EN formulas (liquid or powder) with subsequent patient colonization or infection is also a concern during preparation in a healthcare setting. EN preparation may include the mixing, reconstitution, or dilution of modular products and formula with water, and/or pouring the formula into an administration container. The sterility of the commercially-available liquid EN products, as well as that of the sterile bags and administration sets, is disrupted by any manipulation thereby raising the risk for contamination. Therefore, the environment in which EN preparation takes place should be controlled to reduce the risk for contamination. Critical points for contamination are documented to include the dietetic unit/kitchen and the patient care unit.[21] For example, some pathogenic organisms may readily attach to and form biofilm on stainless steel surfaces as well as on enteral access devices, further reinforcing the need to prevent contamination in the first place.[22] EN formulas prepared in a kitchen or in a patient

care unit are at much higher risk for contamination than those prepared under aseptic conditions or that undergo sterilization prior to patient administration. As many as 30%-57% of enteral formulas prepared in the hospital and over 80% of those prepared in the home have been found to be contaminated with bacteria.[21,23,24] Approximately half of the contaminated EN formulas in the hospital contained bacterial counts that exceed federal limits for foods (10^4 CFU/mL).[21] Some admixtures were contaminated with more than one organism.[21] Isolates have included Gram-negative bacilli, Gram-positive organisms, anaerobes, and yeast.[25,26] Subsequent growth of a contaminant organism will depend on storage conditions. For EN formulas not used immediately after preparation, refrigeration may reduce bacterial growth potential. Bacterial contamination may also reduce nutrient composition available to the patient.[27] Patient colonization and infection with organisms that are identical to those isolated from their EN formulas has been clearly documented.[28,29] One salmonella outbreak among children and staff was linked to preparation of EN formulas in the hospital's formula room where cross contamination occurred.[30]

Reconstitution of any component or initiating a multi-step preparation of an EN formula is best performed by trained personnel in an appropriate environment to reduce contamination.[31] The fact that powdered formulas are not commercially sterile requires meticulous adherence to aseptic procedures in the handling and reconstitution process, especially for infants or immunocompromised patients. With the availability of closed EN systems, contamination in the preparation of individualized EN admixtures for adult patients is considered a less frequent event compared with the larger numbers of infants and children requiring such a preparation. Preparing infant formula is best done within a clean environment (ie, International Organization for Standardization [ISO] Class 5 hood), by personnel trained in aseptic technique, wearing appropriate attire. The preparation area should be separate from any storage area to avoid particulate matter contamination. Any instruments or utensils used in EN preparation should either be disposable or undergo heat sterilization prior to use. Hand hygiene and aseptic practices should be in place to prevent EN formula contamination during preparation. Centers for Disease Control and Prevention (CDC) recommendations for handwashing can be found at http://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf. These recommendations include hand washing to the elbow with soap and water, and using a Food and Drug Administration (FDA)-approved antimicrobial persistence alcohol hand rub between glove changes, as well as prohibition of watches, rings, piercings or artificial nails. Wearing disposable gowns, mask, gloves, and head covers may reduce the spread of airborne pathogens.[32] Infants and immunocompromised children are considered among the most vulnerable patients; many hospitalized immuno-compromised adults are also at risk. Consideration should be given to applying the U.S. Pharmacopoeia (USP) Compounding Category 1 (non-sterile, simple) or Category 2 (non-sterile, complex) moniker (name, label) and wording to all EN formula preparation which carry the expectation of adhering to good compounding practices for nonsterile preparations.[1] Category 3 is reserved for low-risk but sterile preparations.[1] This is based on the corresponding probability of contamination and suggests specific preparation and quality assurance practices.[1] Such a quality control process may then support hang times for prepared EN formulations of up to 12 hours without compromising the open system.[31,33]

HBM Preparation, Storage, and Administration

Reduction of bacterial growth during the period between expression of milk and delivery of milk to the infant, because expressed breast milk is not sterile, and to avoid transmission of microbes (eg, hepatitis B or methicillin-resistant Staphylococcus aureus [MRSA]) in milk to infants unrelated to the donor mother is essential to maintain safe HBM. Mothers are given their own collection kits to be attached to hospital-grade electric pumps. The collection kits should be cleaned according to manufacturer's directions after each use and sterilized daily. Pumps can be used by multiple mothers and sanitized between uses. These pumps should be checked by the hospital biomedical engineering department annually, whenever milk accidentally enters the pump, or when not working properly.[16] HBM should be stored in the hospital in containers approved for food storage such as glass or food-grade plastic (polypropylene or polycarbonate) containers.[34] Either sterile or aseptic containers may be used to store HBM.[34,35] Containers should have a cap to produce an airtight seal in order to avoid leakage or contamination; the use of a nipple on a container is not appropriate for storage.[36] Commercially- available containers designed for HBM collection feature universal threading so that they can be used to connect with pump directly in order to minimize touch contamination. Loss of immunologic factors occurs during storage of breast milk; the least losses occur with use of glass or hard plastic containers for storage compared to other containers.

Most hospitals provide a mother with a new storage container each time she expresses her milk. If the mother reuses the storage container, it can be sterilized following the same directions for the collection kits.[16] Storage bags intended for HBM storage are sterile and can be used for the infant at home. For the hospitalized infant, storage bags do not provide a closed system, may leak or tear, and are difficult to manage in the preparation of HBM for administration. There may be increased loss of fat and

fat-soluble vitamins with the polyethylene bags.[37,38] If a mother has already used these bags for the storage of her milk, they should be put into another double-zipped food-storage bag and used only if no other milk container is available.[16] While in storage, HBM from each lacatating mother must be segregated from any other mother's milk by storage in bins or zip-lock bags that are clearly labeled with the correct infant(s) name and medical record number. Dedicated refrigerators and freezers for infant feedings is suggested.[16,34] HBM that is appropriately labeled should be stored in an area that has controlled access.

Feeding an infant fresh HBM which has been expressed in the past 48 hours is preferable.[39] When fresh HBM is not available, frozen milk can used, starting with the oldest first; colostrum, then transitional, and finally, mature milk. It is important to completely thaw an entire container, because using only the unfrozen part of the milk may result in unequal distribution of milk components.[16] HBM should be thawed and warmed according to policies based on evidence-based protocols such as the American Dietetic Association's *Guidelines for Preparation of Formula and Breast Milk in Health Care Facilities*.[16]

HBM should be prepared with aseptic technique. After performing hand hygiene, the preparer should wear gloves.[40] The Occupational Safety and Health Administration (OSHA) has stated that HBM does not constitute occupational exposure based on the lack of evidence that any healthcare worker has acquired a viral infection via breast milk.[41] It is recommended that healthcare workers who are frequently exposed to HBM wear gloves.[16]

Due to sterility concerns about powdered additives, whenever a nutritionally adequate liquid fortifier is available, it is advocated for use as a fortifier of HBM, with this preparation also taking place in a controlled environment.[16] Because the volumes are often low when HBM is given as a continuous infusion via an enteral access device, a syringe pump is typically used to deliver the HBM. This also avoids the adherence of fat from the HBM to the enteral pump bag. Mothers often express their milk at home and transport it to the hospital. If the milk is to be used fresh—within 48 hours of expression—the milk can be refrigerated at home and transported chilled (35°-42° F or 2°-6° C). Otherwise the milk should be frozen at home, transported frozen, and stored in the hospital freezer designated for HBM storage.

HBM that is transported to or from the hospital in a frozen state should be tightly packed in a cooler without ice, because water freezes at a temperature higher than HBM and the ice is warmer than the frozen HBM and may thaw the frozen containers. Freezer gel packs are preferred over ice because they have a lower freezing temperature. Any dead space in the cooler should be filled with clean towels, foam chips or newspaper. If the HBM is to be in-transit for an extended length of time,

dry ice can be used in an insulated container. Hospitals often have guidelines and training for personnel involved in the transport of frozen biological material, with instructions regarding special labeling, weight limits for dry ice, use of non air-tight external containers, or the advisability of contacting a shipping company. If < 50% of the volume of frozen milk becomes partially thawed during transport, the milk can be safely refrozen. If the milk is > 50% thawed, the milk should either be used within 24 hours or discarded.

The Human Milk Banking Association of North America recommends dedicated freezers and refrigerators for the storage of HBM.[34] HBM in the freezer or refrigerator should be stored in bins for each patient with the name and medical record number clearly marked to avoid misadministration. Bins can be reused after washing thoroughly with soap and water. HBM should be arranged in the bins by date so that the oldest milk can be used first.[16]

The temperature of the refrigerators and freezers must be monitored to ensure that they stay in a safe range, ≤40°F (≤4°C) for refrigerators and -4°F (-20°C) for freezers. Alarms can be linked to the hospital security system to alert personnel to a problem to avoid the unnecessary loss of frozen HBM. The refrigerators should also be plugged into the emergency outlets that provide generator backup in the event of a power failure.[16] Due to the concern for the safety and security of HBM, some institutions limit access to the freezers and refrigerators to hospital staff.

Misadministration of HBM occurs when another mother's milk is administered to an infant. Each hospital should have a policy to address this issue. All breast milk preparation, storage, and administration policies should strive to create an atmosphere where there is a very low likelihood of this occurring, but should have a procedure in place in case a misadministration occurs. An example of a policy is available elsewhere.[16]

Handling/Administration

Introduction of potentially pathogenic micro-organisms may also occur during handling of feeding systems and during EN administration. In general, it has become clear that hospital-acquired infections associated with contaminated substances occur predominantly in the patient care area, especially when basic hygiene measures are not followed.[42] Setting up and manipulating the EN feeding systems in the patient care unit accounts for much of the contamination with potential pathogens.[29,43] Contaminated enteral feeding systems can contribute to the etiology of diarrhea in patients receiving EN.[44] From a prospective, controlled epidemiologic study, the acquisition of *Clostridium difficile* (20% vs 8%, $P = .03$) and subsequent organism-associated diarrhea (9% vs 1%, $P = .03$) is

significantly more likely in patients receiving EN.[45] In addition, post-pyloric feeding is a risk factor for *C. difficile* infection.[45] This occurred in an environment using an open feeding system, with an 8-hour hang time and administration sets changed every 24 hours. The most likely sources for contamination were the EN formulas and the healthcare personnel themselves.[45] Although irrigation trays may serve a practical purpose, they may also be a source of contamination (especially when hand hygiene and aseptic practices are not in place), and should be considered an open system and changed every 4-8 hours. Patient colonization and infection with organisms that are identical to those isolated from their EN formulations have been documented.[28,29]

Retrograde movement of pathogens along the enteral administration tubing has been suggested as an intrinsic mode of contamination of the EN formula. Two studies on this issue found that contamination did not occur when the tubing had a drip chamber.[46,47] If the retrograde colonization load is high or is from some particularly bad pathogens, it can be problematic, especially if the patient is already sick. While food in general is not sterile, it goes directly to the body's defense mechanisms (hydrocholoric acid and bile) which kill off many organisms in healthy individuals. Tube feeding products are perfect growth media. In addition, "exogenous" contamination can occur from healthcare providers.[48] Enteral access device contamination has been attributed to the lack of standard precautions in place when accessing the feeding hub.[49] The hub of the enterostomy tube should be cleaned with alcohol wipes at each change of tubing connection. Hands must be washed and/or alcohol hand rub applied between changing of gloves when moving from a dirty procedure (eg, aspirating gastric residuals) to a clean procedure (eg, handling equipment or EN formulas).[49] This research identified cross-contamination among 2 different patient care units when using molecular typing to assess hub bacteria as a source of enteral tubing contamination.[49] Under conditions simulating clinical use, 24% of EN delivery sets contained bacterial counts $\geq 10^5$ CFU/mL at 24 hours, suggesting that administration sets should be changed at least every 24 hours.[50] Contamination rates were examined for up to 72 hours, but not at any time point less than 24 hours in this study. Touch contamination in handling closed EN feeding systems has resulted in a 10-fold increase in contamination rates with 6-hour hang times[44] and recovery of a Gram-negative organism in 13%-87% of samples collected at the distal end of the administration set during a 24-hour simulated infusion.[51] Disinfection of connection sites with isopropyl alcohol after being manipulated using faulty technique may reduce contamination with select systems.[52] No part of the delivery system, including the EN formula itself, should come into contact with hands, skin, clothing or any other non-disinfected surface.[53] Aseptic technique in the patient care area can reduce the infectious risk to the patient.[54]

2. Hang Time for Enteral Formula and Issues of Enteral Set Usage

Hang Time

Contamination of EN formula or administration sets can occur at any step in the delivery process (see Figure 7). For that reason, criteria have been established for how long various types of formula can hang safely at ambient conditions. In 1995, the FDA revised their standards on what constitutes unacceptable levels of contamination in enteral formulas. The criteria include: any aerobic agar plate growing $>10^4$ CFU/mL, three or more samples $>10^3$ CFU/mL, or any pure culture of *Bacillus cerus, Listeria monocytogenes, Staphlococcus aureus* or *coliforms*.[55,56] Recommended hang times for formula and recommended set usage are summarized in Figure 8.

In response to the previously cited death of an infant from contaminated infant formula, the FDA has recommended that reconstituted enteral formulas prepared from mixing powdered formula should hang no more than 4 hours. It is not possible to commercially sterilize powdered formulas, so they should be reconstituted with sterile water and hung for 4 hours only.[17,16,52] When nutritionally appropriate sterile liquid formulas are available, they should replace powdered products due to sterility issues.[23,51,52,16] Formulas, either decanted with modular additives or reconstituted, should hang no longer than 4 hours. A recent report validated the safety of hospital-prepared enteral formulas and decanted formulas using a 4-hour hang time and replacing administration sets every 8 hours in burn patients.[57] Prepared formulas and HBM decanted into an open delivery system for use with neonates and immuncompromised patients of any age should hang no longer than 4 hours.[16,23,45]

In an early study of various administration sets that were deliberately contaminated, investigators found sterile, decanted formula to have low-to-no bacterial contamination for up to 12 hours when clean gloves were worn when adding the formula to the bag.[58] They also found that a recessed spike set allowed for limited exposure of the port-to-touch contamination, regardless of the type of container used. Weenk and Kemen compared various feeding systems and found a sterile glass bottle containing enteral formula to be associated with the lowest level of microbial growth from touch contamination.[43] They also found that decanted formula poured from a screw cap (as opposed to a flip top such as a can of soda) into a feeding bag was associated with lower levels of microbial growth. A later study looking

Figure 8.   Formula Hang Time Based on Source of Preparation

| 0 hours | 4 | 8 | 12 | 24 | 36 | 48 |

| **Sterile** Formula In an Open System (Neonate) |

| **Non-Sterile** Powder Formula |

| **Non-Sterile** Additives |

| **HBM** |

| **Sterile** Formula In an Open System |

| **Sterile** Formula In an Open System (at home) |

| **Sterile** Formula In a Closed System * |
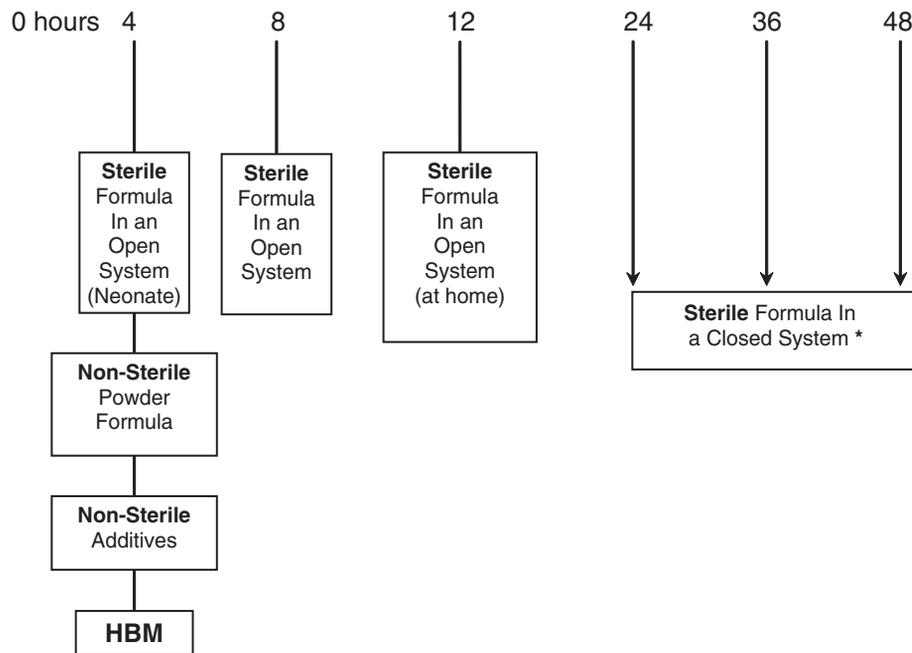
* Per manufacturer's guidelines. HBM, human breast milk

at closed vs open feeding systems found that open systems had no contamination at 7.5-13.3 hours after practice changes were made that included avoiding formula dilution, use of additives, and changing the delivery set every 8 hours.[42] A study of pediatric home care patients also documented the safety of sterile, decanted enteral formulas used for 12 hours during continuous feedings.[30]

Most of this research looks at contamination of EN formulas along a continuum of time, with longer hang times being associated with increasing and unacceptable levels of bacteria. This has led to the preference by many institutions to use a closed system enteral formula as often as possible. This practice has not been feasible in the pediatric sector until recently and even now available products are limited. Many studies in the literature document the safety of a 24-hour hang time for sterile closed systems.[24,30,32,45,58] A few studies looking at hang times of 36 and 48 hours have reported little to no contamination.[24,58,59] One study even validated the safety of using a closed system enteral formula for intermittent bolus feeding in nursing home patients.[47]

Much research has focused on contamination of enteral administration sets with investigators trying to discern if the source of bacterial growth is from healthcare providers' hands vs endogenous retrograde growth from the patient. One study used DNA extraction for molecular typing to determine the source of bacteria growth, and found both enteric bacteria indicating retrograde bacterial migration and skin contaminants likely originating from healthcare workers' hands.[49] An earlier study by Payne-James looked at contaminated formula and retrograde movement of bacteria in tubing sets with no drip chamber, a drip chamber, and a drip chamber plus an anti-reflux valve. [46] Results showed no bacterial contamination of the EN formula when tubing with a drip chamber was used.[46]

Two studies done in the Netherlands in intensive care unit (ICU) patients looked at bacterial contamination of enteral administration sets and found them to be unacceptably contaminated after a 24-hour hang time.[48,60] These studies suggested that retrograde migration of bacteria from the stomach and lungs are a problem. The recommended time for use of delivery sets varies with the type of formula being administered.

Early studies using open systems also validate concerns that enteral administration sets used for more than 24 hours in hospitalized patients result in unacceptably high levels of bacteria. Kohn documented a 23.8% contamination level for administration sets used

for 24 hours and a 42.9% contamination rate for sets used 48 hours.[50] Perez also found higher levels of bacterial growth in enteral administration sets after 48 hours of use. [61] They looked at initial diluents for enteral formula and compared sterile vs tap water but found that after 24 hours the bacterial growth was unacceptable using either type of water.[61] A recent study of pediatric homecare patients did document bacterial growth in enteral administration set tubing after 48-hour use, but contamination did not increase between 24- and 48-hour use and none of the patients had any clinical signs of problems from 48-hour administration set use in the home.[62] Administration sets are typically changed every 4 hours when HBM is being administered.[16]

Reducing Contamination

Although contamination and potential for clinical infection continue to exist, most healthcare institutions do not routinely maintain records of contamination rates and identify the critical points. Implementation of quality control measures and corrective action can reduce the bacterial contamination rates and therefore, undesired patient exposure to potentially pathogenic micro-organisms.[31] Reducing contamination rates implies knowledge of a baseline contamination rate. Solutions to the problem of enteral feeding systems with unacceptable levels of bacterial contamination have been repeatedly provided in the literature. Over 20 years ago, concern for contamination and subsequent patient infection led investigators to suggest use of sterile, non-manipulated, closed systems for EN administration and good hygiene, along with routine microbial surveillance.[55,63] The use of closed system enteral administration sets has been demonstrated to be safe for 24-48 hours.[64,65] Different administration sets have been evaluated for risk of inadvertent contamination in the process of filling the container.[43,66] The authors concluded that the adherence to strict aseptic technique is the key to prevention of contamination during the filling process. While use of closed EN systems may reduce contamination associated with preparation, this should still be supplemented with careful hygiene and technique to prevent touch contamination. The Hazard Analysis Critical Care Points (HACCP) system has been used to identify significant safety problems in EN administration as well as to highlight implementation of corrective practices.[67-69]

Administration set hang time was increased from 4 hours to 8 hours following the results of a well-designed study of several EN formulas including a modular product, without a significant increase in microbial contamination, provided that the bag contained no more than a 4-hour amount of formula.[57] Even when EN formulas in cans are administered, quality control mechanisms are important. For example, a clean area should be used in which contact

precautions are maintained: wipe down can/bottle lids with isopropyl alcohol, allow them to dry, and pour them into containers that can be sealed and clearly labeled, as previously described, with a hang time not to exceed 4-8 hours. Administration sets and bags containing any unused enteral formula should be discarded after this time. The CDC recommends that if a dry powder EN product is selected to meet a patient's needs, the preparation should be performed by trained personnel following strict aseptic technique.[17] Reconstituted formula should not be exposed to room temperature for longer than 4 hours. In addition, the reconstituted formula should be refrigerated if not immediately used and any remaining formula discarded within 24 hours of preparation. In the absence of federal regulation on preparation and handling of EN formulas within institutional settings, the American Dietetic Association (ADA) infant feeding guidelines are widely used.[16] The ADA safety guidelines can be applied to all patients receiving EN as can be said about the detailed material related to good compounding practices as described by the USP.[1]

A study published by Beattie and Anderson in 2001 demonstrated a reduction in microbial contamination of EN formula when manufacturer's recommendations were followed (using deliberately contaminated hands) and faulty handling.[58] Four types of containers and spike sets were studied and results showed using disposable gloves and following manufacturer's instructions when pouring decanted formula into a bag did result in acceptable low-to-no microbial contamination. In summary, all of these studies validate the safety of formulas in clinical practice and advocate strict adherence to standard precautions and manufacturer's recommendations when handling formula that is decanted.

