ENTERAL NUTRITION: PROCEDURES AND GUIDELINES

Steps in performing tube feeding

1. Check if the formula is the appropriate one for the patient
    a. Check the name, room number
    b. Check the content or formula name
    c. Determine the volume and the rate of delivery
    d. Check time of preparation and expiration (as determined by protocol)
2. Check the tube placement:
    a. Go to EN Specific Procedures and Guidelines #2: Checking placement
3. Check the access passage areas
    a. Go to EN Specific Procedures and Guidelines #3: Checking tube passages
4. Once sure of the tube placement and site of entry, deliver the formula:
    a. Go to EN Specific Procedures and Guidelines #4: Delivery Method
    b. Go to EN Specific Procedures and Guidelines #5: Initiation of Feeding
    c. Flushing: Go to EN Specific Procedures and Guidelines #6: Flushing
    d. Gastric residual: Go to EN Specific Procedures and Guideline #7: Gastric residuals
    e. Aspiration: Go to EN Specific Procedures and Guideline #8: Aspiration prevention, detection, and management
5. Tube feeding methods:
    a. Go to EN Specific Procedures and Guideline #9: PEG insertion, maintenance, and replacement
    b. Go to EN Specific Procedures and Guideline #10: Nasoenteric, insertion and maintenance
    c. Go to EN Specific Procedures and Guideline #11: Jejunostomy, insertion and maintenance

Enteral Nutrition Specific Procedures and Guidelines #2: Nutrient Delivery, Checking Tube Placement

Main Reference: (1)

1. **Principles:**
   a. Feeding tubes require regular assessment and monitoring to <u>ensure continued correct placement.</u>
   b. When problems arise, early intervention is key to maintaining enteral access.
2. **Oro- or nasogastric and oro- or nasoenteric tubes:**
   a. Checking placement.
       i. Placement of the tube should be checked every 8 hours during continuous feedings and before each intermittent feeding.
       ii. Verification methods include:
           1. X-ray,
           2. Marking the tube where it exits the patient and measuring it,
           3. Checking the pH of the aspirate,
           4. Observing the color of the aspirate, and
           5. Auscultation**. (2,12) – Documentation of tube placement**
               a. Auscultation of air insufflation over the midepigastrium has been used to document passage of the tube into the stomach. Caution is needed because inadvertent pulmonary placement can result in bronchial sounds being transmitted through the diaphragm, simulating gastric placement.
               b. Auscultation alone should not be used to confirm tube placement. However, a positive air insufflation test combined with aspiration of gastric contents is a fairly reliable predictor of successful placement.
               c. X-ray verification of tube placement remains the gold standard; it also shows whether the tube is in the preferred antral position or is curled.
           6. Any time tube misplacement or displacement is suspected, a roentgenogram should be taken.
3. **Gastrostomy and jejunostomy tubes.**
   a. The care of these tubes includes maintaining patency, protecting the skin at the exit site, and preserving proper placement and integrity of the tube. **(3,4-6)**
   b. **Checking placement**
       a) For traditional gastrostomy and jejunostomy tubes,
           1. Measure the length of the tube protruding from the abdomen and document the external length in the medical record daily.
           2. If no external markings are on the tube, an indelible mark can be made on the tube and used to monitor position.**(7)**
           3. **Gastrostomy tubes with internal bumpers should be pushed in several centimeters and the tube rotated 360°.**
           4. **In pediatric patients, the tube is rotated 360° but not pushed in.**
           5. **If this is not possible, a buried bumper may be developing, and the patient will need to be referred to an experienced health care provider for further care and ultimate replacement.(8, 9)**
       b) LPDs (Low Profile Device) should also be monitored daily.
           1. The tube should have some movement (ie, you should be able to slide the tube in and out about 0.5 inch).

       2. An LPD should be gently pushed in approximately 0.5 inch and rotated 360° daily to prevent the balloon or internal bumper from adhering to the gastric wall.

       3. For infants and small children, the LPD should be pushed in approximately one-eighth inch and rotated.

a) Dressings.

     a. Dressings are commonly used for 48 hours after initial placement when the tract is considered an open wound,

     b. when the tract is soiled, or

     c. when the patient is at high risk for inadvertent tube removal.

b) Tube stabilization. Stabilizing a tube can reduce the risk of tube displacement, pain, and enlargement of the tract.

     a. Sutures or T- fasteners may be present to secure gastrostomy or jejunostomy tubes. If a gastrostomy tube has anchoring sutures or T- fasteners, check with the physician about possible removal when the tract is healed.

     b. Most jejunostomy tubes require a secure suture at all times.

     c. Anchoring devices can secure the tube and protect the skin from the effects of frequent dressing changes.**(10,11)**

        i. Anchoring devices typically last twice as long as tape.

        ii. Examples of anchoring devices are Hollister Drain/Tube Attachment Device (Hollister, Libertyville, IL), Cath-Secure (MC Johnson, Naples, FL), and Flexi-Trak (ConvaTec, Skillman, NJ).

        iii. If adhesive tube holders are used, the exit site must be cleaned around the tube daily and as needed to prevent accumulation of tissue debris.

     d. If the tube has a balloon, check the water in the balloon at least once a week.

References:

1. Kirby DF, Opilla M. Implementation of enteral feedings, Enteral nutrition implementation and management. In Merritt R, Editor in Chief. The A.S.P.E.N. Nutrition Support Practice Manual 2nd edition. A.S.P.E.N. 8630 Fenton St, Suite 412; Silver Spring, MD; 2005; 59.
2. Metheny N. Verification of feeding tube placement. In: Silver E, Gussler JD, eds. *Current Issues in Enteral Nutrition Support: Report of the First Ross Conference on Enteral Devices.* Columbus, OH: Ross Products Division, Abbott Laboratories; 1996:34–41.
3. Townsend LC. Practical considerations of the gastrostomy button. *Gastroenterol Nurs.* 1991;14:18–26.
4. Teasley-Strausburg KM, Lehmann S. Guidelines for administration of nutrition support and nutrition support service forms. In: Teasley-Strausburg KM, Cerra FB, Lehmann S, Shronts EP, eds. *Nutrition Support Handbook: A Compendium of Products with Guidelines for Usage.* Cincinnati, OH: Harvey Whitney Books; 1992:321–330.
5. Eisenberg PG. Gastrostomy and jejunostomy tubes. *RN.* 1994;57:54–59.
6. Broscious SK. Preventing complications of PEG tubes. *Dimens Crit Care Nurs.* 1995; 14: 37–41.
7. Iber FL, Livak A, Patel M. Importance of fungus colonization in failure of silicone rubber percutaneous gastrostomy tubes (PEGs). *Dig Dis Sci.* 1996; 41: 226–231.
8. Kirby DF, DeLegge MH, Fleming CR. American Gastroenterological Association technical review of tube feeding for enteral nutrition. *Gastroenterology.* 1995; 108: 1282–1301.

9. Boyd JW, DeLegge MH, Shamburek RD, Kirby DF. The buried bumper syndrome: a review of the literature and a new technique for safe, endoscopic PEG removal. *Gastrointest Endosc.* 1995; 41: 508–11.
10. Blaylock B, Clayton G, Milnes M, Foster C. A catheter anchoring device. *Ostomy Wound Management.* 1993; 39: 36–43.
11. Wilson RE. Case study: a system for stabilizing percutaneous tubes. *Ostomy Wound Management.* 1994; 40: 44–9.
12. Metheny N, McSweeney M, Wehrle MA, Wiesema L. Effectiveness of the auscultatory method in predicting feeding tube location. *Nurs Res.* 1990;39:262–267.

Enteral Nutrition Specific Procedures and Guidelines #3: Nutrient Delivery, Checking Tube Passages
Main Reference (1)

1. **Principles:**
    a. Care of Feeding Tubes: Feeding tubes require regular assessment and monitoring to:
        i. To ensure continued correct placement and
        ii. To avoid complications such as skin breakdown or infection.
    b. When problems arise, early intervention is key to maintaining enteral access.
2. **Oro- or nasogastric and oro- or nasoenteric tubes:**
    a. Care of orally or nasally inserted tubes requires vigilance in checking placement, protecting the mucosal surfaces, and flushing routinely.
    b. Protecting the mucosal surfaces.**(2)** Mucosal irritation of the nasopharynx may occur anywhere along the path of the feeding tube.
        a) Inspect the nares, mouth, and pharynx daily for skin irritation, ulceration, pressure necrosis, and lesions.
        b) Clean the nares daily with warm water or saline and keep mucous membranes moist with petroleum jelly. If the nares are crusty, clean them with dilute hydrogen peroxide and then moisturize.
        c) Change the fixator device or tape on the nose or mouth as needed if loose or soiled and at least every 3 to 5 days. Incorrect taping can lead to pressure necrosis.
        d) Maintain good oral hygiene.
            1. Even when patients are not eating, their teeth should be brushed at least twice a day.
            2. If gum inflammation is present, the patient may benefit from an oral antiseptic rinse (eg chlorhexidene gluconate).
            3. Tube-fed patients receiving antibiotics may benefit from an oral antifungal formulation (eg, nystatin 500, 000 units applied to the oral cavity 4 times a day) to help prevent overgrowth of fungus.
3. **Gastrostomy and jejunostomy tubes.**
    a. The care of these tubes includes maintaining patency, protecting the skin at the exit site, and preserving proper placement and integrity of the tube.**(3,2,4-5)**
    b. Care of exit site and tube
        i. Exit site assessment.
            1. Check for erythema (initially, a small amount of serosanguineous drainage can be expected), edema, warmth, and exudate.
            2. Foul-smelling drainage is a sign of infection.
        ii. Also monitor for:
            1. Skin breakdown,
            2. Pressure necrosis,