Aside from contamination issues, feeding set composition has been a concern. The FDA has recommended all feeding sets and tubing used for male infants be di(2-ethylhexyl) phthalate (DEHP) free. This mandate is a result of liver toxicity and testicular atrophy in animal studies.[70] DEHP is a plasticizer that has been removed from most products used for pediatric enteral feedings. There are no regulations for female infants or adults at this time.

3. *Enteral Formula Stability*

The stability of each component of an EN formula is important to maintaining the product's integrity and the patient's nutrition status. There are very few studies specifically examining nutrient stability in EN formulas. The conditions of storage (temperature, light, and oxygen exposure) as well as the composition of the container can influence stability. A product available in a dry powder form that requires reconstitution will lend itself to stability concerns, with the instability varying in part with the degree of dilution.[71]

The data on enteral formulation stability is limited so far. Over a 6-hour simulated administration period, instability was noted in the fat and carbohydrate fractions without a change in pH or clogging of the enteral access device.[71] The proportion of unsaturated fatty acids within a product and the accompanying level of antioxidants may in part determine its stability. The potential for lipid peroxidation during storage, administration, and exposure of an enteral formula to light has also been evaluated.[72] A 6-hour simulated administration revealed increases in peroxidation compared to the control situation whether or not protected from room lighting.[72] The degree of fatty acid oxidation increases with storage time as well as with increasing temperatures; some losses even occurring with refrigerated storage at 4°C.[73] The ratio of 6:3 fatty acids may also increase with time. [73] Although the clinical implications are still not clear, there may be reason to consider storing all EN formulas under controlled conditions for the sake of product integrity. This has been most appropriate for reconstituted formulations with time-limited stability. Commerc ially available liquid EN formulas undergo heat sterilization to limit any micro-organism contaminants from reaching a patient. The influence of this process on macronutrient composition and bioavailability has been evaluated and found to be less likely at higher product water content, and with shorter periods of heat exposure.[74] Exposure of 1-liter, closed feeding systems to temperatures of 37°C for 24 hours did not compromise product stability although this was based solely on visual assessment rather than physicochemical analysis.[75]

Loss of nutrient value over time may extend to micronutrients as well. The activity of thiamine, vitamin A, and vitamin E decreased over time in enteral feeding formulations with a 1-year shelf life. Losses were greater at 20°C and 30°C compared with refrigeration at 4°C.[76] Over a storage period of just 9 months at room temperature, losses of thiamine, vitamin A, and vitamin E were 47%-53%, 88%-98%, and 45%-49% respectively in the products tested.[76] The type of container may be an additional variable to the stability of a formula across the product's shelf-life. The stability of vitamin A, vitamin E, and riboflavin from an EN formula did not differ between polyvinyl chloride and polyethylene/ethyl vinyl acetate enteral feeding containers.[59] Following a freeze-thaw cycle, losses of these vitamins remained not more than 10%.[59] Although the labeling of many enteral formulas are not yet based on percent values of the most current Dietary Reference Intakes, it is not known whether the micronutrient contents of EN formulas include overages relative to their label claims to account for instability over time. It would be valuable for the manufacturers to provide stability data on components of commercially available EN formulas.

Practice Recommendations

1. Each institution should define an ongoing quality control process for EN formula preparation, distribution, storage, handling, and administration. (B)
2. Institutions should maintain written policies and procedures for safe EN formula and HBM preparation and handling, as well as maintain an ongoing surveillance program for contamination. These should be based on the ADA infant feeding guidelines, HACCP, and the USP good compounding practices. (B)
3. EN formulas should be prepared for patient use in a clean environment using aseptic technique by specially trained personnel. Strict aseptic technique should be used in the preparation and administration of enteral formulas. (A)
4. All personnel involved in preparing, storing, and administering EN formulas and HBM should be capable and qualified for the tasks, and follow accepted best practices. (C)
5. Sterile, liquid EN formulas should be used in preference to powdered, reconstituted formulas whenever possible. (A)
6. Store unopened commercially-available liquid EN formulas under controlled (dark, dry, cool) conditions. (B)
7. Maintain a rapid enteral feeding formula inventory turnover well within the product's expiration date. (C)
8. Formulas reconstituted in advance should be immediately refrigerated, and discarded within 24 hours of preparation if not used; formulas should be exposed to room temperature for no longer than 4 hours, after which they should be discarded. (B)
9. Use a purified water or sterile water for irrigation supply for formula reconstitution and medication dilution. Consider purified water for enteral access device flushes in at-risk patients. (B)
10. Strict adherence to manufacturer's recommendations for product use results in less contamination of EN. (B)
11. Use of disposable gloves is recommended in the administration of EN. (A)
12. Formula decanted from a screw cap is preferable instead of a flip top. (A)
13. A recessed spike on a closed system container is preferable. (B)
14. A feeding pump with a drip chamber prevents retrograde contamination of the EN formula from the feeding tube. (A)
15. Sterile, decanted formula should have an 8-hour hang time unless used for a neonate where hang time should be limited to 4 hours. (B)

16. Administration sets for open system enteral feedings should be changed at least every 24 hours. (B)

17. Powdered, reconstituted formula, HBM, and EN formula with additives should have a 4-hour hang time. (C)

18. Closed-system EN formulas can hang for 24-48 hours per manufacturer's guidelines. (A)

19. Administration sets for closed-system EN formulas should be changed per manufacturer guidelines. (A)

20. Administration sets for HBM should be changed every 4 hours. (C)

21. All products used for pediatric patients should be DEHP free. (B)

References

1. United States Pharmacopoeial Convention. *United States Pharmacopoeia/ National Formulary*, edition 31/26. Rockville, MD: United States Pharmacopoeial Convention, Inc., 2008.

2. Environmental Protection Agency. *National Primary Drinking Water Regulations*. 40 CFR §141-142, 2002.

3. World Health Organization. *Guidelines for drinking-water quality*. Geneva, Switzerland: WHO, 2004.

4. Marrie TJ, Haldane D, MacDonald S, et al. Control of endemic nosocomial legionnaires' disease by using sterile potable water for high risk patients. *Epidemiol Infect*. 1991;107:591-605.

5. Venezia RA, Agresta MD, Hanley EM, Urquhart K, Schoonmaker D. Nosocomial legionellosis associated with aspiration of nasogastric feedings diluted in tap water. *Infect Control Hosp Epidemiol*. 1994;15:529-533.

6. Bert F, Maubec E, Bruneau B, Berry P, Lambert-Zechovsky N. Multi-resistant Pseudomonas aeruginosa outbreak associated with contaminated tap water in a neurosurgery intensive care unit. *J Hosp Infect*. 1998;39:53-62.

7. Rogues AM, Boulestreau H, Lashéras A, et al. Contribution of tap water to patient colonisation with Pseudomonas aeruginosa in a medical intensive care unit. *J Hosp Infect*. 2007;67:72-78.

8. Communicable Disease Report. Ice as a source of infection acquired in hospital. *CDR Weekly*. 1993;3:241.

9. Communicable Disease Report. Cryptosporidium in water and the immunocompromised. *CDR Weekly*. 1999;9:289,292.

10. Anaissie EJ, Penzak SR, Dignani MC. The hospital water supply as a source of nosocomial infections: a plea for action. *Arch Intern Med*. 2002;162:1483-1492.

11. Johansson RJH, Andersson K, Wiebe T, Schalén C, Bernander S. Nosocomial transmission of *Legionella pneumophila* to a child from a hospital's cold-water supply. *Scan J Inf Dis*. 2006;38: 1023-1027.

12. Vonberg RP, Eckmanns T, Bruderek J, Rüden H, Gastmeier P. Use of terminal tap water filter systems for prevention of nosocomial legionellosis. *J Hosp Inf*. 2005;60:159-162.

13. White R, Bradnam V. *Handbook of Drug Administration via Enteral Feeding Tubes*. London, UK:Pharmaceutical Press, 2007.

14. U.S. Environmental Protection Agency. Ground water and drinking water. September 26, 2008. http://www.epa.gov/safewater/. Accessed October 2008.

15. Centers for Disease Control and Prevention. Water-related diseases. October 1, 2007. http://www.cdc.gov/ncidod/diseases/water/index.htm. Accessed October 2008.

16. Robbins ST, Beker LT. *Infant Feedings: Guidelines for Preparation of Formula and Breastmilk in Health Care Facilities*. Chicago, IL: American Dietetic Association, 2004.

17. Centers for Disease Control and Prevention. Enterobacter sakazakii infections associated with the use of powdered infant formula – Tennessee, 2001. *MMWR*. 2002;51:297-300.

18. Muytjens HL, Roelofswillemse H, Jaspar GHJ. Quality of powdered substitutes for breast-milk with regard to members of the family Enterobacteriaceae. *J Clin Microbiol*. 1988;26:743-746.

19. Nazarowec White M, Farber JM. Thermal resistance of *Enterobacter sakazakii* in reconstituted dried-infant formula. *Lett Appl Microbiol*. 1997;24:9-13.

20. ESPGHAN Committee on Nutrition. Preparation and handling of powdered infant formula: a commentary. *J Pediatr Gastroenterol Nutr*. 2004;39:320-322.

21. Roy S, Rigal M, Doit C, et al. Bacterial contamination of enteral nutrition in a pediatric hospital. *J Hosp Infect*. 2005;59:311-316.

22. Kim H, Ryu JH, Beuchat LR. Attachment of and biofilm formation by *Enterobacter sakazakii* on stainless steel and enteral feeding tubes. *Appl Environ Microbiol*. 2006;72:5846-5856.

23. Anderton A, Nwoguh CE, McKune I, Morrison L, Grieg M, Clark B. A comparative study of the numbers of bacteria present in enteral feeds prepared and administered in hospital and the home. *J Hosp Inf*. 1993;23:43-49.

24. Bott L, Husson MO, Guimber D, et al. Contamination of gastrostomy feeding systems in children in a home-based enteral nutrition program. *J Pediatr Gastroenterol Nutr*. 2001;33:266-270.

25. de Leeuw IH, Vandewoude MF. Bacterial contamination of enteral diets. *Gut*. 1986;27(suppl 1):56-67.

26. Marion ND, Rupp ME. Infection control issues of enteral feeding systems. *Curr Opin Clin Nutr Metab Care*. 2000;3:363-366.

27. van Alsenoy J, de Leeuw I, Delvigne C, Vandewoude M. Ascending contamination of a jejunostomy feeding reservoir. *Clin Nutr*. 1985; 4:95-98.

28. Levy J, van Laethem Y, Verhaegen G, Perpete C, Butzler JP, Wenzel RP. Contaminated enteral nutrition solutions as a cause of nosocomial bloodstream infection: a study using plasmid fingerprinting. *JPEN J Parenter Enteral Nutr*. 1989;13:228-234.

29. Thurn J, Crossley K, Gerdts A, Maki M, Johnson J. Enteral hyperalimentation as a source of nosocomial infection. *J Hosp Inf*. 1990;15:203-217.

30. Bornemann R, Zerr DM, Heath J, et al. An outbreak of salmonella serotype saintpaul in a children's hospital. *Inf Control Hosp Epidemiol*. 2002;23:671-676.

31. Fagerman KE. Limiting bacterial contamination of enteral nutrient solutions: 6-year history with reduction of contamination at two institutions. *Nutr Clin Pract*. 1992;7:31-36.

32. Bischoff WE, Tucker BK, Wallis ML, et al. Preventing the airborne spread of *Staphylococcus aureus* by persons with the common cold: effect of surgical scrubs, gowns, and masks. *Infect Control Hosp Epidemiol*. 2007;28:1148-1154.

33. Rupp ME, Weseman RA, Marion N, Iwen PC. Evaluation of bacterial contamination of a sterile, non-air-dependent enteral feeding system in immunocompromised patients. *Nutr Clin Pract*. 1999;14:135-137.

34. Arnold L. *Recommendations for Collection, Storage, and Handling of a Mother's Milk for Her Own Infant in the Hospital Setting*. 3rd ed. Denver, CO: The Human Milk Banking Association of North America, Inc.; 1999.

35. Pittard W, Geddes K, Brown S. Bacterial contamination of human milk container and method of expression. *Am J Perinatol*. 1991;8:25-27.

36. Lawrence RA, Lawrence RM. The collection and storage of human milk and human milk banking. In: Lawrence RA, Lawrence RM, eds. *Breastfeeding: A Guide for the Medical Profession*. St. Louis, MO: Mosby; 1999:677-710.

37. Meier P, Brown L, Hurst N. Breastfeeding the preterm intern. In: Riordan J, Auerbach KG, eds. *Breastfeeding and Human Lactation*. 2nd ed. Sudbury, MA: Jones and Bartlett; 1998:449-481.

38. Hamosh M, Ellis LA, Pollock D, et al. Breastfeeding and the working mother: effect of time and temperature of short term storage on proteolysis, lipolysis, and bacterial growth in milk. *Pediatrics*. 1996;97:492-498.

39. Meier P, Brown L. Breastfeeding for mothers and low birth weight infants. *Nurs Clin North Amer*. 1996;31:351-365.

40. Nommsen-Rivers L. Universal precautions are not needed for health care workers handling breast milk. *J Hum Lact*. 1997:13:267-268.

41. Occupational Safety and Health Administration. Breast milk does not constitute occupational exposure as defined by Standard No. 1910.1030. Interpretation and compliance letters. http://www.osha.gov. Accessed November 1, 2007.

42. Vonberg RP, Gastmeier P. Hospital-acquired infections related to contaminated substances. *J Hosp Inf*. 2007;65:15-23.

43. Weenk GH, Kemen M, Wernert HP. Risks of microbiological contamination of enteral feeds during the set up of enteral feeding systems. *J Hum Nutr Diet*. 1993;6:307-316.

44. Okuma T, Nakamura M, Totake H, Fukunaga Y. Microbial contamination of enteral feeding formulas and diarrhea. *Nutrition*. 2000;16:719-722.

45. Bliss DZ, Johnson S, Savik K, Clabots CR, Willard K, Gerding DN. Acquisition of *Clostridium difficile* and *Clostridium difficile*-associated diarrhea in hospitalized patients receiving tube feeding. *Ann Intern Med*. 1998;129:1012-1019.

46. Payne-James JJ, Rana SK, Bray MJ, et al. Retrograde (ascending) bacterial contamination of enteral diet administration systems. *JPEN J Parenter Enteral Nutr*. 1992;16:369-373.

47. Moffitt SK, Gohman SM, Sass KM, et al. Clinical and laboratory evaluation of a closed enteral feeding system under cyclic feeding conditions: a microbial and cost evaluation. *Appl Nutr Invest*. 1997;13:622-628.

48. Mathus-Vliegen EMH, Bredius MWJ, Binnekade JM. Analysis of sites of bacterial contamination in an enteral feeding system. *JPEN J Parenter Enteral Nutr*. 2006;30:519-525.

49. Matlow A, Jacobson M, Wray R, et al. Enteral tube hub as a reservoir for transmissible enteric bacteria. *Am J Infect Control*. 2006;34:131-133.

50. Kohn CL. The relationship between enteral formula contamination and length of enteral delivery set usage. *JPEN J Parenter Enteral Nutr*. 1991;15:567-571.

51. Beattie TK, Anderton A. Microbiological evaluation of four enteral feeding systems which have been deliberately subjected to faulty handling procedures. *J Hosp Inf*. 1999;42:11-20.

52. Beattie TK, Anderton A. Bacterial contamination of enteral feeding systems due to faulty handling procedures – a comparison of a new system with two established systems. *J Hum Nutr Diet*. 1998; 11:313-321.

53. Stroud M, Duncan H, Nightingale J. Guidelines for enteral feeding in adult hospital patients. *Gut*. 2003;52(suppl 7):1-12.

54. Johnson S, Gerding DN, Olson MM, et al. Prospective controlled study of vinyl glove use to interrupt *Clostridium difficile* nosocomial transmission. *Am J Med*. 1990;88:137-140.

55. Anderson KR, Norris DJ, Godfrey LB, Avent CK, Butterworth CE. Bacterial contamination of tube-feeding formulas. *JPEN J Parenter Enteral Nutr*. 1984;8:673-678.

56. Food and Drug Administration. *Compliance Program Guidance Manual. Food Composition, Standards, Labeling and Economics, Chapter 21, Compliance Program 7321.002*, May 3, 1995.

57. Neely AN, Mayes T, Gardner J, Kagan RJ, Gottschlich MM. A microbiologic study of enteral feeding hang time in a burn hospital: can feeding costs be reduced without compromising patient safety? *Nutr Clin Pract*. 2006;21:610-616.

58. Beattie TK , Anderton A. Decanting versus sterile pre-filled nutrient containers– the microbiological risks in enteral feeding. *Intern Environ Health Res*. 2001;11:81-93.

59. Davis AT, Fagerman KE, Downer FD, Dean RE. Effect of enteral feeding bag composition and freezing and thawing upon vitamin stability in an enteral feeding solution. *JPEN J Parenter Enteral Nutr*. 1986;10:245-246.

60. Mathus-Vliegan LM, Binnekade JM, deHaan RJ. Bacterial contamination of ready to use 1-L feeding bottles and administration sets in severely compromised intensive care patients. *Crit Care Med*. 2000;28:67-73.

61. Perez SK, Brandt K. Enteral feeding contamination: comparison of diluents and feeding bag usage. *JPEN J Parenter Enteral Nutr*. 1989;13:306-308.

62. Roberts CA, Lyman E. Microbial contamination of enteral feeding sets used in the home of pediatric patients. *Nutr Clin Pract*. 2008;23:85-89.

63. Schroeder P, Fisher D, Volz M, Paloucek J. Microbial contamination of enteral feeding solutions in a community hospital. *JPEN J Parenter Enteral Nutr*. 1983;7:364-368.

64. Vanek V. Closed versus open enteral delivery systems: a quality improvement study. *Nutr Clin Pract*. 2000;15:234-243.

65. Wagner DR, Elmore MF, Knoll DM. Evaluation of "closed" versus "open" systems for the delivery of peptide-based enteral diets. *JPEN J Parenter Enteral Nutr*. 1994;18:453-457.

66. Keohane P, Attrill H, Love M, et al. A controlled trial of aseptic enteral diet preparation – significant effects on bacterial contamination and nitrogen balance. *Clin Nutr*. 1983;2: 119-122.

67. Carvalho MLR, Morais TB, Amaral DF, Sigulem DM. Hazard analysis and critical control point system approach in the evaluation of environmental and procedural sources of contamination of enteral feedings in three hospitals. *JPEN J Parent Enteral Nutr*. 2000;24:296-303.

68. Oliviera MH, Bonelli R, Aidoo KE, Batista CRV. Microbiological quality of reconstituted enteral formulations used in hospitals. *Nutrition*. 2000;16:729-733.

69. Oliveira MR, Batista CRV, Aidoo KE. Application of hazard analysis critical control points system to enteral tube feeding in hospital. *J Hum Nutr Dietet*. 2001;14:397-403.

70. Food and Drug Administration, Centers for Devices and Radiological Health. *Safety Assessment of di(2-ethylhexyl)phthalate (DEHP) Released from PVC Medical Devices*. Rockville, MD: Food and Drug Administration;2002.

71. Galt LG, Josephson RV. Stability and osmolality of a nutritional food supplement during simulated nasogastric administration. *Am J Hosp Pharm*. 1982;39:1009-1012.

72. van Zoeren-Grobben D, Moison RMW, Ester WM, Berger HM. Lipid peroxidation in human milk and infant formula: effect of storage, tube feeding and exposure to phototherapy. *Acta Paediatrica*. 1993;82:645-649.

73. Rufián-Henares JÁ, Guerra-Hernández E, García-Villanova B. Evolution of fatty acid profile and lipid oxidation during enteral formula storage. *JPEN J Parenter Enteral Nutr*. 2005;29:204-211.

74. Lowry KR, Fly AD, Izquierdo OA, Baker DH. Effect of heat processing and storage on protein quality and lysine bioavailability of a commercial enteral product. *JPEN J Parenter Enteral Nutr*. 1990;14:68-73.

75. Hsu TC, Chen NR, Sullivan MM, et al. Effect of ambient temperature on contamination and physical stability of one-liter ready-to-hang enteral delivery systems. *Nutrition*. 2000;16: 165-167.

76. Frias J, Vidal-Valverde C. Stability of thiamine and vitamins E and A during storage of enteral feeding formula. *J Agric Food Chem*. 2001;49:2313-2317.

V. ENTERAL ACCESS DEVICES: SELECTION, INSERTION, AND MAINTENANCE CONSIDERATIONS

When oral feedings are not an option or do not adequately meet nutrition needs, selection of the enteral access device can strongly affect the success of EN. The optimal device and location (gastric vs small bowel) must be determined. The placement of any enteral access device entails risks associated with placement.

A. Selection of Enteral Access Devices

The selection of an enteral access device requires an evaluation of the patient's disease state, GI anatomy taking into account past surgeries, gastric and intestinal motility and function, and the estimated length of therapy. The decision must be made regarding whether to place the distal tip of the enteral access device in the stomach or small bowel. In general, gastric access relies on a functional stomach free of delayed gastric emptying, obstruction, or fistula. Small bowel feedings are most appropriate for patients with gastric outlet obstruction, gastroparesis, pancreatitis and in those with known reflux and aspiration of gastric contents. Patients who need simultaneous gastric decompression with small bowel feedings can be best accommodated by a dual-lumen gastrojejunal tube.

Enteral access devices inserted via the nasal and oral routes are usually placed for short-term use in the hospitalized patient. However, there may be situations when use of a nasogastric (NG) access in the outpatient setting is appropriate. Some patients are able to self-place an enteral access device. A concern with NG feedings in ICU patients has been the risk of reflux with bronchopulmonary aspiration; multiple small studies have attemped to address this issue. Subsequently, 3 meta-analyses have addressed this question.[1-3] The oldest analysis from 2002 that utilized 10 studies and an aggregate population of 612 patients found a significant reduction in ventilator-associated pneumonia with small bowel feedings but no difference in mortality rates.[1] Two subsequent meta-analyses—one with 11 studies and 637 aggregate patients, and another with 9 studies and 522 aggregate patients—found no evidence of increased pneumonia or change in length of ICU stay in patients receiving gastric vs post-pyloric feedings.[2,3] These 2 meta-analyses also found that gastric feedings were initiated sooner because they avoided the delay from post-pyloric placement difficulties.

The decision concerning placement of long-term access is dependent on the estimated length of therapy, the patient's disposition, and the special needs of the patient and caregivers. Two studies of adult patients with persistent dysphagia due to neurological diseases randomized patients to NG feedings or percutaneous endoscopic gastrostomy (PEG) placement.[4,5] These studies found that the patients with PEGs had greater weight gain and fewer missed feedings.[4,5] The patients fed by NG had a significant decrease in the amount of formula they received because of tube difficulties compared to the PEG patients who had no such difficulties.[4,5] One of the studies allowed patients with NGs to crossover to PEGs for repeated tube difficulties (usually displacement), so only 1 of 19 patients had NGs in place for 4 weeks.[5] At the end of the study, this patient opted for a PEG stating that the NG was cosmetically unacceptable.

Practice Recommendations

1. Select an enteral access device based on patient-specific factors. (C)
2. Nasojejunal route for enteral feedings in ICU patients are not required unless gastric feeding intolerance is present. (A)
3. Patients with persistent dysphagia should have a long-term enteral access device placed. (B)

B. Insertion of Enteral Access Devices

Short-Term Enteral Devices

Nasal or oral insertion of an enteral access device is often performed at the bedside. Nasojejunal tubes may be placed with the assistance of endoscopy or fluoroscopy. Confirmation of correct position of a newly inserted tube is mandatory before feedings or medications are administered. A variety of bedside tests to determine tube placement are used with varying degrees of accuracy. Usually bedside detection methods serve as precursors to radiographic confirmation, often serving to decrease the number of radiographs needed to one. The gold standard for confirming correct placement of a blindly-inserted enteral access device is a properly obtained and interpreted radiograph that visualizes the entire course of the tube.[6-8]

Radiographic confirmation is more readily used in adults than in children. A report from an interdisciplinary task force on NG tube placement at Children's Hospital in Boston recommended the use of bedside pH of the gastric aspirate; however, they noted that this was not reliable if the patient was on gastric acid suppression therapy.[9] The task force also created a list of special high risk medical/surgical conditions that required "special considerations." Their protocol gave wide latitude to nursing judgment, stating that an X-ray should be obtained if any questions arose concerning the placement. The

dilemma in children is that the only currently proven method to accurately document enteral access device placement is an X-ray, but this method poses a radiation risk and is not always easy to obtain.

Detection of Inadvertent Tracheopulmonary Placement

Although observing for respiratory symptoms is warranted during enteral access device insertion, malpositioning may occur without any apparent symptoms.[10,11] The appearance and pH of aspirates from a feeding tube may provide useful clues to an enteral access device location. For example, fluid withdrawn from a tube that has perforated into the pleural space typically has a pale yellow serous appearance and a pH of 7 or higher, while fasting gastric fluid typically is clear and colorless or grassy green with a pH of 5 or less.[12-16] However, appearance and pH of aspirates are not sufficiently accurate to distinguish between gastric and bronchopulmonary placement. Multiple case reports clearly indicate that clinicians cannot differentiate between respiratory and gastric placement by the auscultatory method.[10,17-24] Several studies have indicated that capnography can be helpful in determining when a tube has taken the wrong course into the trachea during the insertion process.[25-28] However, it is important to point out that this method cannot distinguish between enteral access device placement in the esophagus and the stomach. Thus, even though capnography may indicate non-bronchotracheal placement of a newly inserted tube, a radiograph is still required to assure proper placement in the stomach. Other bedside assessments have been suggested for distinguishing between respiratory and gastric placement but are not available for widespread use. Among these are testing for enzymes in fluid aspirated through the enteral access device and using an electromagnetic tracking device during tube insertion. [29-31] There is insufficient evidence that these methods can replace radiographic confirmation of enteral access device location.

Detecting Esophageal Placement

It is difficult to obtain an aspirate from an enteral access device when the tip lies in the esophagus. On the occasions when an aspirate can be obtained, it is likely refluxed gastric juice or swallowed saliva.[12] Thus, observing the aspirate's pH and appearance is of little or no benefit in this situation. The auscultatory method also cannot differentiate between the esophagus and stomach. Because it is difficult to rule out esophageal placement by bedside methods, a radiograph is mandatory (especially when large volumes of fluid are to be administered via the tube).[6] Life-threatening bronchopulmonary aspiration was reported in a patient who received 4 liters of a bowel

preparation solution via a tube improperly positioned in the esophagus; the tube was erroneously believed to be in the stomach based on the auscultatory method.[32]

Distinguishing Between Gastric and Small Bowel Placement

A study that examined feeding tube placement in 201 children (nasogastric or nasojejunal) found that an X-ray on the day of placement demonstrated a placement error in 15.9% of the patients.[33] When the study followed the children over time, 20.9% of the children had a placement error at least once. A tube is said to be malpositioned if it is located in the stomach of a patient receiving small bowel feedings for slow gastric emptying. An experimental study found that experienced nurses could not distinguish between gastric and small bowel placement by the auscultatory method.[34] A higher level of accurate placement has been reported when clinicians observe the appearance and pH of the feeding tube aspirate.[35] Small bowel aspirates are typically bile-stained, while fasting gastric fluid is typically clear and colorless or green.[13] Gastric fluid usually has a lower pH than that of small bowel secretions. For example, Griffith et al found that most gastric pH readings were ≤ 5, with or without the use of gastric acid suppression therapy.[15] Investigators who evaluated gastric pH in critically ill children found that it is similar to that observed in adults. For example, Gharpure et al reported that the mean pH of fasting gastric aspirates from a group of 43 critically ill children was 4; in contrast, the mean pH of fasting small bowel aspirates was 7 in 25 patients.[35] It should be noted that when gastric pH is ≥6, the pH method is of no benefit in predicting tube location in the GI tract (nor in ruling out tracheopulmonary placement). Other bedside assessments (ie, testing for bilirubin and enzymes in GI contents aspirated through the enteral access device, and use of electromagnetic devices) that are less available may be useful in distinguishing between gastric and small bowel placement, but they lack sufficient agreement with radiographic findings to preclude radiographic confirmation of tube location.[29-31]

C. *Maintenance Considerations*

After feedings have been started, it is necessary to assure that the tube has remained in the desired location (either the stomach or small bowel). Unfortunately, a small bowel tube may dislocate upward into the stomach or a gastric tube may migrate downward into the small bowel; a worse scenario is when a tube's tip dislocates upward into the esophagus.[36] Obviously, an X-ray cannot be obtained several times a day to confirm tube location; thus, clinicians are forced to rely on a variety of bedside methods for this purpose. Among the methods that may be useful are

determining if the external length of the tubing has changed since the time of the confirmatory radiograph, [37] observing for negative pressure when attempting to withdraw fluid from the feeding tube, observing for unexpected changes in residual volumes, and measuring pH of the feeding tube aspirates.[37,38] In a prospective study, observing for changes in external tube length was helpful in identifying upward dislocations of feeding tubes into the esophagus, as well as from the small bowel into the stomach.[38] Negative pressure is more likely to be felt during attempts to aspirate fluid from a small bowel tube than from a gastric tube. [39,40] A sharp increase in gastric residual volume may indicate displacement of a small bowel tube into the stomach.[37,40] Testing the pH of feeding tube aspirates is most likely to be helpful when intermittent feedings are used. As indicated above, the auscultatory method cannot distinguish between gastric and small bowel placement, nor can it detect when a tube's tip is in the esophagus. [32,34]

Practice Recommendations

1. Obtain radiographic confirmation that any blindly-placed tube (small-bore or large-bore) is properly positioned in the GI tract prior to its initial use for administering feedings and medications in adult patients. (B)

2. When attempting to insert a feeding tube into the stomach of an adult patient, it may be helpful to use capnography to detect inadvertent entry of the tube into the trachea. Be aware that a radiograph is still needed before the tube is used for feedings. (B)

3. When attempting to insert a feeding tube into the small bowel, observe for a change in the pH and in the appearance of aspirates as the tube progresses from the stomach into the small bowel; use the findings to determine when a radiograph is likely to confirm small bowel placement. (B)

4. In adult patients, do not rely on the ausculatory method to differentiate between gastric and respiratory placement. The auscultatory method may be used as an adjunct method in the pediatric population. (A)

5. Do not rely on the auscultatory method to differentiate between gastric and small bowel placement. (A)

6. Mark the exit site of a feeding tube at the time of the initial radiograph; observe for a change in the external tube length during feedings. If a significant increase in the external length is observed, use other bedside tests to help determine if the tube has become dislocated. If in doubt, obtain a radiograph to determine tube location. (B)

7. In pediatrics and neonates, all methods but X-ray verification of enteral tube placement have been shown to be inaccurate. X-ray use in children should be as judicious as possible given the radiation exposure. (B)

D. Long-Term Enteral Access

Insertion options for feeding-tube enterostomies include endoscopic, laparoscopic, fluoroscopic, and open techniques. Success in long-term enteral feeding is in part dependent on careful selection of the appropriate enteral access device and placement technique together with proper maintenance and care. Therefore, knowledge of the GI anatomy and motility, prior GI surgery, patency of the upper GI tract, intended use, and intended length of therapy must be part of the decision-making process.

The patient's potential risks from anesthesia, effects of pre-existing co-morbidities, and expected patient outcomes must be assessed prior to placement of a long-term enteral access device. Predictive factors in early mortality after PEG tube placement were described in a study by Light et al.[42] Two statistically significant predictors of mortality at 1 week post-PEG were urinary tract infection and previous history of aspiration, and if combined with age greater than 75 years, the 1-month mortality was significant. Tanswell et al described the recommendations of the 2004 National Confidential Enquiry into Patient Outcome and Death which investigated deaths after therapeutic endoscopy, including PEG placement.[43,44] Their recommendations included an in-depth, multidisciplinary team assessment of the potential benefits to the individual prior to PEG insertion and the need for guidelines for the use of PEG feedings, including patient selection. In their study, this assessment included biochemical parameters, comorbidities, indication for PEG placement, and reason to place or not to place the PEG. Their study showed that careful pre-assessment screening reduced the occurrence of early post-PEG mortality.

The potential to develop gastroesophageal reflux in children following PEG tube placement appears to be minimal even when predicted based on pre-placement studies.[42] This does not appear to hold true when the child has some sort of neurological abnormality.[45] When 46 pediatric patients (93% of whom were neurologically impaired) had pre-PEG placement assessment with a pH probe study, those with normal values had infrequent clinical reflux afterwards.[46] The patients with abnormal pH probe results prior to PEG placement were more likely to require intervention (19 of 24 patients on medication, 7 of 24 patients required fundoplication).[46]

A study that examined the results of long-term feeding tube placement in patients with cerebral palsy found that 95% had minor complications following placement.[47] These complications included: diarrhea and constipation, tube

obstruction, infections around the tube site, accidental dislodgement, leakage around the tube, and problems with tube valve. Additionally, 28% of the families cited stresses brought about by tube feedings. These included difficulty finding respite care, restriction of mobility, changed relationship with the child, and missing the taste of food. Despite these complications, 86% of the families felt that tube feedings had a positive impact in their child's care. [47]

Patients that require jejunal feedings can utilize a jejunal tube placed through a previous gastrostomy. This requires a longer tube and has the potential for displacement compared to a tube with direct access to the jejunum. A study in adults with gastric dysfunction compared 56 patients with a directly placed jejunostomy (percutaneous endoscopic jejunostomy [PEJ]) compared to 49 with a jejunostomy via a gastrostomy (percutaneous endoscopic gastrojejunostomy [PEGJ]). [48] Patients with a PEJ required an endoscopy for replacement only 13.5% of the time compared to 55.9% percent of PEGJ patients. Six months after placement there were significantly more patent PEJ tubes than PEGJ tubes. A study in children with gastric dysfunction found that 14 patients had a jejunal tube via gastrostomy and 6 went straight to jejunostomy; 7 of the children with a PEGJ eventually required conversion to PEJs. [49] The PEGJ tubes required 4.6 adjustments per year and 3.9 hospitalizations a year compared to PEJs that required 1.5 manipulations per year and 1.4 hospitalizations.

Problem areas related to long-term enteral access devices include the inappropriate use of urinary drainage catheters and other tubes not designed or intended for enteral feeding, premature removal, accidental catheter tip malposition, and excessive traction of the feeding device. Ideally, long-term enteral access devices should have some form of internal and external retention device to prevent the migration of the catheter further into the GI tract than intended. Tube migration as seen in use of urinary catheters can lead to gastric and intestinal obstruction, aspiration, and leakage of gastric and intestinal secretions onto the skin. Intestinal intussusception was documented in a case reported by Ciaccia et al as a result of a Foley-type catheter.[50] Leakage of gastric and intestinal secretions is also seen with the use of other types of catheters without internal and external retention devices. Prolonged exposure of the skin to these secretions can lead to pain, cellulitis, and possible disruption of enteral feedings.

Peritonitis can result from the premature removal of the long-term enteral access tube, within the first few weeks after insertion. The stomach or small bowel falls away from the abdominal wall with removal of the access device or accidental malposition of the tip of the catheter from the GI tract into the peritoneum and can lead to enteral formula infusing into the peritoneal cavity and peritonitis. Excessive traction on the feeding device can result in Buried Bumper Syndrome, the embedding of the internal retention device

into the gastric mucosa resulting in pain, tube obstruction, peritonitis, and stoma site drainage. Placing the external bumper too tight leads to Buried Bumper Syndrome, while placing it too loose leads to leakage and peritonitis following initial placement. Failure to recognize the type of tube inserted (gastric vs small bowel), the insertion technique, and the location of the distal catheter tip can result in incorrect feeding technique and complications in tube replacement and removal.

Follow-up of a long-term feeding device is indicated to assure that the enteral retention device is properly approximated to the abdominal wall, there is no tube migration, and excessive tension to the exterior portion of the tube is avoided, as well as assessment of the condition of the surrounding skin.

Practice Recommendations

1. Long-term feeding devices should be considered when the need for enteral feeding is at least 4 weeks in adults, children, and infants after term age. (C)

2. Premature infants who do not have anomalies associated with inability to eat by mouth at the normal time for development of oral feeding skills should not have a long-term device considered before the usual age of development of independent oral feeding. (C)

3. Evaluation by a multidisciplinary team is indicated prior to insertion of a long-term feeding device to establish whether:
   a. benefit outweighs the risk of access placement;
   b. insertion of feeding tubes near end of life is warranted; or
   c. insertion of feeding tubes is indicated in the situation where patients are close to achieving oral feeding. (B)

4. Abdominal imaging should be performed prior to permanent feeding device placement if a possible anatomic difficulty exists. (C)

5. Gastrostomy tube placement does not mandate fundoplication. The possible exception is children with neurological abnormalities who also have abnormal pH probe findings. (B)

6. Direct placement of a jejunostomy tube is indicated in patients requiring a long-term jejunostomy. (B)

7. Document tube type, tip location, and external markings in the medical record and in follow-up examinations. (C)

8. Avoid placement of catheters or tubes not intended for use as enteral feeding devices, such as urinary or GI drainage tubes which usually are without an external anchoring device. Use of such tubes leads to enteral misconnection as well as tube migration, which can potentially cause obstruction of the gastric pylorus or small bowel and aspiration. (B)

E. Initiation of Feedings after Placement of a Long-Term Enteral Access Device

Traditional surgery dogma was that post-operative feedings should wait until there was evidence that bowel function had returned as evidenced by flatus or a bowel movement. This was not based on any studies but on the fear that the feedings were associated with complications. Anesthetics were believed to result in an ileus and if the patient was fed too soon they could vomit and aspirate. This has been challenged in recent literature with a variety of studies supporting earlier feedings. These studies are difficult to compare because of the wide variety of surgeries done before the trials. There is also little literature as to what the first feedings should consist of and the rate at which they should be initiated and advanced.

The change in approach was clearly demonstrated in the recent article by Collier et al that fed patients with open abdomens following trauma.[51] The patients with an open abdomen, fed within 4 days of admission, had earlier wound closure, less fistulas, and lower hospital charges. The most concerning patients are those that undergo some sort of GI surgery. However, a study that utilized a protocol in patients undergoing elective segmental intestinal or rectal resection introduced solids the evening of post-operative day 1, without waiting for flatus or a stool, and found that these patients were discharged earlier and had no increase in complications.[52] A similar study began a regular diet at 8 hours post-operation and found good tolerance.[52] Patients undergoing gastrectomy for gastric cancers were found to tolerate an oral diet when introduced on postoperative day 3 with these patients having earlier discharge.[54] Utilizing a group of patients that were even sicker, Malhotra et al studied patients presenting emergently with enteric perforations.[55] All of these patients had sepsis and peritonitis, but half were randomized to receive NG feedings within 48 hours of surgery and suffered no increase in complications and less weight loss. Even newborns begun on small feedings by NG tube within 24 hours of surgery for GI anomalies, rather than waiting for flatus or stool passage, tolerated the feedings without complications, stooled, and were discharged sooner.[56] A meta-analysis of 11 studies that began feedings within 24 hours of surgery vs standard waiting demonstrated no advantage to waiting, and that early feedings had a lower infection rate and were discharged 0.84 days sooner.[57]

There have been very few complications reported with early postoperative feedings. The most serious complication has been bowel necrosis in a total of 32 patients.[58] Melis et al's review of the literature indicated that distention and sepsis or worsening general condition should prompt evaluation and discontinuation of the feedings.[58]

Several studies of feeding after PEG placements in adults have been published. Two studies with >20 patients in each group found no difference in complications with patients fed 3 hours after placement compared to those fed the following day.[59,60] Another study in adults infused 50 mL of diatrizoate sodium into PEGs 3 hours after placement and found no evidence of leakage following an X-ray of the abdomen.[61] There also has been a more rigorous study in adults that randomized patients to receive formula feedings at 4 hours vs 24 hours after PEG placement. This study had over 50 patients in each group and measured post-feeding residuals.[62] No differences were noted in the incidence of complications or in the amount of gastric residuals. In an older review paper, Kirby et al reviewed their first 55 PEGs and stated that they began a trial administration of water at 2 hours postprocedure without increased complications.[63] A recent Spanish article reports a randomized trial of immediate feeding in over 30 patients with no increase in complications. [64]

In the pediatric literature, the shortest time course to using a PEG was described in a clinical report by Werlin et al.[65] This study was uncontrolled, but the authors reported no unusual complications that led to feeding discontinuation in 24 pediatric patients started on Pedialyte® (Abbott Laboratories) 6 hours after PEG placement.