3. Hypergranulation (keep site dry),
4. Gastric leakage (identify the cause; do not just try to repair),
5. Displacement (tube movement >1 inch for adults and >0.25 inches for infants and small children), and
6. Enlargement of the stoma tract (stabilize tube; avoid excessive tube movement.

c. Skin care.
   i. When the tube tract is new and has drainage or crusting, clean the exit site with diluted hydrogen peroxide.
   ii. After the tract is healed, clean the site daily with soap and water.
   iii. Clean carefully under external bumpers or disks to keep dry and clean and to check for excessive pressure.
   iv. External bumpers and disks should be just above skin level and not taut against the skin.
   v. Dressings are commonly placed:
      1. For 48 hours after initial placement when the tract is considered an open wound,
      2. When the tract is soiled, or
      3. When the patient is at high risk for inadvertent tube removal.
   vi. Patients with enteral devices or tubes may shower or bathe according to the directions of their health care provider. If a bumper or disk is present, the skin underneath it should be dried carefully to prevent maceration from trapped moisture.(6,3)

d. Problem skin care. The most crucial step in preventing or minimizing skin problems is early identification and removal of the problem.
   vii. Hypergranulation (everted mucosa)
      1. typically develops when the exit site remains moist or the tube is not stabilized and moves in the stoma.
      2. Keeping the site dry and stabilizing the tube may help prevent this problem.
      3. Excessive growth (>0.25 inch for adults; >2 mm for pediatric patients) of granulation tissue can be eliminated around the tube by carefully cauterizing with silver nitrate sticks.(3,7)
   i. For other skin problems, the cause should be identified and removed, if possible. Certain liquid or solid barriers can be used to protect the skin as it heals.(8,9)
   ii. Minor skin breakdown. If there is slight irritation, place a protective skin barrier (eg, zinc oxide).
   iii. Skin that is already denuded.
      1. Dry the skin well and dust with a powder (eg, Stomadhesive [ConvaTec, Skillman, NJ]).
      2. Then apply a waterproof ointment (eg, Critic Aid Skin Paste [Coloplast, Marietta, GA]).
      3. If the patient is not receiving an acid-suppressing medication (eg, histamine-2 receptor antagonist [eg, ranitidine, famotidine] or a proton pump inhibitor [eg, omeprazole]), then this may be necessary to decrease the risk of acid damage to the skin.
   iv. Hydrocolloids and pectin wafers (eg, Stomadhesive, DuoDERM [ConvaTec, Skillman, NJ]) can also be used to prevent skin breakdown at the exit site and at sites distant from the exit site. These should be placed on clean, dry skin and changed when soiled to prevent trapped moisture.

References:

1. Kirby DF, Opilla M. Implementation of enteral feedings, Enteral nutrition implementation and management. In Merritt R, Editor in Chief. The A.S.P.E.N. Nutrition Support Practice Manual 2nd edition. A.S.P.E.N. 8630 Fenton St, Suite 412; Silver Spring, MD; 2005; 59.
2. Teasley-Strausburg KM, Lehmann S. Guidelines for administration of nutrition support and nutrition support service forms. In: Teasley-Strausburg KM, Cerra FB, Lehmann S, Shronts EP, eds. *Nutrition Support Handbook: A Compendium of Products with Guidelines for Usage.* Cincinnati, OH: Harvey Whitney Books; 1992:321–330.
3. Townsend LC. Practical considerations of the gastrostomy button. *Gastroenterol Nurs.* 1991;14:18–26.
4. Eisenberg PG. Gastrostomy and jejunostomy tubes. *RN.* 1994;57:54–59.
5. Broscious SK. Preventing complications of PEG tubes. *Dimens Crit Care Nurs.* 1995;14:37–41.
6. Faller NA, Lawrence KG, Ferraro CB. Gastrostomy replacement feeding tube: the long and short of it. *Ostomy Wound Management.* 1993;39:26–33.
7. Kaufman MW, Faller NA, Lawrence KG. Low profile gastrostomy devices. *Gastroenterol Nurs.* 1995;18:171–176.
8. Maklebust J. Using wound care products to promote a healing environment. *Crit Care Nurs Clin N Am.* 1996;8:141–158.
9. Hagelgans NA, Janusz HB. Pediatric skin care issues for the home care nurse: part 2. *Pediatr Nurs.* 1994;20:69–75.

Enteral Nutrition Specific Procedures and Guidelines #4: Nutrient Delivery, Delivery Methods
Main Reference: (1)

Delivery methods
1. Gravity controlled
   A.   This manually controlled method of infusing formula is used almost exclusively for gastric feedings.
      1.   A specific volume of formulation is hung in a plastic feeding bag or rigid plastic container with tubing on an intravenous (IV) pole above the insertion site of the feeding tube.
      2.   The tubing is fitted with a roller clamp, to control the infusion rate of the formulation, and a connector, to permit attachment to the patient's feeding tube.
      3.   Feedings may be provided over several minutes to hours depending on patient tolerance.
      4.   A drawback to this method is that the formula infusion rate can fluctuate during the feeding as a result of positional changes or increases in gastric pressure.**(2)**
      5.   Gravity-controlled feedings are indicated only for neurologically intact patients who can reliably protect their airways.
      6.   Most often this method is used with ambulatory patients (ie, in-home care or long-term care facilities).
   B.   Continuous gravity feedings.

1. These feedings are provided over 24 hours and can be accomplished with the use of high-quality gravity-feeding equipment and a roller clamp to control the infusion rate.
2. This method may result in occasional incidents of unintentionally rapid infusion rates or interruptions.
3. Poor-quality tubing or clamps make controlling the rate very difficult, and the patient may inadvertently receive a bolus feeding.
   C. Intermittent gravity feedings.
      1. Intermittent feedings are generally well tolerated if a maximum of 200 to 300 mL is administered over 30 to 60 minutes every 4 to 6 hours. **(3)**
      2. A prescription for an intermittent gravity feeding might read as follows: provide 240 mL of formula every 4 hours; infuse over 1 hour; precede and follow with a 30-mL flush of tap water.
   D. Bolus feedings.
      1. Bolus feedings are the infusion of a predetermined volume of formula at specified intervals by gravity or by syringe over a short period.
      2. The rate of infusion is controlled by either regulating the roller clamp or adjusting the syringe pressure.
      3. Feedings are generally accomplished over several minutes but may be best tolerated when provided at less than 60 mL/minute.
      4. In some settings, a large piston syringe (usually 50 mL or larger) is used to draw up and administer formula directly into the patient's feeding tube.
      5. When a syringe is used, the infusion rate can be gravity-controlled by either raising or lowering the syringe (plunger absent) or by slowly pushing the plunger inward.
      6. Rapid infusion of formula may cause discomfort, leading to the misconception that the formula instead of the administration method is not being tolerated.
      7. A feeding prescription might read as follows:
         a) provide 240 mL of formula every 3 hours over at least 4 minutes;
         b) precede and follow with a 30-mL flush of tap water.
      8. Bolus feedings are the easiest, least expensive delivery method and are more physiologic because they mimic normal feedings. The patient reaps the additional benefit of freedom of movement and breaks from feeding.
      9. Disadvantages include increased risk of aspiration, volume intolerance, vomiting, or delayed gastric emptying.**(4)**
2. **Pump assisted**
   A. Continuous pump feedings
      1. Indicated:
         a) when there is a high risk for aspiration,
         b) with volume sensitivity,
         c) with small-bowel feedings,
         d) sometimes with delayed gastric motility, and
         e) in sicker or hospitalized patients.
      2. Continuous feedings allow for maximal nutrient absorption and improved tolerance.**(4)**
      3. Pump-assisted feedings help to prevent GI complications associated with rapid infusion, such as nausea, cramping, and diarrhea.

        4.   Pumps are also more appropriate in patients who have tenuous fluid balance; if programmed correctly, they can help to prevent fluid overload.

        5.   Usual equipment includes a disposable pump set (container and tubing with drip chamber and connector) and the pump itself.

        6.   Controlled infusion is accomplished by threading the tubing through the pump's electronic sensors and cassette or pumping mechanism.

        7.   Portable "backpack"-style pumps are available for patients who require feedings while participating in their normal daily activities.

        8.   Continuous pump feedings are delivered via a stationary or ambulatory pump at a prescribed rate without interruption.**(5)**

    B.   Cyclic feedings

        1.   Generally administered over 8 to 20 hours per day, depending on the patient's volume tolerance.

        2.   This cycle allows for freedom from the feeding equipment for at least a few hours each day.

        3.   Transitioning from continuous to cyclic feedings typically is attempted as the patient recovers mobility and independence.