Practice Recommendations

1. Enteral feedings should be started postoperatively in surgical patients without waiting for flatus or a bowel movement. The current literature indicates that these feedings can be initiated within 24-48 hours. (A)
2. A PEG tube may be utilized for feedings within several hours of placement: current literature supports within 2 hours in adults and 6 hours in infants and children. (B)

References

1. Heyland DK, Drover JW, Dhaliwal R Greenwood J. Optimizing the benefits and minimizing the risks of enteral nutrition in the critically ill: role of small bowel feeding. *JPEN J Parenter Enteral Nutr.* 2003;26(6 Suppl):S51-S57.
2. Ho KM, Dobb GJ, Webb SAR. A comparison of early gastric and post-pyloric feeding in critically ill patients: a meta-analysis. *Intens Care Med.* 2006;32:639-649.
3. Marik PE, Zaloga GP. Gastric versus post-pyloric feeding: a systematic review. *Crit Care.* 2003;7:R46-R51.
4. Norton B, Homer-Ward M, Donnelly MT, et al. A randomised prospective comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding after acute dysphagic stroke. *BMJ.* 1996;312:13-16.
5. Park RHR, Allison MC, Lang J, et al. Randomised comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding in patients with persisting neurological dysphagia. *BMJ.* 1992;304:1406-1409.
6. Baskin WN. Acute complications associated with bedside placement of feeding tubes. *Nutr Clin Pract.* 2006;21:40-55.

7. Metheny NA, Meert KL. Monitoring feeding tube placement. *Nutr Clin Pract.* 2004;19:487-495.

8. Metheny NA, Meert KL, Clouse RE. Complications related to feeding tube placement. *Curr Opin Gastroenterol.* 2007;23:178-182.

9. Richardson DS, Branowicki PA, Zeidman-Rogers L, et al. An evidence-based approach to nasogastric tube management: special considerations. *J Pediatr Nurs.* 2006;21:388-393.

10. Rassias A, Ball P, Corwin HL. A prospective study of tracheopulmonary complications associated with the placement of narrowbore enteral feeding tubes. *Crit Care.* 1998;2:25-28.

11. Metheny N, Dettenmeier P, Hampton K, Wiersema L, Williams P. Detection of inadvertent respiratory placement of small-bore feeding tubes: a report of 10 cases. *Heart Lung.* 1990;19:631-638.

12. Metheny NA, Clouse RE, Clark JM, Reed L, Wehrle MA, Wiersema L. pH testing of feeding-tube aspirates to determine placement. *Nutr Clin Pract.* 1994;9:185-190.

13. Metheny N, Reed L, Berglund B, Wehrle MA. Visual characteristics of aspirates from feeding tubes as a method for predicting tube location. *Nurs Res.* 1994;43:282-287.

14. Metheny NA, Reed L, Wiersema L, McSweeney M, Wehrle MA, Clark J. Effectiveness of pH measurements in predicting feeding tube placement: an update. *Nurs Res.* 1993;42:324-331.

15. Griffith DP, McNally AT, Battey CH, et al. Intravenous erythromycin facilitates bedside placement of postpyloric feeding tubes in critically ill adults: a double-blind, randomized, placebo-controlled study. *Crit Care Med.* 2003;31:39-44.

16. Metheny NA, Aud MA, Ignatavicius DD. Detection of improperly positioned feeding tubes. *J Healthc Risk Manag.* 1998;18:37-48.

17. Harris CR, Filandrinos D. Accidental administration of activated charcoal into the lung: aspiration by proxy. *Ann Emerg Med.* 1993;22:1470-1473.

18. Kawati R, Rubertsson S. Malpositioning of fine bore feeding tube: a serious complication. *Acta Anaesthesiol Scand.* 2005;49:58-61.

19. el Gamel A, Watson DC. Transbronchial intubation of the right pleural space: a rare complication of nasogastric intubation with a polyvinylchloride tube--a case study. *Heart Lung.* 1993;22:224-225.

20. Hendry PJ, Akyurekli Y, McIntyre R, Quarrington A, Keon WJ. Bronchopleural complications of nasogastric feeding tubes. *Crit Care Med.* 1986;14:892-894.

21. Lipman TO, Kessler T, Arabian A. Nasopulmonary intubation with feeding tubes: case reports and review of the literature. *JPEN J Parenter Enteral Nutr.* 1985;9:618-620.

22. Miller KS, Tomlinson JR, Sahn SA. Pleuropulmonary complications of enteral tube feedings. Two reports, review of the literature, and recommendations. *Chest.* 1985;88:230-233.

23. Kolbitsch C, Pomaroli A, Lorenz I, Gassner M, Luger TJ. Pneumothorax following nasogastric feeding tube insertion in a tracheostomized patient after bilateral lung transplantation. *Intensive Care Med.* 1997;23:440-442.

24. Torrington KG, Bowman MA. Fatal hydrothorax and empyema complicating a malpositioned nasogastric tube. *Chest.* 1981;79:240-242.

25. Asai T. Use of a capnograph during feeding tube insertion. *Crit Care Med.* 2002;30:1674.

26. Araujo-Preza CE, Melhado ME, Gutierrez FJ, et al. Use of capnometry to verify feeding tube placement. *Crit Care Med.* 2002;30:2255-2259.

27. Kindopp AS, Drover JW, Heyland DK. Capnography confirms correct feeding tube placement in intensive care unit patients. *Can J Anaesth.* 2001;48:705-710.

28. Burns SM, Carpenter R, Truwit JD. Report on the development of a procedure to prevent placement of feeding tubes into the lungs using end-tidal CO2 measurements. *Crit Care Med.* 2001;29:936-939.

29. Metheny N, Smith L, Stewart B. Development of a reliable and valid bedside test for bilirubin and its utility for improving prediction of feeding tube location. *Nurs Res.* 2000;49:302-309.

30. Metheny NA, Stewart BJ, Smith L, Yan H, Diebold M, Clouse RE. pH and concentrations of pepsin and trypsin in feeding tube aspirates as predictors of tube placement. *JPEN J Parenter Enteral Nutr.* 1997;21:279-285.

31. Ackerman MH, Mick DJ. Technologic approaches to determining proper placement of enteral feeding tubes. *AACN Adv Crit Care.* 2006;17:246-249.

32. Metheny NA. Preventing respiratory complications of tube feedings: evidence-based practice. *Am J Crit Care.* 2006;15:360-369.

33. Ellett MLC, Maahs J, Forsee S. Prevalence of feeding tube placement errors & associated risk factors in children. *MCN Am J Matern Child Nurs.* 1998;23:234-239.

34. Metheny N, McSweeney M, Wehrle MA, Wiersema L. Effectiveness of the auscultatory method in predicting feeding tube location. *Nurs Res.* 1990;39:262-267.

35. Gharpure V, Meert KL, Sarnaik AP, Metheny NA. Indicators of postpyloric feeding tube placement in children. *Crit Care Med.* 2000;28:2962-2966.

36. Metheny NA, Spies M, Eisenberg P. Frequency of nasoenteral tube displacement and associated risk factors. *Res Nurs Health.* 1986;9:241-247.

37. Metheny NA, Schnelker R, McGinnis J, et al. Indicators of tubesite during feedings. *J Neurosc Nurs.* 2005;37:320-325.

38. Metheny NA, Titler MG. Assessing placement of feeding tubes. *Am J Nurs.* 2001;101:36-45.

39. Harrison AM, Clay B, Grant MJ, et al. Nonradiographic assessment of enteral feeding tube position. *Crit Care Med.*1997;25:2055-2059.

40. Welch SK, Hanlon MD, Waits M, Foulks CJ. Comparison of four bedside indicators used to predict duodenal feeding tube placement with radiography. *JPEN J Parenter Enteral Nutr.* 1994;18:525-530.

41. Day L, Stotts NA, Frankfurt A, et al. Gastric versus duodenal feeding in patients with neurological disease: a pilot study. *J Neurosci Nurs.* 2001;33:148-149, 155-159.

42. Light VL, Slezak FA, Porter JA, et al. Predictive factors for early mortality after percutaneous endoscopic gastrostomy. *Gastrointest Endosc.* 1995;42:330-335.

43. Tanswell I, Barrett D, Emm C, et al. Assessment by a multidisciplinary clinical nutrition team before percutaneous endoscopic gastrostomy placement reduces early postoperative mortality. *JPEN J Parenter Enteral Nutr.* 2007;31:205-211.

44. National Confidential Enquiry into Patient Outcome and Death. Scoping Our Practice: The 2004 Report of the National Confidential Enquiry into Patient Outcome and Death. London NCEPOD 2004. http://www.ncepod.org.uk/pdf/2004/04sum.pdf. Accessed October 28, 2008.

45. Isch JA, Rescorla FJ, Scherer LRT, et al. The development of gastroesophageal reflux after percutaneous endoscopic gastrostomy. *J Pediatr Surg.* 1997;32:321-323.

46. Sulaman E, Udall JN, Brown RF, et al. Gastroesophageal reflux and Nissen fundoplication following percutaneous endoscopic gastrostomy in children. *J Pediatr Gastroenterol Nutr.* 1998;26:269-273.

47. Smith SW, Camfield C, Camfield P. Living with cerebral palsy and tube feeding: a population-based follow-up study. *J Pediatr.* 1999;135:307-310.

48. Fan AC, Baron TH, Rumalla A, Harewood GC. Comparison of direct percutaneous endoscopic jejunostomy and PEG with jejunal extension. *Gastrointest Endosc.* 2002;56:890-894.

49. Raval MV, Phillips D. Optimal enteral feeding in children with gastric dysfunction: surgical jejunostomy vs image-guided gastrojejunal tube placement. *J Pediatr Surg.* 2006;41:1679.

50. Ciaccia D, Quigley RL, Shami PJ. A case of retrograde jejunoduodenal intussusception caused by a feeding gastrostomy tube. *Nutr Clin Pract.* 1994;9:18-21.
51. Collier B, Guillamondegui O, Cotton B, et al. Feeding the open abdomen. *JPEN J Parenter Enteral Nutr.* 2007;31:410-415.
52. Delaney CP, Zutshi M, Senagore AJ, Remzi FH, Hammel J, Fazio VW. Prospective, randomized, controlled trial between a pathway of controlled rehabilitation with early ambulation and diet and traditional postoperative care after laparotomy and intestinal resection. *Dis Colon Rectum.* 2003;46:851-859.
53. Lucha PA Jr, Butler R, Plichta J, Francis M. The economic impact of early enteral feeding in gastrointestinal surgery: a prospective survey of 51 consecutive patients. *Amer Surg.* 2005;71:187-190.
54. Hirao M, Tsujinaka T, Takeno A, Fujitani K, Kurata M. Patient-controlled dietary schedule improves clinical outcome after gastrectomy for gastric cancer. *World J Surg.* 2005;29:853-857.
55. Malhotra A, Mathur AK, Gupta S. Early enteral nutrition after surgical treatment of gut perforations: a prospective randomised study. *J Postgrad Med.* 2004;50:102-106.
56. Ekingen G, Ceran C, Guvenc BH, Tuzlaci A, Kahraman H. Early enteral feeding in newborn surgical patients. *Nutrition.* 2005;21: 142-146.
57. Lewis SJ, Egger M, Sylvester PA, Thomas S. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. *BMJ.* 2001; 323:1-5.
58. Melis M, Fichera A, Ferguson MK. Bowel necrosis associated with early jejunal feeding. *Arch Surg.* 2006;141:701-704.
59. Brown DN, Miedema BW, King PD, Marshall JB. Safety of early feeding after percutaneous endoscopic gastrostomy. *J Clin Gastroenterol.* 1995;21:330-331.
60. Choudhry U, Barde CJ, Markert R, Gopalswamy N. Percutaneous endoscopic gastrostomy: a randomized prospective comparison of early and delayed feeding. *Gastrointest Endosc.* 1996;44:164-167.
61. Nolan TF, Callon R, Choudry U, Reisinger P, Shaar CJ. Same day use of percutaneous endoscopic gastrostomy tubes: radiographic evidence of safety. *Am J Gastroenterol.* 1994;89:1743.
62. McCarter TL, Condon SC, Aguilar RC, et al. Randomized prospective trial of early versus delayed feeding after percutaneous endoscopic gastrostomy placement. *Am J Gastroenterol.* 1998;93:419-421.
63. Kirby DF, Craig RM, Tsang T-K, Plotnick BH. Percutaneous endoscopic gastrostomies: a prospective evaluation and review of the literature. *JPEN J Parenter Enteral Nutr.* 1986;10:155-159.
64. Carmona-Sanchez R, Navarro-Cano G. Percutaneous endoscopic gastrostomy. Is it safe to start eating immediately? *Rev Gastroenterol Mex.* 2002;67:6-10.
65. Werlin SL, Glicklich M, Cohen RD. Early feeding after percutaneous endoscopic gastrostomy is safe in children. *Gastrointest Endosc.* 1994;40:692-693.

VI. ENTERAL NUTRITION ADMINISTRATION

A. Initiation and Advancement of an Enteral Nutrition Regimen

Background

Administration of enteral nutrition (EN) should be guided by the patient's age, underlying disease, nutrition status and requirements, enteral access device, and condition of the gastrointestinal (GI) tract. EN may be administered using bolus, intermittent or continuous techniques, or a combination of these methods. In general, diluting enteral formulas in the initial stages of tube feeding is not necessary. The practice of diluting formulas may actually increase the risk of intolerance due to diarrhea secondary to microbial contamination.[1] Lower osmolality and higher pH of dilute formulas support microbial growth better than full-strength formulas.[2] There are limited prospective data to form strong recommendations for the best starting administration rate for initiation of enteral feeding. Stable patients tolerate a fairly rapid progression of EN, generally reaching the established goal within 24-48 hours of initiation.[3]

Beginning and advancing enteral feedings in pediatric patients is guided by clinical judgment and institutional practices in the absence of prospective controlled clinical trials. Generally children are started on an isotonic formula at a rate of 1-2 mL/kg/h for smaller children and 1mL/kg/h for larger children over 35-40 kg.[4] The rate is advanced based on tolerance by the child with the goal of providing 25% of the total calorie needs on day 1. When giving gastric feedings, it is possible to concentrate formula once feeding tolerance is demonstrated which allows fluid restricted children to receive more calories. Feedings are advanced to goal calories within 24-48 hours and then bolus feedings are started, if indicated. Bolus feedings are given via gravity or over a longer period of time via an enteral feeding pump. Combinations of daytime bolus and night gravity feedings can allow parents to sleep and yet advance the child toward full bolus feeds at home. When the plan involves beginning with bolus feedings, a volume of 2.5-5 mL/kg can be given 5-8 times per day with gradual increases in this volume to decrease the number of feedings to closer to 5 times daily.[5] Bolus feedings can be given over shorter periods of time by gradually increasing the volume infused per hour. At no time should a bolus feeding be given in a shorter period of time than a child would be expected to consume if given a bottle feeding. Maximum volumes for continuous and bolus feedings are determined by the child's response to the regimen, weight gains, and overall GI status.

Initiation and Advancement of Enteral Feedings

Adults: Bolus feedings and gravity-controlled feedings. Usually the bolus and gravity methods are tolerated when infused into the stomach. The feedings may be initiated with full-strength formula 3-8 times per day, with increases of 60-120 mL every 8-12 hours as tolerated up to the goal volume.

Formula (eg, elemental, hypertonic, polymeric, or isotonic) does not require dilution. When additional water is necessary to meet fluid requirements, it is administered intermittently as flushes throughout the

day. Monitoring of gastric residual volumes and assessment of GI tolerance are essential in formula titration to the goal volume. Bolus feedings are defined as formula delivered by gravity via a syringe over approximately 15 minutes. Intermittent feedings are delivered via a feeding container or bag over 30-45 minutes with or without an enteral feeding pump.[6]

Pump-assisted feedings. A pump is generally required for small-bowel feedings and is preferred for gastric feedings in critically ill patients, as the slower administration rate of continuous feedings often enhances tolerance. Conservative initiation and advancement rates are recommended for patients who are critically ill, or have not been fed enterally for some time. In practice, formulas are frequently initiated at full strength at 10-40 mL/h and advanced to the goal rate in increments of 10-20 mL/h every 8-12 hours as tolerated. This approach can usually be used with isotonic as well as high-osmolality or elemental products.[6] There is some evidence that EN can begin at goal rates in stable, adult patients.[7,8]

Children: Bolus feedings and gravity-controlled feedings. Bolus feedings may be started with 25% of the goal volume divided into the desired number of daily feedings. Formula volume may be increased by 25% per day as tolerated, divided equally between feedings.[9]

Pump-assisted feedings. A full-strength, isotonic formula can be started at 1-2 mL/kg/h and advanced by 0.5-1 mL/kg/h every 6-24 hours until the goal volume is achieved.[6] Preterm, critically ill, or malnourished children who have not been fed enterally for an extended period may require a lower initial volume of 0.5-1 mL/kg/hour.[10] Caregivers should be adequately trained on EN techniques and feeding pump operations prior to the patient being discharged on home EN.

Practice Recommendations

1. Base enteral delivery method and initiation and advancement of EN regimens on patient condition, age, enteral route (gastric vs small bowel), nutrition requirements, and GI status. (C)
2. Choose full strength, isotonic formulas for initial feeding regimen. (C)
3. Initiation and advancement of enteral formula in pediatric patients is best done over several days in a hospital setting using a flexible nutrition plan. (C)

References

1. Worthington P, Reyen L. Initiating and managing enteral nutrition. In: Worthington PH, ed. *Practical Aspects of Nutritional Support.* Philadelphia, PA: Saunders, 2004;311-342.
2. Campbell SM. *Preventing Microbial Contamination of Enteral Formulas and Delivery Systems.* Columbus, OH: Abbott Laboratories, Ross Products Division, 2000.
3. Marian M, McGinnis C. Overview of enteral nutrition. In: Gottschlich MM, ed. *The A.S.P.E.N. Nutrition Support Core Curriculum: A Case Based Approach–The Adult Patient.* Silver Spring, MD: American Society for Parenteral and Enteral Nutrition, 2007;187-208.
4. Marchand V. Enteral nutrition tube feedings. In: Baker S, Baker R, Davis A, eds. *Pediatric Nutrition Support.* Boston, MA: Jones and Bartlett; 2007;249-260.
5. Nevin-Folino N, Miller M. Enteral nutrition. In: Queen Samour P, King Helm K, Lang CE, eds. *Handbook of Pediatric Nutrition.* 2nd ed. Boston, MA: Jones and Bartlett; 2004;499-524.
6. Lord L, Harrington M. Enteral nutrition implementation and management. In: Merritt R, ed. *The A.S.P.E.N. Nutrition Support Practice Manual.* 2nd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2005;76-89.
7. Rees RG, Keohane PP, Grimble GK, Frost PG, Attrill H, Silk DB. Tolerance of elemental diet administered without starter regimen. *Br Med J.* 1985;290:1869-1870.
8. Mentec H, Dupont H, Bocchetti M, et al. Upper digestive intolerance during enteral nutrition in critically ill patients: frequency, risk factors, and complications. *Crit Care Med.* 2001;29: 1955-1961.
9. Harrington M, Lyman B. Special considerations for the pediatric patient. In: Guenter P, Silkroski M, eds. *Tube Feeding: Practical Guidelines and Nursing Protocols.* Gaithersburg, MD: Aspen Publishers; 2001:139-188.
10. Akers SM, Groh-Wargo SL. Normal nutrition during infancy. In: Queen Samour P, King Helm K, Lang CE, eds. *Pediatric Nutrition.* Gaithersburg, MD: Aspen Publishers; 1999:65-97.