        4.   Feedings may be provided at night (nocturnal feedings) in an effort to allow patients to experience hunger and gradually increase their oral intake during the day**. (6)**

    C.   Intermittent pump feedings

        1.   Used to deliver predetermined volumes more accurately over a specified period.

        2.   This accuracy is helpful in managing patients that are at risk for aspiration resulting from a rapid infusion rate.

References:
1. Lord L, Harrington M. Implementation of enteral feedings, Enteral nutrition implementation and management. In Merritt R, Editor in Chief. The A.S.P.E.N. Nutrition Support Practice Manual 2nd edition. A.S.P.E.N. 8630 Fenton St, Suite 412; Silver Spring, MD; 2005; 77-8.
2. Nevin-Folino N, Miller M. Enteral nutrition. In: Queen Samour P, King Helm K, Lang CE, eds. *Pediatric Nutrition.* Gaithersburg, MD: Aspen Publishers; 1999:513–549.
3. Heitkemper M, Martin D, Hansen B, et al. Rate and volume of intermittent enteral feeding. *J Parenter Enteral Nutr.* 1981;5:312–316.
4. Smith B, Pederson A. Nutrition focus tube feeding update. *Nutr Focus.* 1990;5:1–6.
5. Weckwerth J, Nelson J, O'Shea R. Home nutrition support. In: Gottschlich M, Matarese L, Shronts E, eds. *Nutrition Support Dietetics Core Curriculum.* Silver Spring, MD: A.S.P.E.N; 1993:467–473.
6. 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.

Enteral Nutrition Specific Procedures and Guidelines #5: Nutrient Delivery and Initiation of Feeding
Main Reference: (1)

Initiation of enteral feedings

1. Recommendations:

   a. Currently, it is recommended that feedings in adults and children be initiated with full-strength formula at a slow rate and steadily advanced.

   b. This approach allows goal rates to be achieved earlier and reduces the risk of microbial contamination by minimizing the number of times the formula is manipulated.

   c. Experience has shown these regimens to be well tolerated, partially because of the widespread use of pumps for controlling infusion rates.

   d. Protocols for introducing tube feedings vary and should be individualized to fit the needs of the patient as well as the realities of the care environment.

   e. During feeding advancement, only one change should be made at a time to allow for tolerance assessment.

   f. If poor tolerance of the enteral regimen is demonstrated, either the formula volume or the concentration should be decreased.

   g. It is important to allow adequate time for the patient to tolerate the modified regimen before further advances are attempted. Occasionally it becomes necessary to change the formula to achieve improved feeding tolerance.

   h. After the patient is receiving and tolerating the goal regimen, modifications to the feeding schedule may be attempted to accommodate the patient's and family's lifestyle.**(2)**

2. **Bolus feedings and gravity-controlled feedings**

   a. Adults.

      i. Usually only gastric feedings are well tolerated when provided as a bolus or gravity feeding.

      ii. The feedings are usually initiated with full-strength formula 3 to 8 times per day, with increases of 60 to 120 mL every 8 to 12 hours as tolerated up to the goal volume.

      iii. Formula (ie, elemental, hypertonic, polymeric, or isotonic) does not require dilution unless additional water is necessary to meet fluid requirements.

      iv. Careful monitoring of gastric residual volumes and GI tolerance may help to facilitate increases in formula intake to the goal volume.

      v. Some patients may require bolus feedings to be delivered by gravity over 15 to 20 minutes or in smaller volumes more frequently.

   b. Children.

      i. Bolus feedings may be started with 25% of the goal volume divided into the desired number of daily feedings.

      ii. Formula volume may be increased by 25% per day as tolerated, divided equally between feedings.**(2)**

3. **Pump-assisted feedings.**

   a. Considerations:

      i. A pump is usually required for small-bowel feedings and is preferred for gastric feedings in critically ill patients, as the slower infusion rate of continuous feedings often enhances tolerance.

      ii. Conservative initiation and advancement rates are recommended for patients who are critically ill, have not been fed enterally for some time, or require hydrolyzed or high-osmolality formula.

   b. Adults.

      i. Formulas are initiated at full strength at 10 to 40 mL/hour and advanced to the goal rate in increments of 10 to 20 mL/hour every 8 to 12 hours as tolerated.

      ii. This approach can usually be used with isotonic as well as high-osmolality or elemental products.

    c. **Children.**
        i. A full-strength, isotonic formula can be started at 1 to 2 mL/kg/hour and advanced by 0.5 to 1 mL/kg/hour every 6 to 24 hours until the goal volume is achieved.
        ii. 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 to 1 mL/kg/hour**. (3)**

References:

1. Lord L, Harrington M. Implementation of enteral feedings, Enteral nutrition implementation and management. In Merritt R, Editor in Chief. The A.S.P.E.N. Nutrition Support Practice Manual 2nd edition. A.S.P.E.N. 8630 Fenton St, Suite 412; Silver Spring, MD; 2005; 76-7.
2. 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.
3. 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.

Enteral Nutrition Specific Procedures and Guidelines #6: Flushing
Main Reference: (1)

1. **Methods to irrigate the tube**
    a. Adults.
        i. To keep tubes patent, feeding ports should be flushed with warm water (at least 20–30 mL for adults) every 4 hours for continuous feedings as well as before and after each intermittent feeding or medication**. (2)**
        ii. Medications should be administered separately, and 5 to 10 mL of water should be provided between each one.
        iii. Gastric acids coagulate most intact protein formulations, so it is recommended that a feeding tube be flushed with 30 mL of warm tap water before and after checking for feeding residuals.**(3)**
        iv. It is important to subtract the amount of water flushed from the obtained residual volume.
    b. Children.
        i. Most pediatric tubes are not routinely flushed with water to prevent clogging unless recurrent problems occur.
        ii. It is important to consider the size of the child when providing flushes.
        iii. Infants' feeding tubes should be flushed with only 3 to 5 mL of water before and after medication administration, because they may not tolerate large amounts of calorie-free fluid.
        iv. Older toddlers are also provided small volumes of flushes following medication administration in an effort to prevent fluid excess **(4)**
2. **Choice of irrigant:**
    a. No irrigant has been shown to be more effective than water in preventing tube clogging.
    b. Water and carbonated beverages were shown to be equally effective in preventing tube clogging, and both were superior to cranberry juice. The lower pH of cranberry juice can cause clogging by precipitating certain proteins**. (5)**

References:
1. Lord L, Harrington M. Implementation of enteral feedings, Enteral nutrition implementation and management. In Merritt R, Editor in Chief. The A.S.P.E.N. Nutrition Support Practice Manual 2nd edition. A.S.P.E.N. 8630 Fenton St, Suite 412; Silver Spring, MD; 2005; 81.
2. Scanlan M, Frisch S. Nasoduodenal feeding tubes: prevention of occlusion. *J Neurosci Nurs.* 1992;24:256–259.
3. Marcuard S, Perkins A. Clogging of feeding tubes. *J Parenter Enteral Nutr.* 1988;12:403–405.
4. 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.
5. Methany N, Eisenberg P, McSweeney M. Effect of feeding tube properties and three irrigants on clogging rates. *Nurs Res.* 1988;37:165–169.

Enteral Nutrition Specific Procedures and Guidelines #7: Gastric residuals
Main Reference: (1)

1. Gastric residuals are frequently used to monitor the safety and gastric emptying of tube feedings.
    A. When gastric emptying is delayed or gastric secretion is excessive, fluid accumulates in the stomach and may result in:
        1. vomiting,
        2. aspiration,
        3. abdominal distention,
        4. or cramping.
    B. To prevent these potential complications, the volume of fluid remaining in the stomach during feeding (the residual volume) is measured to monitor the safety of advancing or continuing enteral feeds. **(2,3)**
    C. Gastric motility is affected by:
        1. disease,
        2. mechanical obstruction, and
        3. certain medications.**(4)**
    D. One episode of high residual volume should not automatically prompt cessation of feedings in the absence of physical examination or radiographic abnormalities; rather, signs and symptoms of intolerance should be monitored carefully. (2-5)
    E. Patients with frequently elevated gastric residual volumes may benefit from feeding tube placement beyond the ligament of Treitz. **(4)**
2. **Frequency of checking residuals:** Gastric emptying of enteral feedings can be assessed by checking residuals **prior to each intermittent feed or every 4 hours with continuous feeds**.**(6)**
3. Method for obtaining residuals.
    A. Residuals are obtained by aspirating through the feeding tube with a syringe and measuring the formula and fluid withdrawn.
    B. The aspirating syringe needs to be fairly large, generally at least 50 mL for small-bore (12F or less) feeding tubes and at least 30 mL for gastrostomy tubes.
    C. Smaller syringes exert a higher pressure per square inch and may cause the tube to collapse.
    D. If unable to aspirate, inject 3 to 5 mL of air or water into the feeding tube and reattempt.

E. Residuals contain formula, digestive juices, and electrolytes and therefore should be reinstilled through the feeding tube (unless there is a large amount).

4. Parameters for holding feedings.
  A. Characteristics:
    1. Isolated episodes of high gastric residuals are not always associated with abdominal symptoms.
    2. The amount of gastric residuals obtained depends on:
      a) the amount and timing of the last feeding,
      b) medications, and
      c) the location of the feeding tube tip.
    3. The patient's activity and positioning may also affect the gastric emptying rate.**(6)**
    4. The residual may be clear, indicating the presence of gastric juices, or may contain partially digested formula.
  B. ADULTS: When a residual reaches =200 mL with a nasogastric tube or =100 mL with a gastrostomy tube, associated signs or symptoms of intolerance should be assessed. (3)
  C. INFANTS AND CHILDREN: Slowing or stopping feedings in infants and children has been recommended if residual volume exceeds twice the hourly infusion volume during continuous feedings or exceeds 50% of the infusion volume during bolus feedings. (7)

5. Observations:
  A. It is believed that aspiration from a gastrostomy tube is less likely to yield gastric residuals because of the tube's positioning in the anterior portion of the stomach, compared with a nasogastric tube.
  B. Therefore, high residuals from a gastrostomy tube are more worrisome.
  C. If abdominal discomfort or distension is present, feedings should be held.
  D. Further workup with roentgenograms may be indicated.
  E. If the abdominal exam is benign, feedings should be delayed for at least 1 hour and residuals rechecked.
  F. If high residuals persist without associated clinical signs and symptoms, a promotility agent (eg, erythromycin, metoclopramide) may be tried.
  G. Another option is to insert a transpyloric feeding tube and perform gastric decompression as necessary.
  H. Residuals cannot always be aspirated from jejunal or duodenal tubes.**(6)**
  I. Intolerance of small-bowel feedings can be identified when a patient experiences:
    1. abdominal distention,
    2. discomfort,
    3. and/or diarrhea.
  J. If a patient develops feeding intolerance with small-bowel feedings, the previously tolerated formula strength or volume should be reinstituted and feeds gradually advanced as tolerated.**(8)**

References:
  1. Lord L, Harrington M. Implementation of enteral feedings, Enteral nutrition implementation and management. In Merritt R, Editor in Chief. The A.S.P.E.N. Nutrition Support Practice Manual 2nd edition. A.S.P.E.N. 8630 Fenton St, Suite 412; Silver Spring, MD; 2005; 79.
  2. Burd RS, Lentz C. The limitations of using gastric residual volumes to monitor enteral feedings: a mathematical model. *Nutr Clin Pract.* 2001;16:349–354.

3. McClave SA, Snider HI, Lowen CC, et al. Use of residual volume as a marker for enteral feeding intolerance: prospective blinded comparison with physical examination and radiographic findings. *J Parenter Enteral Nutr.* 1992;16:99–105.
4. A.S.P.E.N. Board of Directors. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *J Parenter Enteral Nutr.* 2002;26:33SA–35SA.
5. Murphy LM, Bickford V. Gastric residuals in tube feeding: how much is too much? *Nutr Clin Pract.* 1999;14:304–306. Smith B, Pederson A. Nutrition focus tube feeding update. *Nutr Focus.* 1990;5:1–6.
6. Smith B, Pederson A. Nutrition focus tube feeding update. *Nutr Focus.* 1990;5:1–6.
7. Schanler RJ. The low birth weight infant: perinatal nutrition. In: Walker WA, Watkins JB, eds. *Nutrition in Pediatrics: Basic Science and Clinical Applications.* Hamilton, Ontario;B.C. Decker;1996:387–407.
8. Marian M. Pediatric nutrition support. *Nutr Clin Pract.* 1993;8:199–209.

Enteral Nutrition Specific Procedures and Guidelines #8: Aspiration detection, management, and prevention
Main Reference: (1)

1. **Aspiration precautions**
   A.   Tube-feeding residuals – Please read <u>Enteral Nutrition Specific Guidelines #7: Gastric Residuals</u>
   B.   Head-of-bed elevation.
      1.   The effect of head elevation in patients fed through small-bore tubes or enterostomies has not been determined; however, the semirecumbent position (=30° elevation) has been recommended for all tube-fed patients to minimize the potentially life-threatening consequences of aspiration. **(2,3)**
      2.   Aspiration of pharyngeal and gastric secretions can still occur in some patients (even those not fed), and large-bore tubes may disrupt the function of the lower esophageal sphincter (LES), increasing the risk of aspiration.
2. **Aspiration detection**
   A.   Clinical signs and symptoms.
      1.   When a significant amount of enteral formula is aspirated, sudden onset of dyspnea, tachypnea, wheezing, rales, tachycardia, cyanosis, decreased oxygenation, anxiety, and agitation can occur.
      2.   Smaller amounts of formula may be aspirated over time with no apparent clinical symptoms.
      3.   A subsequent fever can signal the development of aspiration pneumonia.
   B.   Roentgenogram findings are nonspecific and lack sensitivity for the detection of aspiration.
      1.   There are many causes of pulmonary infiltrates, including pneumonia, contusion, atelectasis, and hemorrhage.
      2.   The appearance of new infiltrates in dependent lung fields in a patient lacking other causes of infiltrates suggests aspiration.
   C.   Use of coloring agents.
      1.   Blue dye has been used to tint tube-feeding formulas as a method for determining the presence of formula in tracheal aspirates. It was thought that this method would help detect pulmonary aspiration in tube-fed patients.

2. The sensitivity, specificity, and safety of this method have not been adequately evaluated.
3. The percentage of patients who will develop clinically significant aspiration whether or not coloring is detected has not been determined.
4. Most important, a Food and Drug Administration Public Health Advisory issued September 29, 2003, reported blue discoloration and death in patients receiving tube feedings containing FD&C Blue No. 1 dye. **(4)**
5. Blue discoloration of the skin, urine, feces, and serum has been reported in patients receiving this dye in their tube feedings, and in some the dye has been associated with refractory hypotension, metabolic acidosis, and death.
6. Case reports reveal that critically ill patients, especially those who have increased intestinal permeability, are at risk for these complications.
7. Based on these reports, patients with sepsis, severe burns, trauma, shock, surgical interventions, renal failure, celiac sprue, and inflammatory bowel disease may be at risk for systemic toxicity of blue dye absorption from enteral tube feedings.
8. Other disadvantages of this method include the false elevation of gastric pH, positive Hemoccult stool tests, formula manipulation, and the potential to induce an allergic response.
9. Blue food colorings or methylene blue may still be used when checking for fistulas (ie, tracheal-esophageal fistula) in hemodynamically stable patients, if provided in unit-of-use containers (ie, an ampule of methylene blue) to minimize contamination risk.

D. Tracheal glucose measurements.
1. It has been reported that aspiration of tube-feeding formulas may be determined by a positive-glucose result in the tracheal aspirate, **(5)** but the sensitivity and specificity of this method have not been adequately tested.
2. High tracheal concentrations of glucose have been found in intubated patients, both fed and not fed, and often are not associated with clinical evidence of aspiration.
3. High tracheal concentrations of glucose also may be found in diabetic patients with high serum concentrations of glucose.**(6)**

References:
1. Lord L, Harrington M. Implementation of enteral feedings, Enteral nutrition implementation and management. In Merritt R, Editor in Chief. The A.S.P.E.N. Nutrition Support Practice Manual 2nd edition. A.S.P.E.N. 8630 Fenton St, Suite 412; Silver Spring, MD; 2005; 79.
2. 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.
3. Ibanez J, Penafiel A, Raurich JM, et al. Gastroesophageal reflux in intubated patients receiving enteral nutrition: effect of supine and semirecumbent positions. *J Parenter Enteral Nutr.* 1992;16:419–422.
4. FDA Public Health Advisory. *Reports of Blue Discoloration and Death in Patients Receiving Enteral Feedings Tinted with the Dye, FD&C Blue no. 1.* Rockville, MD. US Food and Drug Administration; 2003.

5. Winterbauer RH, Durning RB Jr, Barron E, et al. Aspirated nasogastric feeding solution detected by glucose strips. *Ann Intern Med.* 1981;95:67–68.
6. Kinsey GC, Murray MJ, Swensen SJ, et al. Glucose content of tracheal aspirates: implications for the detection of tube feeding aspiration. *Crit Care Med.* 1994;22:1557–1562.

Enteral Nutrition Specific Procedures and Guidelines #9: PEG – placement, maintenance, and replacement
Main Reference: (1)

Placement:
1. Who has the interest and expertise to place PEG tubes?
    a. Gastroenterologists
    b. Surgeons
    c. Radiologists
    d. Most specialists favor specific tubes and access methods, so the route of insertion varies among them.
    e. Documentation of competency should be provided by the operator
2. **Gastrostomy insertion methods.**
    a. **PEG.**
        i. Prior to an attempt to place a PEG, a screening upper endoscopy is performed to make sure that there are no contraindications to the procedure such as a large ulcer (higher risk of ulcer perforation) or a gastric or duodenal mass or obstruction.
        ii. Conscious sedation is usually sufficient to perform the procedure, but occasionally deep sedation with propofol or even general anesthesia may be required.
        iii. Procedure:
            1. After the initial endoscopy, the patient is place supine and an area of transillumination in the left upper quadrant is identified.
            2. When a proposed site is located, palpation with a finger is used to indent the insufflated stomach.
            3. The site is then prepped with iodine swabs and infiltrated with 1% lidocaine solution.
            4. A 1-cm skin incision is made, and a catheter is placed through the incision into the stomach.
            5. A suture or guidewire is placed through the catheter and grasped with a snare.
            6. The endoscope, snare, and suture are removed from the patient.
            7. The PEG tube is tied onto the suture coming from the mouth and then pulled through the mouth, esophagus, and stomach to reach the anterior abdominal wall.
            8. The endoscope is reinserted and the intragastric position of the PEG bumper is visualized.
            9. The endoscope is removed from the patient, and the external bumper and a feeding adapter are placed.
        iv. Kits are commercially available with tube sizes from 14F to 28F.
            1. Adults commonly have 20F tubes placed.
            2. Larger tubes may be required to insert a smaller feeding tube into the small intestine if small bowel feedings are desired.