Special Considerations for the Preterm Infant

Infants with growth failure have a high risk of poor developmental outcome.[1] Infants with necrotizing enterocolitis (NEC) have been shown to have significantly more neurodevelopmental impairment than age-matched peers.[2] Whether that is inevitable or can be changed by nutrition intervention is not known. Infants with NEC do not tolerate nutrition while they are stressed, because the infants become hyperglycemic on a normal amount of glucose infusion and have increased morbidity.[3]

PN is the initial mode of nutrition support for the premature infant, begun as soon as possible after birth.[4] The timing of the initiation of EN is dependent on the gestational age of the infant and the clinical condition. The concern about NEC governs the timing and advancement of enteral feedings. So far, over 40 years of research has failed to identify the optimal feeding method to prevent NEC.[4]

An evidence-based guideline for NEC for infants weighing < 1500 g has been published, including EN recommendations.[5] Infants who received human breast milk (HMB) have been found to be 4 times less likely to have confirmed (Bell's Stage II) NEC compared to infants who received an EN formula (risk ratio [RR] 0.25, 95% confidence interval [CI] 0.06-0.98).[5-7] One meta-analysis has shown that providing human milk will

prevent 1 case of NEC per 20 preterm infants.[6] Minimal enteral feeding (MEF) has been advanced as a method to "prime" the GI tract of the immature infant, stimulate enteral hormones, and perhaps decrease the incidence of NEC. A different meta-analysis has shown, however, that the use of MEF had no effect on the risk of NEC.[8] A concern is with the definition that was used for MEF, 37 mL/kg/day for greater than 5 days, is a greater volume than what most clinicians would use: 10-20 mL/kg/day is the more accepted volume. Two more studies were added to the meta-analysis, but did not alter the results. [4,9,10] However, a recent large prospective study showed a decreased incidence rate of NEC in infants maintained at 20 mL/kg/day compared to those infants advanced to goal rate.[11]

One meta-analysis looked at the timing of initiation of enteral feedings, comparing early (days 1-5), and late (days 5-14). The evidence was insufficient to support either time period relative to the risk for NEC.[12-15] It seems reasonable to encourage early enteral feeding since there is no difference in the rate of NEC. Also, there is insufficient evidence to recommend a specific rate of advancement of enteral feedings relative to the risk of NEC. No difference was seen in studies that varied from 10 mL/kg/day vs 35 mL/kg/day.[16,17] While initial trophic feeds may be started more slowly, nutritive feeds are commonly advanced approximately 10-20 mL/kg/day for Extremely Low-Birth Weight (ELBW) and Very Low-Birth Weight (VLBW) infants. There is also a lack of evidence demonstrating an advantage with transpyloric over gastric feeding methods. Similarly, there is no benefit of bolus over continuous feeding in efforts to reduce the risk of NEC.[6,18] Clinicians may need to employ several different methods in individual infants for EN to be successful. Historically, some clinicians have feared enteral feeds while an umbilical artery catheter (UAC) is in place due to fear of reduced perfusion to the gut. One small randomized controlled trial found no difference in the incidence of NEC between infants fed early with a UAC in place and those in which feedings were delayed to 24 hours after the UAC was removed.[19] Overall, there is insufficient evidence to evaluate the risk for NEC with enteral feeding while a UAC is in place or to recommend UAC placement position, high vs low, relative to the risk of NEC.[20]

There is also a lack of evidence regarding the resumption of enteral feeding after the diagnosis of NEC has been made.[4] One retrospective study has evaluated early feedings, < 10 days from diagnosis, suggesting a positive impact with shorter time to full enteral feeds, less catheter related sepsis, and a shorter length of stay.[21] The study was not powered sufficiently to evaluate for the recurrence of NEC.[4]

Practice Recommendations

1. For premature infants weighing < 1500 g and at risk for NEC, it is recommended that mothers be encouraged to supply breast milk for their infants. (A)
2. ELBW and VLBW infants may benefit from minimal enteral feeding starting very slowly at 0.5-1 mL/kg/day and advancing to 20 mL/kg/day. (B)
3. Advance nutritive feedings for VLBW and ELBW infants by a rate of 10-20 mL/kg/day. (C)

References

1. Dusick AM, Poindexter BB, Ehrenkranz RA, et al. Growth failure in the preterm infant: can we catch up? *Semin Perinatol.* 2003;27:302-310.
2. Rees CM, Pierro A, Eaton S. Neurodevelopmental outcomes of neonates with medically and surgically treated necrotizing enterocolitis. *Arch Dis Child.* 2007;92:F193-F198.
3. Hall NJ, Peters M, Eaton S, et al. Hyperglycemia is associated with increased morbidity and mortality rates in neonates with necrotizing enterocolitis. *J Pediatr Surg.* 2004;39:898-901.
4. Greer FR. Nutrition support of the premature infant. In: Baker SR, Baker, RD, Davis, AM, eds. *Pediatric Nutrition Support.* Sudbury, MA: Jones and Bartlett; 2007:383-392.
5. Evidence Based Care Guideline for Infants with Necrotizing Enterocolitis. http://www.cincinnatichildrens.org/svc/alpha/h/gealth-policy/ev-based/default/htm; also available on the www.guideline.gov website. Accessed November 1, 2007.
6. Henderson G, Anthony MY, McGuire W. Formula milk versus maternal breast milk for feeding preterm or low birth weight infants. *Cochrane Database Syst Rev.* 2007;(4):CD002972. doi:10.1002/14651858.CD002972.pub2.
7. Schanler RJ, Lau C, Hurst NM, et al. Randomized trial of donor human milk versus preterm formula as substitutes for mothers' own milk in the feeding of extremely premature infants. *Pediatrics.* 2005;116:400-406.
8. Tyson JE, Kennedy KA. Trophic feedings for parenterally fed infants. *Cochrane Database Syst Rev.* 2005(3): CD000504. doi:10.1002/14651858.CD000504.pub2.
9. McClure RJ, Newell SJ. Randomized controlled study of clinical outcome following trophic feeding. *Arch Dis Child Fetal Neonatal Ed.* 2000;82:F29-F33.
10. Schanler RJ, Schulman RJ, Lau C, et al. Feeding strategies for premature infants: randomized trial of gastrointestinal priming and tube feeding method. *Pediatrics.* 1999;103:434-439.
11. Berseth CL, Bisquerra JA, Paje VU. Prolonging small volumes early in life decreases the incidence of necrotizing enterocolitis in very low birth weight infants. *Pediatrics.* 2003;111:529-534.
12. Bombell S, McGuire W. Delayed introduction of progressive enteral feeds to prevent necrotising enterocolitis in very low birth weight infants. *Cochrane Database Syst Rev.* 2008(2):CD001970. doi:10.1002/14651858.CD001970.pub2.
13. Wilson DC, Cairns P, Halliday HL, et al. Randomized controlled trial of an aggressive nutritional regimen in sick very low birth weight infants. *Arch Dis Child Fetal Neonatal Ed.* 1997; 77:F4-F11.
14. LaGamma EF, Ostertag SG, Birenbaum H. Failure of delayed oral feedings to prevent necrotizing enterocolitis. Results of study in very-low-birthweight neonates. *Am J Dis Child.* 1985;139:385-389.

15. McKeown RE, Marsh TD, Amarnath U, et al. Role of delayed feeding and of feeding increments in necrotizing enterocolitis. *J Pediatr*. 1992; 121:764-770.

16. McGuire W, Bombell S. Slow advancement of enteral feed volumes to prevent necrotising enterocolitis in very low birth weight infants. *Cochrane Database Syst Rev.* 2008(2):CD001241. doi:10.1002/14651858.CD001241.pub2.

17. Kamitsuka MD, Horton ML, Williams MA. The incidence of necrotizing enterocolitis after introducing standardized feeding schedules for infants between 1250 and 2500 grams and less than 34 weeks of gestation. *Pediatrics*. 2000;10:379-384.

18. Premji S, Chessell L. Continuous nasogastric milk feeding versus intermittent bolus milk feeding for premature infants less than 1500 grams. *Cochrane Database Syst Rev.* 2002(4):CD001819. doi: 10.1002/14651858.CD001819.

19. Davey AM, Wagner CL, Cox, C, et al. Feeding premature infants while low umbilical artery catheters are in place: a prospective, randomized trial. *J Pediatr.* 2002;124:795-799.

20. Barrington KJ. Umbilical artery catheters in the newborn: effects of position of the catheter tip. *Cochrane Database Syst Rev.* 1999(1):CD000505. doi:10.1002/14651858.CD000505.

21. Bohnhorst B, Muller S, Dordelman M, et al. Early feeding after necrotizing enterocolitis in preterm infants. *J Pediatr.* 2003;43: 484-487.

B. Enteral Feeding Pumps

Enteral feeding pump design has advanced as the diverse needs of patients receiving enteral feedings has emerged. These pumps are used routinely in every patient care setting and with every patient population. Some pumps have features that are particularly appropriate for patients in a home care environment due to their small size and light weight. Many pumps now have cassettes instead of drip chambers to allow for changes in pump position and to prevent inadvertent flow errors during loading of the chamber. All pumps are designed to be accurate within 10% of the ordered rate unless specifically documented to be lower.[1] While the manufacturer's claim for accuracy may be within accepted recommendations, actual formula delivery may vary widely. A study by Tepaske et al looked at 13 enteral feeding pumps, various enteral tubes and formulas, and accuracy of the feeding pumps.[2] All pumps were studied for 24 hours using a continuous drip rate. Since viscosity of formula and size of the feeding tube may be reasoned to effect enteral feeding pump function, 2 sizes of feeding tubes and several formulas of varying viscosity were tested on each pump. Accuracy of the pumps varied from an 11 mL to 271 mL difference between the ordered amount of formula over 24 hours and the amount delivered. A criticism of this study was that the authors used only 1 pump per manufacturer. However, in a subsequent communication, another group reported equally disappointing results of up to -24mL/hr delivery rate when testing 14 pumps from 1 manufacturer (2 different models of pumps).[3] The authors stressed the importance of periodic calibration of enteral feeding pumps to assure proper function and to assure that the pump used is delivering within 10% of the prescribed amount of formula.[2,3] A pump

also requires periodic maintenance to preserve specifications as would any other mechanical device.

Pediatric and infant enteral pumps require even more accuracy, delivering within 5% of set volume. A pump that is off by 10% in a child that requires full enteral support is problematic. During the first year of life, brain growth is a priority and underfeeding may compromise that. Some infants require use of an IV syringe pump in order to provide small volumes with more accuracy.

The use of enteral feeding pumps allows clinicians and home caregivers to deliver set amounts of enteral formula in a consistent manner. Enteral feeding pumps are used to administer bolus and continuous drip feedings. While the gravity method is often used for bolus feedings, enteral pumps have been shown to result in a decrease in adverse events. A study of 100 immobile patients with PEG tubes looked at regurgitation, vomiting, aspiration, pneumonia, diarrhea, and glucose levels during 6 week trials of gravity- vs enteral-pump delivered enteral formula. This prospective, randomized, cross-over design demonstrated a statistically significant decrease in adverse events in all the above parameters when enteral pumps were used.[4]

Continuous drip feedings using HBM is often indicated for neonates and infants. This can result in loss of fat and protein along with separation of a fat layer within the bag.[5-7] To prevent this from occurring, a syringe pump is often used because it is accurate, has increments of delivery down to 0.1mL/hr, and the syringes can cost-effectively be replaced every 4 hours. Tilting of the pump to at an angle with the syringe tip elevated will prevent loss of fat. Use of conventional enteral feeding pumps has resulted in fat adherence to the enteral bags.[7]

The benefits of enteral feeding pump use in home care patients can be overshadowed by the impact on the patients and/or caregivers. Two studies of home care patients document sleep disturbances by pump alarms and faulty pumps as being 2 of the top problems with home enteral feedings.[8,9]

Families also report inadequate training by the home medical equipment company on pump use. Repeated reports of children tampering with the pump settings has led some manufacturers to add a lock-out feature to pump settings so the caregiver can set the pump and change the lock-out feature as needed, but a child cannot alter the rates once the lock out feature is activated. When tolerated, hand-held bolus feedings may be preferable at home due to the ease of cleaning a syringe, ease of moving around without a pump, and reduced expense.

Practice Recommendations

1. Enteral feeding pumps should deliver the prescribed volume within 10% accuracy for adults. (B)

2. Enteral feeding pumps should deliver the pre-scribed volume within 5% accuracy for neonatal and pediatric patients. (C)

3. Feeding pumps should be calibrated periodically to assure accuracy. (B)

4. HBM infused at low rates should be administered via syringe pump with the syringe tip elevated. (C)

5. Feeding pumps used for patients requiring EN at home should have features that promote safety and minimize sleep disturbances. (B)

References

1. Goff KL. The nuts and bolts of enteral infusion pumps. *MEDSURG Nursing.* 1997;6:9-15.

2. Tepaske R, Binnekade JM, Goedhart PT, Schults MJ, Vroom MB, Mathus-Vliegen EM. Clinically relevant differences in accuracy of enteral nutrition feeding pump systems. *JPEN J Parenter Enteral Nutr.* 2006;30:339-343.

3. Spronk PE, Rommes JH, Kuiper MA. Structural underfeeding due to inaccurate feeding pumps. *JPEN J Parenter Enteral Nutr.* 2006;31:154-155.

4. Shang E, Geiger N, Sturm JW, Post S. Pump-assisted enteral nutrition can prevent aspiration in bedridden percutaneous endoscopic gastrostomy patients. *JPEN J Parenter Enteral Nutr.* 2003;28:180-183.

5. Greer F, McCormick A, Loker J. Changes in fat concentration of human milk during delivery by intermittent bolus and continous mechanical pump infusion. *J Pediatr.* 1984;105;745-749.

6. Narayanan I, Singh B, Harvey D. Fat loss during feeding of human milk. *Arch Dis Child.* 1984;59:475-477.

7. Stocks R, Davies D, Allen F, Sewell D. Loss of breastmilk nutrients during tube feeding. *Arch Dis Child.* 1985;60:164-166.

8. Evans S, Macdonald A, Daly A, Hopkins, V, Holden, C. Home enteral tube feeding in patients with inherited metabolic disorders: safety issues. *J Human Nutr Dietet.* 2007;20:440-445.

9. Evans S, Holden C, Macdonald A. Home enteral feeding audit 1 year post-initiation. *J Human Nutr Dietet.* 2006;19:27-29.

C. Patient Positioning

Background

Evidence exists that a sustained supine position (with the head-of-bed [HOB] flat) increases gastroesophageal reflux (GER) and the probability for aspiration.[1-4] A frequently cited study by Torres et al used 2 methods to assess for aspiration in 19 mechanically-ventilated patients in supine and semirecumbent positions.[1] One method involved instilling technetium-m99 in the stomach and then obtaining radioactive counts in endobronchial secretions; the second method was to culture endobronchial secretions, gastric juice, and pharyngeal secretions. Mean radioactive counts in the endobronchial secretions were significantly higher in the samples collected while the patients were supine than those collected while they were semirecumbent (4154 cpm vs 954 cpm, respectively; $P = .036$). Furthermore, the same microorganisms were isolated from the stomach, pharynx, and endobronchial secretions in 68% of the studies in which the patients were supine as opposed to 32% when they were

semirecumbent. This study suggests that although aspiration is significantly more likely when patients are supine, it also occurs when they are semirecumbent. A similar study by the same research team (performed with 15 mechanically-ventilated patients who had nasogastric [NG] tubes) found gastroesophageal reflux occurred irrespective of body position; however, a semirecumbent position protected against pulmonary aspiration of gastric contents.[5] A recent prospective descriptive study of critically-ill, mechanically ventilated, tube-fed patients found that the 137 patients with a mean HOB elevation < 30º had a significantly greater incidence of aspiration of gastric contents (as defined by finding pepsin in tracheal secretions) than did the 224 patients with an HOB elevation ≥ 30º (34.7% vs 24.3%, respectively, $P < .001$).[6] Another finding from this study was that risk for pneumonia was over 4 times greater in patients who were frequent aspirators as compared to those who aspirated infrequently.

Evidence to Refute Beneficial Effects from Elevated HOB Position

Although most studies support the efficacy of a semirecumbent position in decreasing GER, Ibanez et al found no statistically significant differences in the incidence of GER in 50 intubated patients according to supine and semirecumbent positions (81% [21 of 26] vs 67% [16 of 24], respectively, $P = .26$).[7] In a more recent study, investigators attempted to compare the incidence of pneumonia in 112 critically-ill patients randomly assigned to an HOB elevation of 45º with that of 109 similar patients randomly assigned to a position of 10º.[8] The use of enteral feedings was similar in the 2 groups. The planned comparison was not possible because 85% of the patients assigned to the 45º HOB elevation did not achieve the desired position (mean HOB elevation < 30º). It is not surprising that the incidence of ventilator-associated pneumonia did not differ significantly between the 2 groups.

In summary, based on research-based evidence, authorities recommend HOB elevation of 30º-45º to prevent aspiration and pneumonia, unless otherwise specified in medical orders or contraindicated for other reasons.[9-12] Among the recognized contraindications to a semirecumbent position are an unstable spine, hemodynamic instability, prone positioning, and certain medical procedures (such as a central venous catheter insertion).[10,13]

Poor Application of Elevated HOB Position

Although a head-elevated position is an accepted standard of care for patients receiving EN, there is evidence that it is not adequately adhered to in many clinical settings. For example, Grap et al found that the mean backrest elevation for a group of 66 patients observed over 276 patient days was only 21.7º; further,

72% of the backrest elevations were < 30° and 39% were < 10°.[14] Others have found that only 1.4% (n=5) of 360 critically-ill, tube-fed patients had a mean backrest elevation ≥ 45° over a 3-day period; further, only 38% had a mean backrest elevation ≥ 30°.[6]

To decrease the risk for aspiration, nurses frequently suspend tube feedings temporarily during procedures requiring lowering the HOB (such as linen changes), thus interfering with caloric intake. For example, a study of 45 critically ill patients found that 30% of the cases in which inadequate calories were delivered were due to suspended feedings during the delivery of nursing care; delays of up to 6 hours were sometimes found.[15] There is no benefit from stopping feedings during short periods of HOB lowering. If a prolonged procedure will require HOB lowering, stopping feedings is recommended during this period. However, feedings should be promptly restarted when the procedure is ended.

Strategies to Increase Use of an Elevated HOB Position

Medical Orders. A strategy shown to be effective in improving adherence to HOB elevation is the use of routine written medical orders. For example, following implementation of written orders in a group of critically ill patients, researchers found that the HOB elevations ≥ 30° degrees increased from a mean of 26% at baseline to a mean of 88% after the intervention was implemented.[16] Further, the percent of HOB elevations ≥ 45° increased from 3% at baseline to 28% following the intervention.

Staff Education. There is evidence that some health-care providers fail to recognize the importance of an HOB elevated position; for example, a survey of 93 critical care healthcare providers found that only intensivists and dietitians were aware of the potential benefits of an elevated HOB position.[17] All of the 57 critical care nurses surveyed expressed a fear that an elevated backrest position would increase risk for sacral pressure ulcers. Nurses also reported a belief that underutilization of a semirecumbent position was primarily due to the lack of physicians' orders specifying this position; in contrast, physicians reported a belief that underutilization of a semirecumbent position was due to nursing preference.

Reverse Trendelenberg Position. When an elevated backrest is contraindicated for various reasons (such as an unstable spine), it is recommended that a reverse Trendelenberg position be utilized to the extent possible.[12] Although the effectiveness of this position has not been researched, it is reasonable to assume that the results would be similar to those of a backrest elevated position.

Practice Recommendations

1. Elevate the backrest to a minimum of 30°, and preferably to 45°, for all patients receiving EN unless a medical contraindication exists. (A)
2. Use the reverse Trendelenberg position to elevate the HOB, unless contraindicated, when the patient cannot tolerate a backrest elevated position. (C)
3. If necessary to lower the HOB for a procedure or a medical contraindication, return the patient to an HOB elevated position as soon as feasible. (C)

References

1. Torres A, Serra-Batlles J, Ros E, et al. Pulmonary aspiration of gastric contents in patients receiving mechanical ventilation: the effect of body position. *Ann Intern Med*. 1992;116:540-543.
2. Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogue S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. *Lancet*. 1999;354:1851-1858.
3. Kollef MH, Von Harz B, Prentice D, et al. Patient transport from intensive care increases the risk of developing ventilator-associated pneumonia. *Chest*. 1997;112:765-773.
4. Metheny NA, Chang YH, Ye JS, et al. Pepsin as a marker for pulmonary aspiration. *Am J Crit Care*. 2002;11:150-154.
5. Orozco-Levi M, Torres A, Ferrer M, et al. Semirecumbent position protects from pulmonary aspiration but not completely from gastroesophageal reflux in mechanically ventilated patients. *Am J Respir Crit Care Med*. 1995;152:1387-1390.
6. Metheny NA, Clouse RE, Chang YH, Stewart BJ, Oliver DA, Kollef MH. Tracheobronchial aspiration of gastric contents in critically ill tube-fed patients: frequency, outcomes, and risk factors. *Crit Care Med*. 2006;34:1-9.
7. Ibanez J, Penafiel A, Raurich JM, Marse P, Jorda R, Mata F. Gastroesophageal reflux in intubated patients receiving enteral nutrition: effect of supine and semirecumbent positions. *JPEN J Parenter Enteral Nutr*. 1992;16:419-422.
8. van Nieuwenhoven CA, Vandenbroucke-Grauls C, van Tiel FH, et al. Feasibility and effects of the semirecumbent position to prevent ventilator-associated pneumonia: a randomized study [see comment]. *Crit Care Med*. 2006;34:396-402.
9. Tablan OC, Anderson LJ, Besser R, et al. Guidelines for preventing healthcare-associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *MMWR Recomm Rep*. 2004;53(RR-3):1-36.
10. AACN. Practice alert: ventilator-associated pneumonia. *AACN Adv Crit Care*. 2005;16:105-109.
11. Heyland DK, Cook DJ, Dodek PM. Prevention of ventilator-associated pneumonia: current practice in Canadian intensive care units. *J Crit Care*. 2002;17:161-167.
12. McClave SA, DeMeo MT, DeLegge MH, et al. North American Summit on Aspiration in the Critically Ill Patient: consensus statement. *JPEN J Parenter Enteral Nutr*. 2002;26(6 Suppl):S80-S85.
13. Metheny NA. Risk factors for aspiration. *JPEN J Parenter Enteral Nutr*. 2002;26(6 Suppl):S26-S31.
14. Grap MJ, Munro CL, Hummel RS III, Elswick RK Jr, McKinney JL, Sessler CN. Effect of backrest elevation on the development of ventilator-associated pneumonia. *Am J Crit Care*. 2005;14:325-332.
15. McClave SA, Sexton LK, Spain DA, et al. Enteral tube feeding in the intensive care unit: factors impeding adequate delivery. *Crit Care Med*. 1999;27:1252-1256.
16. Helman DL, Jr., Sherner JH, III, Fitzpatrick TM, Callender ME, Shorr AF. Effect of standardized orders and provider education on head-of-bed positioning in mechanically ventilated patients. *Crit Care Med*. 2003;31:2285-2290.
17. Cook DJ, Meade MO, Hand LE, McMullin JP. Toward understanding evidence uptake: semirecumbency for pneumonia prevention. *Crit Care Med*. 2002;30:1472-1477.

D. *Flushes*

Background

Feeding tubes are prone to clogging for a variety of reasons. One is accumulation of formula sediment in the lower segment of the tube, especially during slow administration rates of calorically dense formulas or those containing fiber.[1] Clogging is also more likely in small diameter tubes.[2-4] As demonstrated in a 3-day laboratory study, silicone tubes clog more often than do polyurethane tubes.[5] A common cause of tube clogging is the improper administration of medications via the tube.[6]

Gastric tubes are reported to clog more frequently than small bowel tubes, presumably because of contact between enteral formula and acidic gastric fluid.[6] In a laboratory study, Marcuard et al studied the effect of pH concentrations on a variety of enteral feeding products by applying 1 mL of each to a series of buffer solutions with pH concentrations from 1 through 10.[7] It was found that premixed intact protein formulas coagulated at an acidic pH but not at an alkaline pH. Because of this finding, Simon and Fink concluded that placing the tube's tip in the alkaline environment of the proximal small intestine may diminish the risk of tube clogging. [3]

Powell et al reported more frequent tube clogging when gastric residual volumes (GRVs) were measured every 4 hours in 15 patients receiving intact protein formulas via small-bore tubes than in 13 others who did not have GRV measurements.[4] Although no gastric pH measurements were reported, the investigators assumed that acidic gastric fluid (pH < 5.0) mixed with the formula to promote clogging during GRV measurements. Patients receiving antacid therapy or acid-suppressing medications were excluded from the study. Prior to and after the GRV measurements, a 10 mL water flush was instilled. It is probable that the flush volume of 10 mL was inadequate to clear the tube of formula mixed with gastric juice. Further, findings from the Powell et al study conducted in 1993 likely have less significance today in that most tube-fed patients receive some form of gastric acid buffering (usually in the form of an H_2 receptor antagonist or a proton pump inhibitor).[8] Another important consideration is that the mere administration of enteral formula into the stomach likely raises gastric pH by buffering gastric acid. For example, Valentine reported in 1986 that gastric pH was at least 5 in 120 of 223 (54%) aspirates from 10 patients continuously fed in the stomach at rates between 50 and 125 mL per hour; none of these patients were receiving other means of stress ulcer prophylaxis.[9]

A protocol to prevent tube occlusion as a result of assessing GRV was evaluated in 135 critically-ill patients receiving continuous tube feedings (71 with gastric tubes and 64 with intestinal tubes).[10] Three-fourths of the patients had 10 Fr feeding tubes and the rest had tubes ranging in size from 14 Fr to 18 Fr. Patients were followed prospectively for 3 days; at 4 hour intervals, a nurse injected 30 ml of air into the tube before attempting to withdraw fluid with a 60 mL syringe. Aspirate was obtained from 72% of the small-bore tubes and from 96% of the large-bore tubes. Following withdrawal of the aspirate, 30 mL of water or normal saline (for selected neurologically impaired patients) was injected into the tube before feedings were resumed. None of the tubes became clogged.

Special Considerations for Pediatrics: Flush volumes for NG tubes in neonatal patients should be limited to 1-3 mL and 3-5 mL in pediatric patients to limit excessive free water administration. This is particularly concerning for a child who is fluid-restricted. Routine tube flushes are not recommended for any tubes other than nasojejunal tubes.

Flush Solutions to Prevent Tube Clogging

The most frequently studied flush solutions to maintain tube patency have been water, carbonated beverages, and cranberry juice.[5,11,12] Water was found to be superior to cranberry juice as an irrigant to maintain the patency of small-bore feeding tubes in 30 patients receiving continuous feedings via pump administration.[12] Other investigators corroborated the superiority of water over cranberry juice in a laboratory study of 108 small-bore feeding tubes.[5] There are no data to show that carbonated beverages are more effective than water as a flush solution. [5] Thus, water is the preferred flush solution since it is easily obtainable at a low cost.[1] In a survey of 235 registered nurses at a midwestern university medical center, tap water was reported to be the most commonly used flush solution to maintain feeding tube patency.[13] Moreover, most nurses stated that they flushed feeding tubes every 4 hours.

Cases of infections resulting from the use of contaminated water in tube-fed patients have been reported.[14-16] For example, Venezia et al speculated that 2 cases of nosocomial legionellosis were due to aspiration of NG tube solutions diluted with tap water.[14] These findings prompted a nursing practice change to use only sterile water to dilute feedings and flush medications for NG tube administration. Multidrug resistant Pseudomonas infections in a neuro-ICU were traced to the tap water source.[15] Others have also switched to the use of sterile water to flush NG tubes and to dilute NG tube feedings in high risk patients following the identification of *Legionella pneumophilia serogroup 1* in the water supply.[16]

It has been suggested that the direct administration of distilled or tap water into the intestine may injure the intestinal epithelium.[17] In a single animal model, the administration of 5 mL of distilled water into the intestine of a 357 g Sprague-Dawley rat caused disruption of the intestinal epithelium more so than did the administration of an equal volume of isotonic saline.[17] It would appear that the equivocal volume of water needed to damage the epithelium of a 70 kilogram individual would be far greater than the usual flush volume of 30 ml every 4 hours.

In an in vitro study that evaluated the ability of 6 solutions to dissolve clotted formula in feeding tubes, Marcuard et al found that the best results were achieved with a solution of Viokase® (Axcan Pharma, Quebec, Canada) and sodium bicarbonate.[18] In a prospective study of 10 patients with occluded feeding tubes, the investigators found that injecting a Viokase solution (pH 7.9) via a Drum catheter into the occluded feeding tubes resulted in clearing of 7 of the tubes.[18] To help prevent clogging of difficult-to-replace tubes, Lord[1] reported that it is helpful to administer activated Viokase solution for 30 minutes per week in nasoenteric and jejunal feeding tubes of home patients.

Practice Recommendations

1. Flush feeding tubes with 30 mL of water every 4 hours during continuous feeding or before and after intermittent feedings in an adult patient.[19] (A)

2. Flush the feeding tube with 30 mL of water after residual volume measurements in an adult patient.[10,19] (B)

3. Flushing of feeding tubes in neonatal and pediatric patients should be accomplished with the lowest volume necessary to clear the tube. (C)

4. Sterile water is recommended for use in adult and neonatal/pediatric patients before and after medication administration. (C)

5. Adhere to protocols that call for proper flushing of tubes before and after medication administration.[19,20] (B)

6. Use an administration pump when slow rates of enteral formula are required, such as in the neonatal population, and respond promptly to pump alarms.[1] (C)

7. Use sterile water for tube flushes in immuno-compromised or critically ill patients especially when the safety of tap water cannot be reasonably assumed.[21] (C)

References

1. Lord LM. Restoring and maintaining patency of enteral feeding tubes. *Nutr Clin Pract*. 2003;18:422-426.

2. Hofstetter J, Allen LV Jr. Causes of non-medication-induced nasogastric tube occlusion. *Am J Hosp Pharm*.1992;49:603-607.

3. Simon T, Fink AS. Current management of endoscopic feeding tube dysfunction. *Surg Endo*. 1999;13:403-405.

4. Powell KS, Marcuard SP, Farrior ES, Gallagher ML. Aspirating gastric residuals causes occlusion of small-bore feeding tubes. *JPEN J Parenter Enteral Nutr*. 1993;17:243-246.

5. Metheny NA, Eisenberg P, McSweeney M. Effect of feeding tube properties and three irrigants on clogging rates. *Nurs Res*. 1988;37:165-169.

6. Marcuard SP, Stegall KS. Unclogging feeding tubes with pancreatic enzyme. *JPEN J Parenter Enteral Nutr*. 1990;14:198-200.

7. Marcuard SP, Perkins AM. Clogging of feeding tubes. *JPEN J Parenter Enteral Nutr*. 1988;12:403-405.

8. Metheny NA, Clouse RE, Chang YH, Stewart BJ, Oliver DA, Kollef MH. Tracheobronchial aspiration of gastric contents in critically ill tube-fed patients: frequency, outcomes, and risk factors. *Crit Care Med*. 2006;34:1-9.

9. Valentine RJ, Turner WW Jr, Borman KR, Weigelt JA. Does nasoenteral feeding afford adequate gastroduodenal stress prophylaxis? *Crit Care Med*. 1986;14:599-601.

10. Schallom L, Stewart J, Nuetzel G, et al. Testing a protocol for measuring gastrointestinal residual volumes in tube-fed patients. *Am J Crit Care*. 2004;13:265-266.

11. Nicolau DP, Davis SK. Carbonated beverages as irrigants for feeding tubes. *DICP*. 1990;24(9):840.

12. Wilson MF, Haynes-Johnson V. Cranberry juice or water? A comparison of feeding-tube irrigants. *Nutr Supp Serv*. 1987;7:23-24.

13. Mateo MA. Maintaining the patency of enteral feeding tubes. *Reflections*. 1996;22:22.

14. Venezia RA, Agresta MD, Hanley EM, Urquhart K, Schoonmaker D. Nosocomial legionellosis associated with aspiration of nasogastric feedings diluted in tap water. *Infect Control Hosp Epidemiol*. 1994;15:529-533.

15. Bert F, Maubec E, Bruneau B, Berry P, Lambert-Zechovsky N. Multi-resistant Pseudomonas aeruginosa outbreak associated with contaminated tap water in a neurosurgery intensive care unit. *J Hosp Infect*. 1998;39:53-62.

16. Marrie TJ, Haldane D, MacDonald S, et al. Control of endemic nosocomial legionnaires' disease by using sterile potable water for high risk patients. *Epid Infect*. 1991;107:591-605.

17. Schloerb PR, Wood JG, Casillan AJ, Tawfik O, Udobi K. Bowel necrosis caused by water in jejunal feeding. *JPEN J Parenter Enteral Nutr*. 2004;28:27-29.

18. Marcuard SP, Stegall KL, Trogdon S. Clearing obstructed feeding tubes. *JPEN J Parenter Enteral Nutr*. 1989;13:81-83.

19. Kohn-Keeth C. How to keep feeding tubes flowing freely. *Nursing*. 2000;30:58-59.

20. van den Bemt PM, Cusell MB, Overbeeke PW, et al. Quality improvement of oral medication administration in patients with enteral feeding tubes. *Qual Saf Health Care*. 2006;15:44-47.

21. Padula CA, Kenny A, Planchon C, Lamoureux C. Enteral feedings: what the evidence says. *Am J Nurs*. 2004;104:62-69.

E. Enteral Misconnections

Background

An enteral misconnection is an inadvertent connection between an enteral feeding system and a non-enteral system such as an intravascular catheter, peritoneal dialysis catheter, tracheostomy, medical gas tubing, etc. In each case, serious patient harm—including death—can occur if fluid, medication, or nutritional formula intended for administration into the GI tract, are administered via the wrong route.[1]

Reported enteral misconnections date as far back as 1972 when an inadvertent intravenous (IV) administration of breast milk was published.[2] In one literature review, over 60 references to enteral misconnections appeared in the published literature alone.[3] It is recognized that reporting may greatly underestimate the number of actual cases, and that poor understanding of the causative

factors also hinder a true record of incidents involving feeding connectors. The published reports consistently substantiate the highest level of severity for this type of error, which commonly results in the death of the patient by embolus or sepsis.[1]

In 1996, the Association for the Advancement of Medical Instrumentation (AAMI) Infusion Device Committee convened an expert group to address the safety requirements for enteral feeding set connectors and adaptors. This expert group included members from the FDA, A.S.P.E.N., various safety organizations, such as the Emergency Care Research Institute (ECRI Institute), and manufacturers of feeding sets. The resulting voluntary standard, approved in 1996 and reaffirmed in 2005, called for adapters and connectors used in the enteral system to be incompatible with female luer lock rigid connectors.[4] However, no alternative design standards were ever developed and approved based on that document. Alternative connector designs are referenced in a British Standards document which describes the step connector ("Christmas tree connector").[5] In the 1990s, some feeding sets with these step ("Christmas tree") connectors were developed which were incompatible with luer connectors on IV lines. Following release of the AAMI standard, more manufacturers adopted this design. Unfortunately, these standards are not universally followed by all device manufacturers, and connectors remain a serious hazard to patients.

As recently as April 2006, The Joint Commission issued a Sentinel Event Alert on tubing misconnections.[6] They stated that multiple reports to agencies such as The Joint Commission, the ECRI Institute, U.S. Food and Drug Administration (FDA), Institute for Safe Medication Practices (ISMP), and United States Pharmacopeia (USP) indicated that these misconnection errors occur with significant frequency and, in a number of instances, lead to deadly consequences. In this alert, they identified root causes and risk reduction strategies. Many other healthcare alerts on medical misconnections have been issued by USP, ECRI Institute, FDA, and ISMP from 1986 to the present, yet errors involving misconnections continue.[1] More manufacturers are responding to this issue by developing enteral systems and connections that are not compatible with IV systems.[1] An example of this technology was recently introduced in the U.S., using a screwtop design that minimizes compatibility with IV equipment.

Practice guidelines can be categorized based on education, human factors, and purchasing strategies. A design that prevents cross-connections between IV and enteral products would prevent the problem; any other recommendation decreases risk but does not eliminate it. For example, color-coding enteral connectors (for which there is no current authorized standard color) simply alerts the clinician that this is not an IV connector, but does not prevent the misconnection.

Practice Recommendations

1. Review currently used systems to assess practices that include the potential for misconnection, including nonstandard, rigged work-arounds (luer adapters, etc.).[7] (C)

2. Train nonclinical staff and visitors not to reconnect lines but to seek clinical assistance instead. Only clinicians or users knowledgeable about the use of the device should make a reconnection, and should do so under proper lighting.[8] (C)

3. Do not modify or adapt IV or feeding devices because doing so may compromise the safety features incorporated into their design.[8] (C)

4. When making a reconnection, practitioners should routinely trace lines back to their origins and then ensure that they are secure.[8] Route tubes and catheters that have different purposes in unique and standardized directions (eg, IV lines should be routed toward the patient's head, and enteric lines should be routed toward the feet).[6] (C)

5. When arriving at a new setting or as part of a hand-off process, staff should recheck connections and trace all tubes.[6] (C)

6. Label or color-code feeding tubes and connectors, and educate staff about the labeling or color-coding process in the institution's enteral feeding system.[6] (C)

7. Identify and confirm the EN label, because a 3-in-1 PN admixture can appear similar to an EN formulation bag. Label the bags with large, bold statements such as "WARNING! For Enteral Use Only—NOT for IV Use."[9] (C)

8. Avoid buying enteral equipment that can mate with female luer connectors.[6] Evaluate the need for and reduce the purchases of adapters and connectors that can be modified to make enteral feeding sets compatible with female luer connectors. (C)

9. Purchase an adequate number of enteral pumps so that IV pumps are not used for enteral delivery for adult patients. When syringe pumps are used in neonatal ICUs for human milk or other feedings, they should be clearly distinct from syringe pumps used for IV or other medical purposes. Ideally, they should be a different model, color, or as different in appearance from IV pumps as possible. The enteral feeding pumps should be clearly labeled as enteral feeding pumps. (C)

10. Ensure that hospital purchasing policies mandate buying only enteral feeding sets that are compliant with American National Standards Institute/Association for the Advancement of Medical Instrumentation (ANSI/AAMI)

standard ID54, which effectively excludes any that are compatible with female luer connectors. These devices must also be clearly labeled (eg, "Not for IV Use").[4] (C)

11. Avoid buying pre-filled enteral feeding containers, except for those with design technology labeled non-IV compatible. In all cases, ensure that the enteral administration set is packaged with the enteral feeding bag or container before it is sent to the patient care unit. (The set should be secured to the bag, perhaps with a rubber band, or preattached sets should be requested from the manufacturer). In either case, the objective is to prevent bags or containers from being spiked with IV administration sets.[10] (C)

12. Purchase and use oral syringes instead of luer-lock syringes to draw up and deliver medications into the enteral feeding system. Include pharmacy department recommendations to ensure the correct syringe type, along with dispensing and proper labeling protocols. Other syringes that may be used include large catheter tip syringes that cannot fit into IV systems. (C)

References

1. Guenter P, Hicks RH, Simmons D, et al. Enteral feeding misconnections: a consortium position statement. *Jt Comm J Qual Patient Saf.* 2008;34:285-292.

2. Wallace JR, Payne RW, Mack AJ. Inadvertent intravenous breast milk. *Lancet.* 1972;1(7763):1264-1266.

3. Simmons D, Graves K. Small bore medical connectors reference list. 2007. University of Texas MD Anderson Cancer Center. www.mdanderson.org/pdf/small_bore_medical_connectors_reference_list.pdf. Accessed on June 27, 2007.

4. American National Standards Institute (ANSI)/Association for the Advancement of Medical Instrumentation (AAMI). *Enteral feeding set adapters and connectors.* ANSI/AAMI ID54-1996.

5. British Standard. *Enteral feeding catheters and enteral giving sets for single use and their connectors – Design and testing.* BS EN 1615, 2000.

6. Joint Commission Sentinel Event Alert. *Tubing Misconnections – A Persistent and Potentially Deadly Occurrence, Issue 36*, April 3, 2006. http://www.jointcommission.org/SentinelEvents/SentinelEventAlert/sea_36.htm. Accessed on October 8, 2006.

7. Pratt N. Tubing misconnections: a perilous design flaw. *Mater Manag Health Care.* 2006;15:36-39.

8. ECRI. Preventing misconnections of lines and cables. *Health Devices.* March 2006:81-95.

9. Institute for Safe Medication Practices. ISMP Medication Safety Alert: ISMP Quarterly Action Agenda. Enteral feeding given IV. April 4, 2003. www.ismp.org/Newsletters/acutecare/articles/A2Q03Action.asp?ptr=y. Accessed March 3, 2008.

10. Institute for Safe Medication Practices. ISMP Medication Safety Alert: ISMP Quarterly Action Agenda. IV administration set spiked into enteral nutrition container. April 4, 2001. www.ismp.org/Newsletters/acutecare/articles/A2Q01Action.asp?ptr=y. Accessed March 3, 2008.

VII. MEDICATION ADMINISTRATION

EN often requires administration of medications through the same enteral access device. Appreciating the complexity for drug administration through a feeding tube and maintaining appropriate techniques may help avoid tube obstruction, reduced drug efficacy, or increased drug toxicity.

A. Dosage Forms and Administration

Making the best use of medication in patients receiving EN includes administration techniques that assure bioavailability without further complicating the patient's overall care. Guidelines for administering medication via enteral feeding tubes are available,[1-9] as are a number of surveys of enteral drug administration practices and techniques.[10-16] Surveys suggest that practice differs significantly from guidelines, and several common practices could interfere with appropriate medication delivery.[10-16] Surveys suggest that only 5%-43% of practitioners flush tubes before or between medications, only 32%-51% administer drugs separately from one another, only 44%-64% dilute liquid medication, and only 75%-85% avoid crushing modified-release dosage forms. Some of these practices may contribute to measurable adverse outcomes—namely, tube obstruction, reduced drug efficacy, and increased drug toxicity.

Commercially-available oral drug dosage forms are solids (capsules, tablets) or liquids (solutions, elixers, suspensions). Most tablets and capsules are immediate-release products (ie, compressed tablets, hard gelatin capsules) which contain the active drug molecule mixed with excipients (non-therapeutic ingredients required to formulate the product). These products are designed to allow the drug contents to be released within minutes of reaching the stomach following oral administration. But more and more drugs have been introduced as modified-release products (eg, delayed- or extended-release), or as complex formulations given recent advances in technology.[17,18] Solutions are homogeneous liquid mixtures in which the active medication is totally and uniformly dissolved in the diluent. The diluent often contains water and a variety of other solvents depending on the solubility of the active drug. The viscosity and osmolality of a solution varies with the drug and solvent. Disadvantages of solutions include the increased potential for drug instability due to hydrolysis or oxidation. Suspensions are heterogeneous liquids containing a poorly soluble active medication floating in a liquid medium that contains suspending or thickening agents. Disadvantages of suspensions include their viscosity and the potential for settling out of dispersed particles. This makes it more difficult to deliver the medication to the site of drug absorption through an enteral feeding tube. Regardless of

the container volume, suspensions should be shaken well immediately prior to drug administration.