3. Infants and children often have 14F tubes placed, but later 18F to 20F tubes are necessary to facilitate flow rates commensurate with growth.

b. **Radiologic.**
   i. Gastrostomy tubes may be placed with radiologic guidance, which avoids passage of the endoscope through a bacteria-laden oral cavity.
   ii. This reduces the risk of contamination of the subcutaneous tissues and avoids general anesthesia that may be required for surgical placement.
   iii. In patients with head and neck cancer, there is a very small but real risk of causing PEG stoma site metastases when pulling a tube through the oropharynx.
   iv. This risk can be obviated by doing the procedure radiologically or endoscopically by the introducer technique. **(2,3)**
   v. Fluoroscopy is the most commonly used imaging modality; however, ultrasonography or computed tomography can provide additional information about intra-abdominal structures that may be overlying the stomach or provide a safe tract when endoscopic transillumination fails.
   vi. The size of feeding tubes varies from 10F to 28F.
   vii. The two most common complications associated with radiologic placement are tube clogging and displacement; these complications often lead to catheter replacement.
   viii. If stabilizing sutures are used, larger tubes with a lower rate of dislodgment or clogging can be inserted.

c. **Surgical.**
   i. Most operative gastrostomies are performed under general anesthesia in an operating room, but doing so can escalate costs.
   ii. Surgical gastrostomies have been performed under conscious sedation.
   iii. Operative gastrostomies are very cost-effective when done during another intra-abdominal procedure.
   iv. An operative alternative to laparotomy is laparoscopic insertion.**(4)**
   v. Surgical placement in pediatric patients is most commonly achieved with a Stamm gastrostomy procedure.
       1. This is technically a temporary gastrostomy because the tract closes spontaneously after the tube is removed.
       2. A gastropexy is performed in which the stomach is sutured to the abdominal wall.
       3. Once post-procedure healing is complete, a reliable, established tract for replacing tubes exists.
       4. Gastrostomy tube placement itself may alter the contour of the stomach enough to cause some gastroesophageal reflux.
       5. Children with documented gastroesophageal reflux or gastric aspiration may need a fundoplication procedure performed with the surgical gastrostomy, which may obviate the need for postpyloric feedings.
       6. A pyloroplasty may be performed also if delayed gastric emptying has been documented.

3. **Pros.**
   a. These tubes allow long-term access and are easily cared for and replaceable.
   b. Bolus feeding and administration of medication are possible because of the large caliber of the tube.

4. **Cons.**

      a. Compared with the oral or nasal route, this technique is more invasive.

5. Potential Complications of Gastrostomy (All Methods) (5)
   a. Aspiration
   b. Dislodgement
   c. Tube deterioration
   d. Bleeding
   e. Pneumoperitoneum
   f. Wound infection
   g. Tube occlusion
   h. Stomal leakage

Maintenance:
1. Go to Enteral Nutrition Specific Guideline #2: checking tube placement
2. Go to Enteral Nutrition Specific Guideline #3: checking tube passages
3. Go to Enteral Nutrition Specific Guideline #5: flushing

Replacement:
1. Maturation of the tract
   a. Generally occurs in 2 to 3 weeks in the adult patient and 6 weeks in the pediatric patient.
   b. This process takes longer if the patient is immuno-compromised, diabetic, or severely malnourished.**(6)**
   c. If the tract is disturbed during this time, the stomach may separate from the abdominal wall.
   d. During the maturation process, only a physician should change the gastrostomy tube; a radiologic procedure (eg, fluoroscopy, contrast study) may be indicated to confirm proper tube replacement.
   e. Once the tract is fully mature, nurses may replace tubes — depending on their knowledge and experience, facility policies, and state regulations — if a health care provider orders it.
   f. Some parents/caregivers become comfortable enough to replace their child's gastrostomy tube through a mature tract.
2. If the tube is inadvertently removed:
   a. It should be replaced as soon as possible;
   b. The tract can close within hours of the incident.
   c. The patient can be instructed to take the tube (so caregivers know what type and size tube is being used) to an acute-care facility for replacement, taught how to replace the tube in an emergency situation, or instructed to call a home-care nurse.
3. Gastrostomy tubes should be replaced when:
   a. They show signs of degradation
   b. Balloon breakage
   c. Malfunction
   d. Irreversible occlusion
4. Removal of any tube requires:
   a. Knowledge of the tube type
   b. Initial placement procedure
   c. For example, some endoscopically placed tubes require endoscopy for tube removal.
5. Replacement gastrostomy tubes are usually inserted when the tract is well formed and further endoscopy is not necessary.**(6)**
6. Replacement tube types:

a. Many replacement tubes are made of silicone.
b. If a latex tube (eg, Foley catheter) is selected as a replacement tube, providers should be aware of possible latex sensitivities.
c. There are a variety of replacement gastrostomy tubes and LPDs on the market with balloons or solid bolsters.

References:
1. Kirby DF, Opilla M. Enteral Access and Infusion Equipment. In Merritt R, Editor in Chief. The A.S.P.E.N. Nutrition Support Practice Manual 2nd edition. A.S.P.E.N. 8630 Fenton St, Suite 412; Silver Spring, MD; 2005; 54-58.
2. Thakore JN, Mustafa M, Suryaprasad S, Agrawal S. Percutaneous endoscopic associated gastric metastasis. *J Clin Gastroenterol.* 2003;37:307–311.
3. Hunter JG. Tumor implantation at PEG exit sites in head and neck cancer patients: how much evidence is enough? [editorial]. *J Clin Gastroenterol.* 2003;37:280.
4. Edelman DS, Unger SW. Laparoscopic gastrostomy and jejunostomy: review of 22 cases. *Surg Laparosc Endosc.* 1994;4:297–300.
5. Kirby DF, DeLegge MH. Enteral nutrition: the challenge of access. In: Kirby DF, Dudrick SJ, eds. *Practical Handbook of Nutrition in Clinical Practice.* Boca Raton, FL: CRC Press; 1994:87–117.
6. Eisenberg PG. Gastrostomy and jejunostomy tubes. *RN.* 1994;57:54–59.

Enteral Nutrition Specific Procedures and Guidelines #10: Nasogastric/nasoenteric – placement and maintenance
Main Reference: (1)

Placement:
1. **Nasogastric tubes (NGTs).**
   a. Commonly used, traditional NGTs (eg, Salem sumps) may perform many functions in addition to feeding, such as decompression of the stomach, administration of medication, and measurement of gastric pH or residuals.
   b. NGTs are made in various sizes (5F–18F), but, to avoid clogging, at least a 10F tube is required for commercially available enteral formulations.
   c. For improved patient comfort, some institutions use small-caliber tubes (8F–12F) for short-term nasogastric feedings.
   d. Insertion: uncomplicated
      i. If the tube is to be inserted through the nose, it is important to obtain a history
         1. of sinus problems,
         2. deviated septum,
         3. frequent nosebleeds, known platelet or bleeding disorders,
         4. recent head or facial trauma,
         5. or difficulty with a previous nasal tube passage.
      ii. Before tube passage,
         1. the nasal passages should be inspected.
         2. If the patient already has a tube (nasotracheal) in one nostril, the NGT is best placed in the other nostril.
         3. Hanson's formula[4] has been used to estimate the length of tube needed to pass 1 to 10 cm beyond the gastric cardia in adults: [(*NEX ! 50*)/2] + 50 cm, where N = tip of nose, E = earlobe, and X = xiphoid process.

      iii. Procedure:
1. The tube is marked 50 cm from its tip and, with the patient's head in a neutral position, is placed along the shortest course with the end of the tube at the tip of the nose (*N*) passing to the earlobe (*E*) and then to the xiphoid process (*X*).
2. A second mark is made on the tube at the point where the tube meets the xiphoid process. The length of tube insertion should be halfway between the xiphoid process mark and the 50-cm mark.
3. A simplified method is also used, whereby the tube is measured from the tip of the patient's nose to the earlobe and from the earlobe to the xiphoid process.
4. Some commercially available feeding tubes have markings to denote length.
5. Lubrication of the tube with a water-soluble lubricant facilitates passage;
6. use of local anesthetic jelly (eg, 2% lidocaine jelly) may promote comfort and improve success in an alert patient.
7. To decrease the risk of aspiration, the head of the bed should be raised or the patient should sit up.
8. In comatose or anesthetized patients, the left lateral decubitus position may decrease this risk.
9. The tube is carefully directed back through the nares to the hypopharynx.
10. When the tip is in the posterior pharynx, the patient should be asked to take small sips of water or initiate dry swallows to facilitate passage of the tube past the upper esophageal sphincter (UES).
11. If the patient begins to cough or cannot speak, the tube should be retracted because it may be in the trachea.
12. Once the tube has passed the UES, it is important to be aware of any intrinsic esophageal disease (esophageal stricture, tumor, or diverticulum) that may impede safe passage to the lower esophageal sphincter (LES).
13. Disorders of the LES, such as achalasia, may also hinder tube passage into the stomach.
14. If significant resistance is met, the procedure should be terminated and the reason for the resistance should be assessed. Another method of placement may need to be used.

e. Insertion: complicated
    i. Procedure:
1. A stethotube is a feeding tube that is adapted to a stethoscope.**(2)**
2. If the feeding tube is passed incorrectly into the trachea, there will be a very loud noise, indicating that the tube should be removed and redirected.
3. In comatose or anesthetized patients, a laryngoscope may be used to help guide the tube past the UES into the esophagus and beyond.
4. A physician who is comfortable with the technique generally performs this procedure.

f. Complications (3)
    i. Clogging
    ii. Esophageal perforation
    iii. Nasal mucosal ulceration

iv.   Pneumothorax
         v.   Pulmonary intubation
        vi.   Epistaxis
       vii.   Gastrointestinal bleeding
      viii.   Otitis media
        ix.   Pulmonary aspiration
         x.   Pyriform sinus perforation

2. **Orogastric tubes**
   a. Characteristics:
        i.   The oral route may be preferred when nasal or facial trauma, head injury, sinusitis, or other factors prevent a tube from being placed nasally.
       ii.   In addition, the oral route may be a good option in patients who are sedated, paralyzed, or mechanically ventilated.
      iii. Orogastric tubes are used for premature infants, as they are obligatory nasal breathers.
   b. Pros. The incidence of sinusitis is lower than with nasoenteric tubes.
   c. Cons. Orogastric tubes are not tolerated for prolonged periods in alert patients; tubes may be damaged by teeth.
   d. Complications.
        i.   Except for nasal-related events, the complications are similar to those for nasogastric tubes (See Number 1, letter f (Complications [3]).

3. **Short-Term Nonsurgical Postpyloric Tubes**
   a. **Nasoenteric.**
        i.   These tubes are ideal if short-term feeds are required but the patient is at high risk of aspiration, esophageal reflux, or delayed gastric emptying.
       ii.   It is assumed that if the tip of the tube is placed past the pyloric sphincter, the risk of TFRA is reduced.
      iii.   However, duodenogastric reflux is limited only if the tube is in the distal third of the duodenum and preferably past the ligament of Treitz.**(4)**
      iv. Newer tubes have a separate gastric port for gastric suction, decompression, or medication delivery, with a second lumen for simultaneous small-bowel feeding. These tubes are generally more difficult to place and may require pharmacologic, endoscopic, intraoperative, or radiologic assistance.**(5,6)**
   b. **Nasoenteric tube insertion methods**
        i.   pH sensors.
             1. Small-bowel tubes with pH sensors are available. It is assumed that an increase in pH over the presumed gastric reading is consistent with the end of the tube entering the duodenum.
             2. In one study, the pH profile and radiograph were in agreement in 87% of the cases, but small-bowel tube location was not discussed.**(7)**
       ii.   Pharmacologic measures.
             1. Medications with promotility properties have been used to facilitate passage of feeding tubes into the small intestine.
             2. Metoclopramide (10 mg intravenously) has been studied the most and appears to be most effective when given about 15 minutes before tube insertion.
             3. Only diabetic patients appear to benefit from a dose of metoclopramide given after tube placement.**(8)**
             4. When used in low doses, the antibiotic erythromycin also has promotility properties and can be useful for tube placement.

5. In adults, an intravenous (IV) dose of 500 mg administered prior to tube insertion has been reported to facilitate tube placement. **(8,9)**
6. In children, a dose of 3 mg/kg given intravenously 1 hour prior to tube insertion has been reported**. (10)** (Note that this is an off-label use for erythromycin.)

iii. Fluoroscopy.
1. Radiologic techniques can be very useful for placing nasoenteric tubes.
2. Passage into the third portion of the duodenum or beyond was successful in 86% of attempts in one study.**(11)**
3. Procedures can be performed in the radiology department or at the bedside if portable fluoroscopy is available.

iv. Endoscopy.
1. Endoscopy can facilitate feeding-tube placement into the small bowel; however, in adults, tubes of sufficient length (>105 cm) need to be used.**(12)**
2. Friction from the endoscope may drag tubes back as the endoscope is removed, so postprocedure radiographs are recommended.
3. Success rates of 90% to 95% have been reported with this technique.

v. Pros.
1. Postpyloric feeding tubes are usually of smaller diameter than standard NGTs and cause less patient discomfort.
2. Delayed gastric emptying does not preclude feeding.

vi. Cons.
1. It may be difficult to achieve postpyloric or post–ligament of Treitz positioning.
2. Small-caliber tubes may preclude administration of some medications.
3. Infusion pumps are usually required for infusion of enteral formulations.

vii. Complications ((See Number 1, letter f (Complications [3]).

4. Surgical nasoenteric
   a. Some surgeons provide short-term enteral access postoperatively by manually guiding a nasoenteric tube through the stomach, then through the duodenum, and into the small bowel during laparotomy.
   b. The frequency and success of this practice are not known.

Maintenance:
1. Go to Enteral Nutrition Specific Guideline #2: checking tube placement
2. Go to Enteral Nutrition Specific Guideline #3: checking tube passages
3. Go to Enteral Nutrition Specific Guideline #5: flushing

References:
1. Kirby DF, Opilla M. Enteral Access and Infusion Equipment. In Merritt R, Editor in Chief. The A.S.P.E.N. Nutrition Support Practice Manual 2nd edition. A.S.P.E.N. 8630 Fenton St, Suite 412; Silver Spring, MD; 2005; 54-6.
2. Haddad N, Nawaz T, Potter L, Lipman T. Avoidance of naso-pulmonary intubation by feeding tubes with stethoscopic guidance: the "stethotube" [abstract]. *Gastroenterology*. 1993;104:A623.

3. Kirby DF, DeLegge MH. Enteral nutrition: the challenge of access. In: Kirby DF, Dudrick SJ, eds. *Practical Handbook of Nutrition in Clinical Practice.* Boca Raton, FL: CRC Press; 1994:87–117.
4. Gutske RF, Varma RR, Soergel KH. Gastric reflux during perfusion of the proximal small bowel. *Gastroenterology.* 1970;59:890–895.
5. Patrick PG, Kirby DF, DeLegge MH. Outcome study on nasojejunal feeding in critically ill patients [abstract]. *Gastrointest Endosc.* 1995;41:370.
6. Baskin WN, Johanson JF. An improved approach to the delivery of enteral nutrition in the intensive care unit. *Gastrointest Endosc.* 1995;42:161–165.
7. Heiselman DR, Vidovich RR, Milkovich G, Black LD. Nasointestinal tube placement with a pH sensor feeding tube. *J Parenter Enteral Nutr.* 1993;17:562–565.
8. Booth CM, Heyland DK, Paterson WG. Gastrointestinal promotility drugs in the critical care setting: a systematic review of the evidence. *Crit Care Med.* 2002;30:1429–1435.
9. 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;31:315–316.
10. Di Lorenzo C, Lachman R, Hyman PE. Intravenous erythromycin for postpyloric intubation. *J Pediatr Gastroenterol Nutr.* 1990;11:45–47.
11. Gutierrez ED, Balfe DM. Fluoroscopically guided nasoenteric feeding tube placement: results of a 1-year study. *Radiology.* 1991;178:759–762.
12. Mathus-Vliegen EMH, Tytgat GNJ, Merkus MP. Feeding tubes in endoscopic and clinical practice: the longer the better? *Gastrointest Endosc.* 1993;39:537–542.

Enteral Nutrition Specific Procedures and Guidelines #11: Jejunostomy – indications, placement and maintenance
Main Reference: (1)

Indications:
1. reflux esophagitis,
2. gastric aspiration,
3. gastroparesis,
4. insufficient stomach remnant because of previous resection,
5. and establishment of access for postoperative feeding after major surgical procedures and of feeding access in patients who have unresectable gastric or pancreatic cancers.
6. During urgent abdominal surgery, jejunostomy placement to facilitate early postoperative feeding should be considered.

Duration: Long-term feeding tubes
    a. **Adults: > 4 to 8 weeks**
    b. **Pediatrics: > 4 to 6 weeks**

Placement:
1. Jejunostomy.
    a. If a patient is already undergoing laparotomy, a jejunostomy tube can easily be placed even for short-term use.
    b. For example, someone undergoing a partial gastrectomy may have a gastrostomy and jejunostomy tube placed. The gastrostomy would initially be used for decompression; the jejunostomy would be used for immediate postoperative feedings.
    c. NCJ (Needle Catheter Jejunostomy)
        i. These are small-caliber jejunal tubes that can be easily placed at surgery.
        ii. Older models were 5F, which predisposed them to clogging.

   iii. Newer versions are 7F or 8F, which allows administration of enteral formulations with extra protein or fiber.

2. Methods of insertion **(2-4)**
  a. Percutaneous gastrojejunostomy
    i. Also called a JET-PEG or jejunal extension through a PEG.
    ii. This jejunal feeding tube is a small 9F to 12F tube that is dragged or passed over a guidewire into the small bowel through a previously placed PEG.
    iii. Initial versions of this tube were unsatisfactory in their design, were difficult to place past the proximal duodenum, and often migrated back into the stomach.
    iv. Devices now available are easier to place in the distal duodenum or jejunum and are more reliable because the likelihood of migration is greatly decreased.
    v. To decrease the incidence of TFRA, the feeding port must be located in the distal duodenum or jejunum.
    vi. Although placement of a primary Percutaneous Endoscopic Jejunostomy (PEJ) tube (tube placed with the PEG technique directly into the small intestine) as the initial procedure is not as common as the PEG procedure, it is becoming more widely practiced.
      1. It has been performed in patients with normal anatomy and in those who have had gastric resection.**(5-8)**
    vii. There are also commercially available dual-lumen tubes that have both a gastric and a jejunal port.
      1. These are usually placed through mature gastrostomy tracts and can be placed radiologically or endoscopically.
    viii. The fact that the internal retention device is a balloon often limits these devices' use.
      1. When the balloon fails (usually within 3 months), the entire tube must be replaced.
    ix. These tubes are too large to be used in infants and small pediatric patients.
  b. Radiologic jejunostomy.
    i. Radiologists can insert a small feeding tube through the stomach and fluoroscopically guide it through the pylorus to the duodenojejunal flexure.
    ii. This provides small-bowel feeding with a reduced risk of **TFRA (Tube Feeding Related Aspiration)**, but because smaller catheters (10F) are placed by this technique, a higher obstruction rate is expected.
    iii. One series retrospectively compared surgical gastrostomy with radiologic percutaneous jejunostomy transgastric, in which ultrasound and fluoroscopy were used to insert a feeding tube through the stomach wall and then a 10F catheter was passed to the duodenojejunal junction.**(9)**
    iv. Complications were fewer in the nonsurgical jejunostomy group, despite the fact that the stomach wall was not fixed to the anterior abdominal wall.
    v. However, radiologic techniques do not allow for placement of feeding tubes of sufficient size to provide both gastric and small-bowel access.
    vi. Some centers are now performing dual-lumen gastrojejunostomies.
      1. The gastric port is 16F with a 10F jejunal port.
      2. While this may allow for decompression of the stomach or medication administration and feeding into the jejunum, the tube sizes may be associated with a higher rate of occlusion.
      3. More long-term data are needed.

       vii. Direct percutaneous access to the jejunum has been performed under radiologic control; however, this is technically more difficult.
- c. Open surgery.
  - i. Surgical placement of jejunostomy tubes has been performed for over 100 years.
  - ii. A variety of techniques are available, including:
    1. Witzel jejunostomy (probably the most common),
    2. Roux—en-Y jejunostomy,
    3. serosal tunnel jejunostomy,
    4. button jejunostomy,
    5. and laparoscopic jejunostomy.**(10,11)**
  - iii. Numerous tubes have been used, including:
    1. red rubber catheters,
    2. biliary T tubes,
    3. and dialysis catheters.
    4. Surgical gastrojejunostomy tubes, which allow gastric decompression or medication administration in addition to jejunal feeding, are also available.