Occlusion of feeding tubes or any altered clinical response to drug therapy as a result of inappropriate enteral administration techniques are not typically captured in adverse drug event rates. Regardless of etiology, obstruction ("clogging") of a feeding tube is both time- and resource-intensive to address, and therefore is best prevented. Results of a national survey suggest that drug-related feeding tube obstruction exceeds 10% if modified-release dosage forms were routinely crushed.[15] Complications attributed to medication beyond tube obstruction, such as lack of therapeutic benefit and diarrhea, were significant at 26% and 45% respectively.[15] Severe and even fatal outcomes related to inappropriate drug administration via enteral feeding tubes do occur. After a young woman initially admitted to hospital with pneumonia was stabilized and improved, her medications were converted to oral dosage forms that were crushed and administered via nasogastric tube.[19] The medication regimen included hydralazine, labetalol, and extended-release nifedipine. The patient developed hypotension, bradycardia, and asystolic cardiac arrest before being resuscitated. The following day the same medications were again crushed and administered with the same untoward cardiovascular effects leading to the patient's death.[19]

B. Gastric vs Intestinal Delivery

Administration of oral drug products through an enteral feeding tube requires some considerations. Factors that should be taken into account include the length of a patient's functional bowel, the internal diameter and length of the tube, the composition of the tube, the routine flushing regimen, the location of the distal end of the feeding tube relative to the site of drug absorption, the size of the distal opening(s), the need to keep a drug separate from a tube feeding formula, and the size of the oral syringe for both accurate drug dosing and safe intraluminal pressures. On the last point, only syringes manufactured and intended for oral/enteral use should be used to measure and administer a medication through an enteral feeding tube.[9,20] The tips on oral syringes should be too wide to fit luer ports and devices, and should also have a minimal dead-space volume. All of the above considerations should be taken into account to avoid negative outcomes including tube obstruction, reduced efficacy, and increased drug toxicity.

Commercially-available drugs that are intended for systemic effect via oral administration are designed with the physiology of the healthy, intact gastrointestinal (GI) tract in mind. Immediate-release dosage forms begin to disintegrate and dissolve in the stomach before entering the small bowel milieu where the stage is set for continued dissolution and absorption. Although some drug absorption may generally occur throughout the GI tract by mass effect, there are distinct and occasionally unknown sites of absorption of specific drugs. Administration of a drug via an enteral feeding tube may bypass the required environment for dissolution and absorption. For example, when administered as a medication, iron is predominantly absorbed at the duodenum following gastric dissolution. So administration through a tube with the distal opening in the jejunum risks poor bioavailability of the iron.[9] Prior to administration of medication through a feeding tube, the location of the distal tube tip should be noted.

C. Drug Interactions

Interactions involving medication administered to patients receiving EN include those that pose a *compatibility* problem and those that influence the *stability* of the drug or nutrient. These can result in feeding tube occlusion, altered drug or nutrient delivery and bioavailability, or altered GI tract function. Whenever a drug formulation is altered—whether by pulverizing it, adding it to fluid, or combining it with other substances—drug stability may be compromised. Suboptimal drug administration has been identified more commonly in patient care units that did not establish drug preparation and administration protocols.[21] In most clinical settings, medication may be administered through the same enteral access device, but not admixed with the EN formulation.

Drug Added to EN – In patient care settings that do not use a closed EN feeding system, the opportunity to add medication to EN formulas may still exist. This requires adequate knowledge of a drug's compatibility with the formula, and the stability of each component of the final formula as well. The available data cannot be extrapolated to different formulas of the same medication, different medications in the same drug class, or different enteral feeding formulas. For example, a liquid morphine product of lower concentration may result in phase separation and protein precipitation of an EN formula while a more concentrated version of the same drug might not.[22] Several papers describe the compatibility of a relatively small number of medications when admixed with a limited number of commercially available EN formulas.[22-27] The type and concentration of protein, as well as the fiber and mineral content of the feeding formula are factors involved in incompatibility, while drug product variables include pH, viscosity, osmolality, alcohol, and mineral content.[23,25] Few of these studies evaluate nutrient stability. The evaluations go beyond simple visual examination and identify any alterations in chemical (eg, pH) or physical (eg, osmolality) properties of the admixture using conditions of typical use (ie, 8-12 h administration through an

administration set of clinically-relevant doses). The concentration of the medication may be significantly reduced over time.[24,26] Over 95% of incompatible admixtures result in clogged feeding tubes, of which less than one-third could be resolved by flushing with water.[25] The addition to EN formulas of most of the tested products cannot be recommended.[24] Even when data exist supporting the addition of a medication to a formula in terms of compatibility and stability, an evaluation of therapeutic benefit must also be made to determine if a therapeutic amount of the medication is still available at the optimal site of absorption to allow for the expected therapeutic effects. To avoid interactions, administration of the EN formula is temporarily held while each medication is administered enterally. The period of time that the formula is held will depend on the interaction potential between the administered drug and the EN formula.

Drug Added to Drug – The design of immediate-release oral products is based on the intended use through oral ingestion with 120-240 mL of water. Once in the gastric lumen, the water along with endogenous secretions initiate the process of breaking down the tablet or capsule and dispersing the particles widely with continued dilution in the large volume of the stomach, and subsequent emptying into the duodenum with further dispersion and dilution in the large surface area of the small bowel. The chemical reaction that would take place within the confined space of a mortar under a pestle or other tablet-crushing device between 2 or more medications may be much greater than would occur when combining drugs orally. The applied force used in combining drugs, and the resultant increase in particle surface area exposed, could accelerate changes in molecular structure and formation of complexes with subsequent changes in physical and chemical properties.

When considering the various excipients also occupying that confined non-physiologic space, the potential for chemical reactions increases even further. Any new dosage form created by pulverizing and mixing together 2 or more medications (and their excipients) must still be expected to release each drug in a known and consistent manner following administration.[28] Unfortunately this information is not available for most medications and therefore cannot be recommended.

If planning to combine liquid drug products, knowledge of each solvent's physicochemical properties will be required to minimize disruption of drug solubility and stability. Therefore, combining one liquid drug product with another can be quite complex, altering the solubility products with each new additive in the mix. Again, the stability and compatibility of mixtures is impractical to predict. A balance between the needs of a fluid-restricted patient and the minimal volume required to dilute medications for enteral feeding tube administration must be realized.

D. Crushing and Diluting Medication

Some tablets are very small, very hard, or film-coated, making them difficult to crush. Enteric- and film-coatings do not crush well and tend to aggregate in clumps when diluted in water, thereby increasing the risk of clogging. Modified-release dosage forms should not be crushed for administration via feeding tubes[5,29]; this runs the risk of destroying the protective coating on a drug making it much less effective, or it may result in an excessive dose of the drug being released at one time, as occurred in a recent case fatality.[19] Instead, a more appropriate dosage form or therapeutic equivalent should be considered. Interfering with the integrity of intact liquid-filled gel capsules poses another level of complexity as it is difficult to assure accurate doses, so these are also best avoided in enterally fed patients. Injectable dosage forms are generally not considered appropriate for administration through a feeding tube because they are designed for a physiologic site with different characteristics.

Except for tablets that disperse easily when placed in an oral syringe with water, contents of an appropriate tablet or capsule should be crushed/pulverized to a fine powder before being dispersed, dissolved, or suspended in an appropriate volume of sterile water.[28] Advantages to the smaller particle size are improved suspension and decreased likelihood of obstructing a tube or its distal exit site(s). A disadvantage is increased risk of interaction with other medication particles found in the water. Flushing the enteral feeding tube between medications decreases the incidence of enteral tube occlusions.[30]

Commercially-available liquid formulations of a drug are not necessarily the best delivery option for a patient, depending in large part on the excipients present.[31] Liquid dosage forms often must be further diluted with sterile water prior to administration through an enteral feeding tube depending on viscosity and osmolarity. The viscosity and osmolality of the liquid dosage form, the internal diameter and length of the tube, and the location of the distal tip will all determine the final diluted volume of the liquid drug formulation. Suspensions tend to have much higher viscosity than solutions. Some suspensions are granular and may contain modified-release particles. The resistance to flow through an enteral feeding tube can be reduced through dilution but still may not be adequate to overcome a narrow tube. Dilution of each liquid medication prior to administration is associated with improved delivery of the drug dose to the distal end of the tube.[32,33] Liquid medication formulations can contain a number of excipients in addition to the drug and liquid. A number of poorly-absorbed sweeteners and stabilizers are used in liquid drug products which invariably increases their osmolality and potential to cause diarrhea. Electrolyte- containing liquids also contribute to high osmolality.

Pharmacists can provide necessary information on the physicochemical properties of a drug as well as interpretation of published stability and compatibility data. These can be applied to an individual patient's drug regimen and allow more informed decision-making by the entire healthcare team. A multidisciplinary intervention program involving guidelines, nurse education, and pharmacist recommendations has been shown to be effective in promoting the most appropriate drug administration practices and techniques, thereby reducing tube obstructions and drug errors. [21] The entire medication regimen may be simplified, any medication that is not immediately needed may be temporarily discontinued, and dosing schedules may be altered to avoid administration of medications at the same time.[5] Additionally, dosage forms or routes of administration may be altered or switched to a therapeutically similar product if not available by another dosage form or route.[5] The option of creating extemporaneous formulas for individual patients occurs particularly in pediatric practice settings.[34,35] Specific formulas may be found in the literature.[34-36] Aside from ensuring drug stability, the data should additionally reflect that the labeled drug dose can ultimately be delivered to the distal end of the enteral feeding tube without significant loss.

In the same way that nurses or pharmacists would not routinely mix different medications in the same intravenous bag or syringe without assuring drug stability and compatibility, the same should be said about the preparation of medication for administration through enteral feeding tubes. Best practices in drug administration through enteral feeding tubes will require dedicated time and resources. Implementing standardized protocols for drug administration through an enteral feeding tube should reduce inconsistencies in practice which may otherwise interfere with appropriate medication delivery. [16,31]

Practice Recommendations

1. Do not add medication directly to an enteral feeding formula. (B)
2. Avoid mixing together medications intended for administration through an enteral feeding tube given the risks for physical and chemical incompatibilities, tube obstruction, and altered therapeutic drug responses (ie, do not mix medications together, but do dilute them appropriately prior to administration). (B)
3. Each medication should be administered separately through an appropriate access. Liquid dosage forms should be used when available and if appropriate. Only immediate-release solid dosage forms may be substituted. Grind simple compressed tablets to a fine powder and mix with sterile water. Open hard gelatin capsules and mix powder with sterile water. (B)
4. Prior to administering medication, stop the feeding and flush the tube with at least 15 mL water. Dilute the solid or liquid medication as appropriate and administer using a clean oral syringe (≥ 30 mL in size). Flush the tube again with at least 15 mL water taking into account patient's volume status. Repeat with the next medication (if appropriate). Flush the tube one final time with at least 15 mL water. Note: Dilution/flush should be less for pediatric doses (minimum 50:50 volume) and at least 5 mL when fluid is not restricted. (A)
5. Restart the feeding in a timely manner to avoid compromising nutrition status. Only hold the feeding by 30 minutes or more when separation is indicated to avoid altered drug bioavailability. (A)
6. Use only oral/enteral syringes labeled with 'for oral use only' to measure and administer medication through an enteral feeding tube. (B)
7. Consult with an adult pharmacist or pediatric pharmacist for patients who receive medications co-administered with EN. (C)

References

1. Gora ML, Tschampel MM, Visconti JA. Consideration of drug therapy in patients receiving EN. *Nutr Clin Pract*. 1989;4:105-110.
2. Lehmann S, Barber JR. Giving medications by feeding tube: how to avoid problems. *Nursing*. 1991;21(11):58-61.
3. McConnell EA. Giving medications through an enteral feeding tube. *Nursing*. 1998;28:66.
4. Gilbar PJ. A guide to enteral drug administration in palliative care. *J Pain Symptom Manage*. 1999;17:197-207.
5. Beckwith MC, Feddema SS, Barton RG, Graves C. A guide to drug therapy in patients with enteral feeding tubes: dosage form selection and administration methods. *Hosp Pharm*. 2004;39:225-237.
6. Dickerson RN. Medication administration considerations for patients receiving enteral tube feedings. *Hosp Pharm*. 2004;39:84-89, 96.
7. Magnuson BL, Clifford TM, Hoskins LA, Bernard AC. Enteral nutrition and drug administration, interactions, and complications. *Nutr Clin Pract*. 2005;20:618-624.
8. Rollins C, Thomson C, Crane T. Pharmacotherapeutic issues. In: Rolandelli RH, Bankhead R, Boullata JI, Compher CW, eds. *Clinical Nutrition: Enteral and Tube Feeding*. 4th ed. Philadelphia, PA: Elsevier/Saunders;2005:291-305.
9. White R, Bradnam V. *Handbook of Drug Administration via Enteral Feeding Tubes*. London, UK: Pharmaceutical Press, 2007.
10. Leff RD, Roberts RJ. Enteral drug administration practices: report of a preliminary survey. *Pediatrics*. 1988;81:549-551.
11. Mateo MA. Nursing management of enteral tube feedings. *Heart Lung*. 1996;25:318-323.
12. Belknap DC, Seifert CF, Peterman M. Administration of medications through enteral feeding catheters. *Am J Crit Care*. 1997;6:382-392.
13. Schmieding NJ, Waldman RC. Nasogastric tube feeding and medication administration: a survey of nursing practices. *Gastroenterol Nurs*. 1997;20:118-124.
14. Seifert CF, Johnston BA. Drug administration through enteral feeding catheters [letter]. *Am J Health-Syst Pharm*. 2002;59:378-379.
15. Seifert CF, Johnston BA. A nationwide survey of long-term care facilities to determine the characteristics of medication administration

through enteral feeding catheters. *Nutr Clin Pract*. 2005;20: 354-362.

16. Boullata JI, Hudson LM, Spencer CT, Preston AM, Oakes BA. Drug administration by feeding tube: results of a practice-based survey [abstract]. *Nutr Clin Pract*. 2007;22:126. Abstract NP40.

17. Franceschinis E, Voinovich D, Grassi M, et al. Self-emulsifying pellets prepared by wet granulation in high-shear mixer: influence of formulation variables and preliminary study on the in vitro absorption. *Int J Pharm*. 2005;291:87-97.

18. Matteucci ME, Brettmann BK, Rogers TL, Elder EJ, Williams RO, Johnston KP. Design of potent amorphous drug nanoparticles for rapid generation of highly supersaturated media. *Molec Pharm*. 2007;4:782-793.

19. Schier JG, Howland MA, Hoffman RS, Nelson LS. Fatality from administration of labetalol and crushed extended-release nifedipine. *Ann Pharmacother*. 2003;37:1420-1423.

20. National Health Service. National patient safety agency: patient safety alert. www.npsa.nhs.uk. Accessed June 20, 2007.

21. van den Bemt PMLA, Cusell MBI, Overbeeke PW, et al. Quality improvement of oral medication administration in patients with enteral feeding tubes. *Qual Saf Health Care*. 2006;15:44-47.

22. Udeani GO, Bass J, Johnston TP. Compatibility of oral morphine sulfate solution with enteral feeding products. *Ann Pharmacother*. 1994;28:451-455.

23. Altman E, Cutie AJ. Compatibility of enteral products with commonly employed drug additives. *Nutr Supp Serv*. 1984;4(12):8,10,11,14.

24. Holtz L, Milton J, Sturek JK. Compatibility of medications with enteral feedings. *JPEN J Parenter Enteral Nutr*. 1987;11:183-186.

25. Burns PE, McCall L, Worsching R. Physical compatibility of enteral formulas with various common medications. *J Am Diet Assoc*. 1988;88:1094-1096.

26. Strom JG, Miller SW. Stability of drugs with enteral nutrient formulas. *Ann Pharmacother*. 1990;24:130-134.

27. Crowther RS, Bellanger R, Szauter KE. In vitro stability of ranitidine hydrochloride in enteral nutrient formulas. *Ann Pharmacother*. 1995;29:859-862.

28. United States Pharmacopoeial Convention. *United States Pharmacopoeia/National Formulary, edition 30/25*. Rockville, MD: United States Pharmacopoeial Convention, Inc., 2007.

29. Mitchell JF. *Oral Dosage Forms that Should Not Be Crushed or Chewed [wall chart]*. St. Louis, MO: Wolters Kluwer Health, Inc., 2007.

30. Scanlan M, Frisch S. Nasoduodenal feeding tubes: prevention of occlusion. *J Neurosci Nurs*. 1992;24:256-259.

31. Madigan SM, Courtney DE, MacCauley D. The solution was the problem. *Clin Nutr*. 2002;21:531-532.

32. Clark-Schmidt AL, Garnett WR, Lowe DR, Karnes HT. Loss of carbamazepine suspension through nasogastric feeding tubes. *Am J Hosp Pharm*. 1990;47:2034-2037.

33. Seifert CF, McGoodwin PL, Allen LV. Phenytoin recovery from percutaneous endoscopic gastrostomy Pezzer catheters after long-term in vitro administration. *JPEN J Parenter Enteral Nutr*. 1993;17: 370-374.

34. Trissel LA. *Trissel's Stability of Compounded Formulations*. 3rd ed. Washington, DC: APhA Publications, 2005.

35. Jew RK, Mullen RJ, Soo-Hoo W. *Children's Hospital of Philadelphia Extemporaneous Formulations*, 2nd ed. Bethesda, MD: American Society of Health-System Pharmacists, 2003.

36. Dansereau RJ, Crail DJ. Extemporaneous procedures for dissolving risendronate tablets for oral administration and for feeding tubes. *Ann Pharmacother*. 2005;39:63-67.

VIII. MONITORING ENTERAL NUTRITION ADMINISTRATION

Patients in all settings and age groups must be monitored while undergoing EN support. Monitoring the patient's tolerance to EN is essential in the delivery of EN.[1] This section will focus on refeeding syndrome and monitoring of gastric residual volumes (GRVs).

A. *Monitoring For Refeeding Syndrome*

Monitoring metabolic parameters prior to the initiation of enteral feedings and periodically during enteral therapy should be based on protocols and the patient's underlying disease state and length of therapy. Patients at high risk for refeeding syndrome and other metabolic complications should be followed closely, and depleted minerals and electrolytes should be replaced prior to initiating feedings. Prevention of refeeding syndrome is of utmost importance. This potentially lethal complication of refeeding the malnourished patient can result in potential metabolic and pathophysiological complications, which can affect the cardiac, respiratory, hepatic, and neuromuscular systems leading to clinical complications and even death. Stanga et al highlighted 7 cases of refeeding syndrome, and each case developed one or more features of refeeding syndrome including deficiencies and low plasma levels of potassium, phosphorous, magnesium, and thiamine combined with salt and water retention.[1] These responded to specific interventions. In most cases, these abnormalities could have been anticipated and prevented.[1]

Patients at risk of developing refeeding syndrome should be identified, and electrolyte abnormalities should be corrected prior to the initiation of nutrition support. Nutrition support should be initiated at approximately 25% of the estimated goal and advanced over 3-5 days to the goal rate. Serum electrolytes and vital signs should be monitored carefully after nutrition support is started.[2]

Practice Recommendations

1. Monitor fluid and electrolyte, and other metabolic parameters as needed based on the patient's clinical situation. (B)
2. Check metabolic and nutrition parameters, and correct depleted levels prior to the initiation of enteral feedings. (B)

References

1. Stanga Z, Brunner A, Leuenberger M, et al. Nutrition in clinical practice– the refeeding syndrome: illustrative cases and guidelines for prevention and treatment. *Eur J Clin Nutr*. 2008;62:687-694.

2. Kraft MD, Btaiche IF, Sacks GS. Review of the refeeding syndrome. *Nutr Clin Pract*. 2005;20:625-633.

B. *Monitoring Gastric Residual Volume (GRV)*

In most patient populations, aspiration can result in significant complications such as hypoxia and pneumonia.

Aspiration can be defined as the inhalation of material into the airway. In the critically-ill patient, this material may include nasopharyngeal secretions and bacteria as well as liquids, food, and gastric contents.[1] The risk factors for aspiration include sedation, supine patient positioning, the presence and size of a nasogastric tube, malposition of the feeding tube, mechanical ventilation, vomiting, bolus feeding delivery methods, the presence of a high-risk disease or injury, poor oral health, nursing staffing level, and advanced patient age.[2]

Measurement of GRV

Methodologies to Detect Aspiration. Measurement of GRV is one technique used to prevent aspiration. Research regarding the efficacy of this technique has provided conflicting results. That is, no adequately powered studies have, to date, demonstrated a relationship between aspiration pneumonia and GRV.[3] In addition, no adequately powered studies have demonstrated that elevated GRVs are reliable markers for increased risk of aspiration pneumonia.