3. **Potential Complications of Jejunostomy (12)**
- a. Bleeding
- b. Dislodgment
- c. Tube deterioration
- d. Volvulus
- e. Pneumatosis intestinalis
- f. Tube occlusion
- g. Stomal leakage
- h. Wound infection
- i. Bowel obstruction

Maintenance:
1. Go to Enteral Nutrition Specific Guideline #2: checking tube placement
2. Go to Enteral Nutrition Specific Guideline #3: checking tube passages
3. Go to Enteral Nutrition Specific Guideline #5: flushing
4. **The common belief that only elemental diets should be given through jejunostomy tubes has been shown to be untrue.(13)**
5. **Standard polymeric diets containing fiber can be used; however, the catheter must be flushed routinely to maintain tube patency.**
6. Pros.
   - a. These tubes decrease the risk of TFRA.
   - b. Early postoperative feeding is possible in most patients except those who are hemodynamically unstable, have peritonitis, or have a bowel obstruction.
7. Cons.
   - a. An infusion pump is required.
   - b. Administration of medication is precluded in some instances but is dependent on the size of the T-tube.
   - c. Invasive procedures are required for access.
   - d. Outside connectors are prone to break and may require replacement of the entire T-tube.
   - e. The tubes are difficult if not impossible to replace unless a mature tract has developed.

References:

1. Kirby DF, Opilla M. Enteral Access and Infusion Equipment. In Merritt R, Editor in Chief. The A.S.P.E.N. Nutrition Support Practice Manual 2nd edition. A.S.P.E.N. 8630 Fenton St, Suite 412; Silver Spring, MD; 2005; 56-8.
2. Kirby DF, DeLegge MH. Enteral nutrition: the challenge of access. In: Kirby DF, Dudrick SJ, eds. *Practical Handbook of Nutrition in Clinical Practice.* Boca Raton, FL: CRC Press; 1994:87–117.
3. Parasher VK, Abramowicz CJ, Bell C, et al. Successful placement of percutaneous gastrojejunostomy using steerable guidewire: modified controlled push technique. *Gastrointest Endosc.* 1995;41:52–55.
4. Baskin WN. Enteral access techniques. *Gastroenterologist.* 1996;4(suppl 1):S40–67.
5. Shike M, Schroy P, Ritchie MA, et al. Percutaneous endoscopic jejunostomy in cancer patients with previous gastric resection. *Gastrointest Endosc.* 1987;33:372–374.
6. Mellert JK, Fischer H, Grund KE. Direct endoscopic percutaneous jejunostomy (EPJ): an alternative for operative catheter-jejunostomy [abstract]. *Gastrointest Endosc.* 1993;39:254.
7. Duckworth PF Jr, Kirby DF, McHenry L, et al. Percutaneous endoscopic gastrojejunostomy (PEG/J) made easy: a new over-the-wire technique. *Gastrointest Endosc.* 1994;40:350–353.
8. Patrick PG, Kirby DF, DeLegge MH. Evaluation of percutaneous endoscopic gastrojejunostomy tubes as a long-term feeding option [abstract]. *Gastroenterology.* 1996;110:A830.
9. Ho C-S, Yee ACN, McPherson R. Complications of surgical and percutaneous nonendoscopic gastrostomy: review of 233 patients. *Gastroenterology.* 1998;95:1206–1220.
10. Gorman RC, Morris JB, Metz CA, Mullen JL. The button jejunostomy for long-term jejunal feeding: results of a prospective randomized trial. *J Parenter Enteral Nutr.* 1993;17:428–431.
11. Reed DN. Percutaneous peritoneoscopic jejunostomy. *Surg Gynecol Obstet.* 1992;174:527–529.
12. Kirby DF, DeLegge MH. Enteral nutrition: the challenge of access. In: Kirby DF, Dudrick SJ, eds. *Practical Handbook of Nutrition in Clinical Practice.* Boca Raton, FL: CRC Press; 1994:87–117.
13. Collier P, Kudsk KA, Glezer J, Brown RO. Fiber-containing formula and needle catheter jejunostomy: a clinical evaluation. *Nutr Clin Pract.* 1994;9:101–103.

ESPEN GUIDELINES: PEG

1. **Group members:** Chr. Lo¨ser (a), G. Aschl (b), X. He´buterne (c), E.M.H. Mathus-Vliegen (d), M. Muscaritoli (e), Y. Niv (f), H. Rollins (g), P. Singer (h), R.H. Skelly (i)
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2. **Comments:**
   a. PEG has now replaced the surgical gastrostomy (Witzel gastrostomy, Stamm gastrostomy, Janeway gastrostomy) which was associated with a markedly higher rate of complications. **(2,3)**
   b. Placement of a PEG/PEJ (percutaneous endoscopic jejunostomy) tube is simple, safe and well-tolerated by patients. **(4,5)**
   c. There is a wide range of diets and nutrient preparations suitable for tube feeding currently available.
   d. PEG-feeding, therefore, has rapidly spread to become routine practice worldwide and is currently the method of choice for medium- and long- term enteral feeding.

3. **Comparison of PEG versus NGT:** Several studies compared the various clinical effects of PEG tube feeding and feeding via nasogastric tubes. **(6-10)**13–17
   a. While nasogastric tube feeding was found to have a higher rate of discomfort and complications (irritations, ulceration, bleeding, dislocation, clogging),
   b. PEG feeding proved to have higher subjective and social acceptance, being less stigmatizing, and had reduced rates of oesophageal reflux and aspiration pneumonia. **(6-10)** 13–17
   c. Interestingly it was clearly shown that with regard to nutritional efficacy PEG feeding was superior too. **(7,10)** 14,17
   d. Therefore, in our present understanding, feeding via PEG should be preferred if it can be expected that the patient's nutritional intake is likely to be inadequate and supplementary artificial enteral nutrition is necessary for a period exceeding 2–3 weeks.

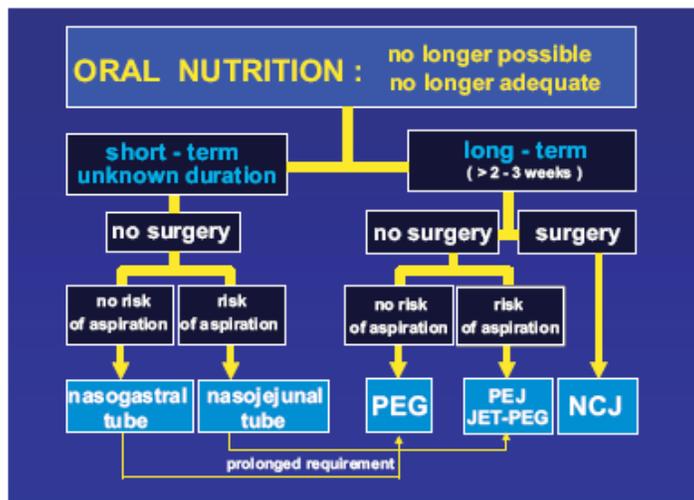4. Decision Tree for gastrointestinal access:

Figure 1 Decision tree for the selection of the appropriate tube system for enteral nutrition (for explanation,
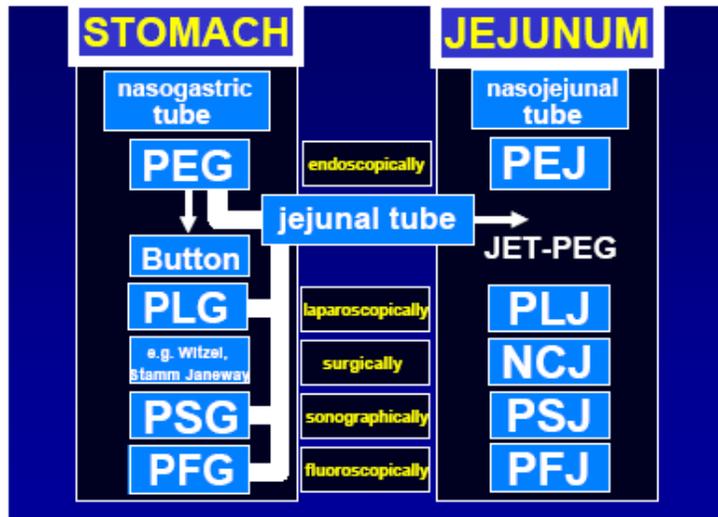
Figure 2 General techniques and modified methods of placement of enteral tube systems for gastric and jejunal nutrition: PEG, Percutaneous Endoscopic Gastrostomy; PLG, Percutaneous Laparoscopic Gastrostomy; PSG, Percutaneous Sonographically Guided Gastrostomy; PFG, Percutaneous Fluoroscopically Guided Gastrostomy; PEJ, Percutaneous Endoscopic Jejunostomy; JET-PEG, Jejunal Tube PEG; PLJ, Percutaneous Laparoscopic Jejunostomy; NCJ, Fine Needle Catheter Jejunostomy; PSJ, Percutaneous Sonographically Guided Jejunostomy; PFJ, Percutaneous Fluoroscopically Guided Jejunostomy.