GRV cannot be correlated with pneumonia (after the initiation of enteral feedings), ICU mortality, or hospital mortality. Studies suggest that "the elevated residual volumes by themselves have little clinical meaning and that only when combined with vomiting, sepsis, sedation, or the need for pressor agents does the correlation with worsening patient outcome emerge."[4]

Elevated and increasing residual volumes may be a symptom of another underlying problem manifesting itself as delayed gastric emptying. If serial measurements reveal a change in GRV, other potential causes must be investigated instead of simply holding the enteral feedings.[4] In the past, blue food coloring was added to enteral formula to attempt to detect aspiration of gastric feedings. This practice lacked standardization in the amount of food coloring added per volume of formula, was implicated as the cause of enteral formula contamination due to the use of multidose bottles, and interfered with guiac testing. The practice is no longer utilized as a result of the FDA Public Health Advisory in September 2003 describing patient fatalities from hypotension, and metabolic acidosis as well as blue discoloration of the skin, organs, and body fluids associated with FD & C Blue #1 dye.[5] Further, the blue dye method has been show to be ineffective in detecting aspiration.[6] The use of glucose oxidase strips to test tracheal secretions for glucose from enteral formula has also been found to be less ideal because glucose was found in tracheal secretions of unfed patients.[7]

Interpreting the Relationship Between Aspiration and GRVs. Research regarding the association between aspiration and GRV has been hampered by 2 problems: (a) use of unreliable methods to detect aspiration and (b) inaccurate measurement of GRVs. The practice of measuring GRVs is poorly defined. Standardization of how to measure GRVs, when to measure them, definition of a high GRV, and what an elevated GRV actually implies, remains controversial and confusing to clinicians. Using a syringe to withdraw gastric contents will not consistently result in aspiration of the total volume of fluid present in the stomach.[8] Many variables can affect bedside GRV measurements. These include the type of feeding tube used when performing the measurement, the position of the feeding tube's ports in the gastric antrum, and the patient's position. Large GRVs are detected more often when large-bore sump tubes are used for the measurement. Using small-bore tubes can underestimate the GRV. For example, a study of 645 dual measurements made by using small-bore feeding tubes and large-bore sump tubes concurrently present in the stomach of 62 critically ill patients indicated that large GRVs were detected 2-3 times more often with large-bore sump tubes.[9] Regardless of the size of the feeding tube used, ports positioned at the gastroesophageal junction will result in a negligible GRV in most cases.[10] Patient positioning may be of greater significance in infants than in adults, but the assumption that it could affect the amount of GRV obtained remains reasonable.[8,10] In a study of 10 critically ill patients, McClave et al found no difference in GRVs obtained when the patients were supine vs in a right lateral decubitus position[30]; similarly, van der Voort & Zandstra reported that GRVs were similar when 19 critically ill patients were prone as opposed to supine.[11] In contrast, Malhotra et al reported significantly higher GRVs from 27 preterm babies when they were supine as opposed to prone.[12]

It has been suggested that gastric residuals be checked more frequently when enteral feedings are first initiated. Numerous studies have documented evaluation of GRV from every 4 to every 12 hours depending on when the feedings were initiated and previous GRV obtained.[10]

The acceptable ranges for GRVs can also vary significantly. Much research has been conducted to define this elusive number, but none have been able to identify the precise level of GRV which places the patient at greatest risk for obvious GI intolerance. There is no clarification of whether the GRV represents the value below which is suggested to advance feedings or the threshold value at which feedings should be discontinued due to potential GI intolerance. One recent literature search suggests that "accepting an isolated gastric residual volume of 250 mL, and evaluating the clinical situation with two or more consecutive volumes of 250 mL before stopping/holding the feeding is associated with greater formula delivery."[3] Others suggest, as a result of the ambiguity of GRV, that enteral feedings should not be stopped for residual volumes < 400-500 mL particularly in the absence of

other signs and symptoms of GI intolerance including emesis, distention, or constipation.[4] Abrupt cessation of enteral feeding upon overt regurgitation or aspiration is appropriate, however. GRV of 200-500 mL should stimulate a step-wise approach to assess the potential of GI intolerance. If the GRV is < 200 mL, assessment of aspiration risk should continue.[13] The Canadian Clinical Practice Guidelines concur that in critically ill, mechanically ventilated patients a higher GRV of 250mL or more should be accepted to improve the delivery of EN in this patient population.[14] In a prospective study of 206 patients fed gastrically, over 3000 tracheal secretions obtained during suctioning were analyzed for pepsin. The pepsin-positive tracheal secretion served as a proxy for aspiration of gastric contents. No direct relationship was found between aspiration and GRVs; that is, patients aspirated even when high GRVs were absent. However, they aspirated significantly more often when high GRVs were present. When GRVs were entered into a regression model with other risk factors for aspiration (including low level of consciousness, low head-of-bed (HOB) elevation, sedation, vomiting, and severity of illness), the following values were found to be significant: 2 or more > 200 mL and 1 or more > 250 mL.[15,16]

Examples of Studies that Support the Use of GRV Measurements. Metheny's prospective study of 206 critically ill, mechanically ventilated patients described the association between GRVs and aspiration of gastric contents. The authors recommended that serial GRV measurements be made when gastric feedings are administered, and that large-diameter sump tubes be used during the first few days of tube feeding to increase the probability of identifying high GRVs.[15] Metheny et al also compared GRVs in 89 critically ill patients identified as frequent aspirators to GRVs in 119 critically ill patients identified as infrequent aspirators. (Aspiration was said to be present if pepsin was present in suctioned tracheobronchial secretions; frequent aspirators were defined as those patients having 40% or more of their secretions positive for pepsin.) When GRVs were entered into a logistic regression equation with other risk factors for aspiration (such as a low level of consciousness, vomiting, and a low HOB elevation), the following GRV categories were found to occur significantly more often in the frequent aspiration group: 2 or more GRVs ≥ 200 ml, and 1 or more GRVs ≥ 250 ml.[17]

Mayer et al measured GRVs in 23 critically ill children (median age 5.8 years).[18] Patients were said to be feed-intolerant if the GRV was > 125% of the hourly feed volume measured 4 hours after a feed challenge. Using 3 objective measures of gastric emptying calculated from a 6-hour paracetamol absorption test, the investigators classified 8 children as feed intolerant and 15 as feed tolerant. Those who were feed intolerant had delayed gastric emptying associated with high GRVs (the median GRV was 321% of the hourly feed volume in the feed intolerant group and 4% in the feed tolerant group). The investigators concluded that the use of GRVs to define feed intolerance is justified in critically ill children.

Mentec et al observed 153 critically ill patients for upper GI intolerance (defined as 1 or more GRVs > 500 mL, 2 consecutive GRVs between 150 and 500 mL, or vomiting) and clinical signs of pneumonia.[19] All patients had 14 Fr feeding tubes, which perhaps explains why 13% of the patients were found to have 1 or more GRVs > 500 mL and 19% were found to have 2 or more consecutive GRVs between 150 and 500 mL. The median time of development of the high GRVs was 2 days, which supports the belief that high GRVs are more likely to occur in the early days of feeding. Over one-fourth (26%) of the patients experienced vomiting. While aspiration was not measured in the study, clinical signs of pneumonia were observed. Patients identified as having upper GI intolerance had a significantly higher incidence of pneumonia than did those without upper GI intolerance (43% vs 24%, respectively, P=.01).

Examples of Studies That Do Not Support the Use of GRV Measurements. A study by Cohen does not support the belief that GRV measurement represents gastric emptying. A paracetamol absorption test was performed on 32 critically ill patients who had a GRV more than twice the hourly administration rate or one that was >150 mL. According to their findings, 8 patients had normal gastric emptying and 24 had abnormal gastric emptying; yet GRVs were similarly elevated in both groups.[20] The practice of GRV measurement may, in fact, impede nutrition support. Administration times are decreased and the incidence of feeding tube clogging is increased.[21] In one study, the incidence of regurgitation was higher numerically in a group of patients with a GRV of 200 mL (35.0% vs 27.8%, P=NS) when compared to a group of patients with a GRV of 400 mL. In this study, the incidence of aspiration was no different between the 2 groups.[22]

McClave studied 40 critically ill, mechanically ventilated patients over a period of 3 days to determine the relationship between aspiration and elevated GRVs.[4] To facilitate detection of aspiration, 0.48 mL of yellow microscopic colorimetric microspheres were added to each 1500 mL bag of enteral formula. A total of 587 tracheal secretions were collected in Luken's specimen traps and examined fluoroscopically in a research laboratory for the presence of the colorimetric microspheres; aspiration was said to be present if a yellow color was detected in the secretions. Three-fourths of the patients had at least 1 episode of aspiration; the mean incidence per patient was 22.1% (range 0%-94%). In addition, 531 secretions were collected from the oropharynx to observe for colorimetric spheres (serving as

a proxy for regurgitation of gastric contents). Of the 40 patients, 34 had at least 1 episode of regurgitation; however, no relationship was found between these events and aspiration. A total of 1,118 GRV measurements were made; of these, 69 (6.2%) were > 150 mL, 54 (4.8%) were > 200 mL, and 17 (1.5%) were > 400 mL. The incidence of aspiration did not vary significantly according to GRVs, causing the authors to conclude that GRVs are a poor predictor of aspiration. The authors recommended that feeds not be stopped for residual volumes below 400-500 mL, in the absence of other signs of intolerance.[4]

Elpern et al conducted a descriptive study of 39 critically ill patients receiving gastric feedings (for a total of 276 feeding days). GRVs were measured every 8 hours; GRVs exceeded 150 ml in 28 measurements in 11 of the patients (28%). Aspiration was defined as being present when formula was visible in suctioned tracheal secretions. Of the 39 patients, only 4 met the criterion for aspiration (1% of feeding days). None of the instances of feeding were associated with vomiting.[23]

Use of Prokinetic Agents as an Algorithmic Approach to Feeding Intolerance. When nursing practices were reviewed, the practice of GRV measurement was identified as a significant contributor to underfeeding with EN. GRVs were frequently cited as a reason to delay feeding and as a method of assessing enteral feeding tolerance.[24] The most common responses to elevated GRVs were initiation of prokinetic agents and decreasing the feeding rate. Significantly less frequent responses were evaluation of feeding tube placement and changing patient position.[24] Pinella randomized patients to either 150 mL GRV threshold value with optional prokinetic therapy, or to 250 mL GRV value with mandatory prokinetic therapy. There was no difference in the incidence of vomiting or intolerance defined as increased GRV or persistent diarrhea.[25]

In a randomized, controlled, double-blind trial comparing the efficacy of combination therapy with erythromycin and metaclopramide to erythromycin alone, the investigators defined feeding intolerance as 1) 2 or more GRVs of ≥ 250 mL within the first 24 hours, or 2) any 6-hour GRV ≥250 mL thereafter while receiving ≥ 40 mL/hour of enteral feedings. They used the 250 mL-threshold for the GRV as an indication for therapy rather than cessation of enteral feeds. They found that the combination therapy is more effective in improving the outcomes of enteral feedings in critical illness.[26]

The response to elevated GRVs should be carefully evaluated in the clinical setting. Low residual volumes should not result in decreased vigilance to signs and symptoms of GI intolerance. Similarly, high GRVs should not automatically result in holding of the enteral feedings. High-risk patient populations should be identified based on diagnosis, clinical factors, and physical findings. If GRVs are regularly measured, trends of increasing volumes should be identified as a potential sign of GI intolerance (distention, emesis, constipation), clinical signs of sepsis, level of sedation, and influence of pressor agents.[2] Furthermore, efforts to minimize aspiration associated with delayed gastric emptying should be emphasized. In critically ill, mechanically ventilated patients who experience feeding intolerance such as high GRVs or emesis, metaclopromide should be considered as a motility agent. Hyperglycemia can affect gastric emptying as well. Although hyperglycemia has not been specifically demonstrated to delay gastric emptying in critically ill patients, it has been shown to have that effect in healthy individuals and in people with diabetes.[26] Hyperglycemia inhibits gastric emptying "by reducing vagal efferent activity and inhibition of the release of nitric oxide from the myenteric plexus." Prokinetic drugs in this patient population may adversely affect gastric emptying.[27]

While GRVs are typically measured from gastric feeding tubes, some facilities also measure residual volumes from nasally or orally placed small bowel feeding tubes. The rationale for this is that it is a useful technique to detect inadvertent upward dislocation of the tip of the feeding tube into the stomach. That is, residual volumes from the small bowel are typically quite low (such as < 10); a sudden sharp increase in residual volume (such as 100 mL or more) is a good indication that the tube has dislocated into the stomach.[28]

Practice Recommendations

1. Evaluate all enterally fed patients for risk of aspiration. (A)
2. Assure that the feeding tube is in the proper position before initiating feedings. (A)
3. Keep the head of the bed elevated at 30º-45º at all times during the administration of enteral feedings. (A)
4. When possible, use a large-bore sump tube for the first 1-2 days of enteral feeding and evaluate gastric residuals using at least a 60 mL syringe. (A)
5. Check gastric residuals every 4 hours during the first 48 hours for gastrically fed patients. After enteral feeding goal rate is achieved and/or the sump tube is replaced with a soft, small-bore feeding tube, gastric residual monitoring may be decreased to every 6-8 hours in non-critically ill patients. (C) However, every-4-hour measurements are prudent in critically ill patients. (B)
6. If the GRV is ≥ 250 mL after a second gastric residual check, a promotility agent should be considered in adult patients. (A)

7. A GRV >500 mL should result in holding EN and reassessing patient tolerance by use of an established algorithm including physical assessment, GI assessment, evaluation of glycemic control, minimization of sedation, and consideration of promotility agent use, if not already prescribed. (B)

8. Consideration of a feeding tube placed below the ligament of Treitz when GRVs are consistently measured at > 500 mL. (B)

9. In acutely ill pediatric patients receiving continuous drip feedings, the GRVs may be checked every 4 hours and held if the volume is greater than or equal to the hourly rate. If feedings are bolus, then the GRV may be checked before the next feeding and held if the residual volume is more than half of the previous feeding volume. (C)

References

1. Zaloga GP. Aspiration-related illnesses: definitions and diagnosis. *JPEN J Parenter Enteral Nutr.* 2002;26(6 Suppl):S2-S7.

2. Metheny NA. Risk factors for aspiration. *JPEN J Parenter Enteral Nutr.* 2002;26(6 Suppl):S26-S31.

3. Kattelmann KK, Hise M, Russell M, Charney P, Stokes M, Compher C. Preliminary evidence for a medical nutrition therapy protocol: enteral feedings for critically ill patients. *J Amer Dietetic Assoc.* 2006;106:1226-1241.

4. McClave SA, Lukan JE, Stefater JA, et al. Poor validity of residual volume as a marker for risk of aspiration in critically ill patients. *Crit Care Med.* 2005;33:324-330.

5. FDA Public Health Advisory September 29, 2003. http://www.cfsan.fda.gov/%7edms/cpl-ltr2html. Accessed October 3, 2007.

6. Metheny NA, Dahms TE, Stewart BJ, et al. Efficacy of dye-stained enteral formula in detecting pulmonary aspiration. *Chest.* 2002;122:276-281.

7. Metheny NA, Dahms TE, Stewart BJ, Stone KS, Frank PA, Clouse RE. Verification of inefficacy of the glucose method in detecting aspiration associated with tube feedings. *MEDSURG Nursing.* 2005;14:112-121.

8. Metheny NA. Preventing respiratory complications of tube feedings: evidence-based practice. *Am J Crit Care.* 2006;15:360-369.

9. Metheny NA, Stewart J, Nuetzel G, Oliver D, Clouse RE. Effect of feeding-tube properties on residual volume measurements in tube-fed patients. *JPEN J Parenter Enteral Nutr.* 2005;29:192-197.

10. McClave SA, Snider HL, Lowen CC, et al. Use of residual volume as a marker for enteral feeding intolerance: prospective blinded comparison with physical examination and radiographic findings. *JPEN J Parenter Enteral Nutr.*1992;16:99-105.

11. van der Voort PH, Zandstra DF. Enteral feeding in the critically ill: comparison between the supine and prone positions: a prospective crossover study in mechanically ventilated patients. *Crit Care.* 2001;5:216-220.

12. Malhotra AK, Deorari AK, Paul VK, Bagga A, Singh M. Gastric residuals in preterm babies. *J Trop Pediatr.* 1992;38:262-264.

13. McClave SA, Demeo MT, DeLegge MH, et al. North American Summit on Aspiration in the Critically Ill Patient: consensus statement. *JPEN J Parenter Enteral Nutr.* 2002;26(6 Suppl):S80-S85.

14. Heyland DK, Dhaliwal R, Drover JW, Gramlich L, Dodek P; Canadian Critical Care Clinical Practice Guidelines Committee. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. *JPEN J Parenter Enteral Nutr.* 2003;27:355-373.

15. Metheny NA, Schallom L, Oliver DA, Clouse RE. Gastric residual volume and aspiration in critically ill patients receiving gastric feedings. *Am J Crit Care.* 2008;17:512-519.

16. Metheny NA, Dahms TE, Chang YH, Stewart BJ, Frank PA, Clouse RE. Detection of pepsin in tracheal secretions after forced small-volume aspirations of gastric juice. *JPEN J Parenter Enteral Nutr.* 2004;28:79-84.

17. Metheny NA. Residual volume measurement should be retained in enteral feeding protocols. *Am J Crit Care.* 2008;17:62-64.

18. Mayer AP, Durward A, Turner C, et al. Amylin is associated with delayed gastric emptying in critically ill children. *Intens Care Med.* 2002;28:336-340.

19. Mentec H, Dupont H, Bocchetti M, et. al. Upper digestive intolerance during enteral nutrition in critically ill patients: frequency, risk factors, and complications. *Crit Care Med.* 2001;29:1955-1961.

20. Cohen J, Aharon A, Singer P. The paracetamol absorption test: a useful addition to the enteral nutrition algorithm? *Clin Nutr.* 2000;19:213-215.

21. McClave SA, Dryden GW. Critical care nutrition: reducing risk of aspiration. *Semin Gastrointest Dis.* 2003;14:2-10.

22. Lukan JK, McClave SA, Stefater AJ, et al. Poor validity of residual volumes as a marker for risk of aspiration. *Crit Care Med.* 2005;33(2):324-330.

23. Elpern EH, Stutz L, Peterson S, Gurka DP, Skipper A. Outcomes associated with enteral tube feedings in a medical intensive care unit. *Am J Crit Care.* 2004;13:221-227.

24. Marshall AP, West SH. Enteral feeding in the critically ill: are nursing practices contributing to hypocaloric feeding? *Int Crit Care Nurs.* 2006;22:95-105.

25. Pinella JC, Samphire J, Arnold C, Liu L, Thiessen B. Comparison of gastrointestinal tolerance to two enteral feeding protocols in critically ill patients: a prospective, randomized, controlled trial. *JPEN J Parenter Enteral Nutr.* 2001;25:81-86.

26. Nguyen NQ, Chapman M, Fraser RJ, Bryant LK, Burgstad C, Holloway RH. Prokinetic therapy for feed intolerance in critical illness: one drug or two? *Crit Care Med*;2007;35:1-7.

27. Chapman MJ, Nguyen NQ, Fraser RJL. Gastrointestinal motility and prokinetics in the critically ill. *Curr Opin Crit Care.* 2007;13:187-194.

28. Fruhwald S, Holzer P, Metzler H. Intestinal motility disturbances in intensive care patients pathogenesis and clinical impact. *Intens Care Med.* 2007;33:36-44.

29. Metheny N, Schnelker R, McGinnis J, et al. Indicators of tubesite during feedings. *J Neuro Nurs.* 2005;37:320-325.

IX. *Summary*

The complexity of EN feedings cannot be underestimated. All healthcare professionals should be vigilant in continous surveillance of high risk practices, products and systems as they relate to the enterally fed patient. Recognition of ordering, administration, and monitoring steps of EN delivery which may increase risk of complications to the enterally fed patient is essential.

While the intent of this document was to provide the clinician with sufficient evidence to optimally provide EN, it was evident prior to initiating this project that there was a lack of evidence-based research to support several

practice guidelines. The reader may find that some practice recommendations, such as the ordering and labeling of enteral products, are based on consensuses of expert opinion. On the other hand, the evidence is much more conclusive in water and enteral formula safety, patient positioning, and medication administration.

Some general conclusions, however, can be made. There is the need for further research and documentation of effectiveness of these practice guidelines and how they effect patient outcomes. Also, there is a need for a multidisciplinary approach in providing EN to such a diverse patient population across various settings, whether as a formal nutrition support service or as teams of caregivers coming together within the practice setting.