5. **Indications: (4,5,11-15)** 4–8,42,43
    a. As a general rule, PEG feeding should be considered if it is expected that the patient's nutritional intake is likely to be qualitatively or quantitatively inadequate for a period exceeding 2–3 weeks.
    b. It is important to try supplementary oral nutrition by special drinks and individual nutritional and swallowing advice first; but if this does not stabilize or improve the patient's situation additional enteral nutrition via PEG should be considered early in ongoing diseases in order to stop the deterioration of the nutritional status and consecutively to stabilize and even improve individual quality of life.
    c. The primary aim of enteral tube feeding is:
        i. to avoid further loss of body weight,
        ii. to correct significant nutritional deficiencies,
        iii. to rehydrate the patient,
        iv. to promote growth in children with growth retardation,
        v. and to stop the related deterioration of the quality of life of the patient due to inadequate oral nutritional intake.
    d. With this aim in view, the range of indications for the use of a PEG tube is wide.
        i. Oncological disorders (stenosing tumours in the ear, nose and throat region or the upper gastrointestinal tract; PEG tubes may be used palliatively in inoperable cases or placed prior to surgery, radiotherapy or chemotherapy

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and removed when the patient has recovered and has a reliable and adequate oral intake).

    ii.   Neurological disorders (dysphagic states after cerebrovascular stroke or craniocerebral trauma, and in patients with cerebral tumours, bulbar paralysis, Parkinson's disease, amyotrophic lateral sclerosis, cerebral palsy).

    iii.   Other clinical conditions (wasting in AIDS, shortbowel syndrome, reconstructive facial surgery, prolonged coma, polytrauma, Crohn0s disease, cystic fibrosis, chronic renal failure, congenital abnormalities, e.g. tracheo-oesophageal fistula).

    iv.   Another indication for use of a PEG system is the palliative drainage of gastric juices and secretions in the small intestine in the presence of a chronic gastrointestinal stenosis or ileus.

6.   Impact of PEG placement on outcome:
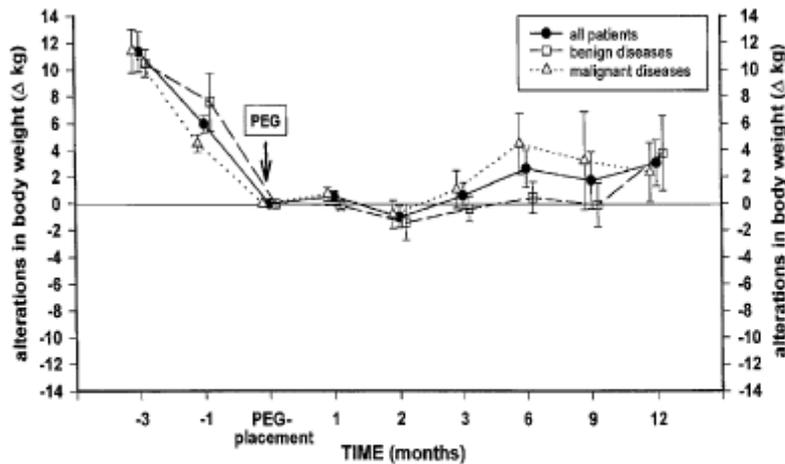
Figure 3 Time-course of body weight in all patients ($n = 210$) and separately in patients with benign or malignant underlying disease retrospectively for 3 months before and prospectively 12 months after PEG placement (Löser et al., Dig Dis Sci 1998; 43: 2549-2557; for comments, see text).

7. **Contraindications for the use of PEG/PEJ systems: (11-13)** 6–8
    a.   Serious coagulation disorders (INR>1.5, Quick<50%, PTT450 s plateletso50,000/mm3),
    b.   Interposed organs (e.g. liver, colon),
    c.   marked peritoneal carcinomatosis,
    d.   severe ascites, peritonitis,
    e.   anorexia nervosa,
    f.   severe psychosis

8.   Procedures:
    a.   As the endoscopic insertion of an enteral feeding tube represents an elective invasive procedure and physical injury from the legal point of view, it is essential to obtain legally valid consent. (16) 41

b. The adult patient should be fasted for at least 8 h prior to the procedure for insertion of a PEG system, or longer in cases in which there is evidence of impairment of gastric motility.

c. Antibiotic: Currently, there is a controversial debate in the literature as to whether a single dose of an antibiotic (e.g. 2 g of a cephazolin i.v.), as a general prophylaxis, provides effective protection against inflammatory complications (for an overview, see).(17,18) 68,69

     i. At present, there are more published studies in which a clinical benefit of a single administration of an antibiotic has been demonstrated, (19-24) 70–75 while there are two studies in which no advantage in respect of the prevention of wound infection was found.(25,26) 76,77

     ii. Additionally, one recently published meta-analysis (18) 69 confirmed the clinical benefits of a single-shot antibiotic prophylaxis.

References:

1. Main reference: Chr. Lo¨ser (a), G. Aschl (b), X. He´buterne (c), E.M.H. Mathus-Vliegen (d), M. Muscaritoli (e), Y. Niv (f), H. Rollins (g), P. Singer (h), R.H. Skelly (i)ESPEN guidelines on artificial enteral nutrition—Percutaneous endoscopic gastrostomy (PEG). Clinical Nutrition (2005); 24: 848–861.
2. (2) Ho CS, Yee ACN, McPherson R. Complications of surgical and percutaneous nonendoscopic gastrostomy: review of 233 patients. Gastroenterology 1988; 95:1206–10.
3. (3) Grant JP. Comparison of percutaneous endoscopic gastrostomy with Stamm gastrostomy. Ann Surg 1988; 207: 598–603.
4. (4) Lo¨ser Chr, Wolters S, Fo¨lsch UR. Enteral long-term nutrition via percutaneous endoscopic gastrostomy (PEG) in 210 patients: a four-year prospective study. Dig Dis Sci 1998; 43:2549–57.
5. (5) Lo¨ser Chr, von Herz U, Ku¨chler Th, Rzehak P, Mu¨ller MJ. Quality of life and nutritional state in patients on home enteral tube feeding. Nutrition 2003;19:605–11.
6. (13) Mekhail TM, Adelstein DJ, Rybicki LA, et al. Enteral nutrition during the treatment of head and neck carcinoma: is a percutaneous endoscopic gastrostomy tube preferable to a nasogastric tube? Cancer 2001;91:1785–90.
7. (14) Park RH, Allison MC, Lang J, et al. Randomised comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding in patients with persisting neurological dysphagia. BMJ 1992;304:1406–9.
8. (15) Baeten C, Hoefnagels J. Feeding via nasogastric tube or percutaneous endoscopic gastrostomy. Scand J Gastroenterol 1992;27(suppl 194):95–8.
9. (16) Wicks C, Gimson A, Vlavianos P, et al. Assessment of the percutaneous endoscopic gastrostomy feeding tube as part of an integrated approach to enteral feeding. Gut 1992; 33: 613–6.
10. (17) Norton B, Homer-Ward M, Donnelly MT, Long RG, Holmes GKT. A randomised prospective comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding after acute dysphagic stroke. BMJ 1996;312:13–6.
11. (6) American Society For Gastrointestinal Endoscopy. Role of PEG/PEJ in enteral feeding. Gastrointest Endosc 1998; 48: 699–701.
12. (7) French Society of Digestive Endoscopy. Guidelines of the French Society of Digestive Endoscopy (SFED): Endoscopic Gastrostomy. Endoscopy 1999; 31(2): 207–8.
13. (8) Lo¨ser Chr, Fo¨lsch UR. Guidelines of the German Association of Gastroenterology (DGVS)—Percutaneous endoscopic gastrostomy (PEG). Z Gastroenterol 1996; 34: 637–41.
14. (42) Lo¨ser C. Clinical aspects of long-term enteral nutrition via percutaneous endoscopic gastrostomy (PEG). J Nutr Health Aging 2000;4:47–51.

15. (43) Aschl G, Kirchgatterer A, Allinger S, et al. Indikationen und Komplikationen der perkutanen endoskopischen Gastrostomie. Wien klin Wochenschr 2003;115:115–20.
16. (41) Lennard-Jones JE. Ethical and legal aspects of clinical hydration and nutritional support. BJU Int 2000; 85: 398–403.
17. (68) Lo¨ser Chr, Keymling M. Antibiotic prophylaxis during placement of percutaneous endoscopic gastrostomy tubes (PEG tubes). Z Gastroenterol 2000;38:271–3.
18. (69) Sharma VK, Howden SW. Meta-analysis of randomized, controlled trials of antibiotic prophylaxis for PEG. Am. J. Gastroenterol 2000;95:3133–6.
19. (70) Ahmad A, Mouncher A, Abdoolah R, et al. Antibiotic prophylaxis for percutaneous endoscopic gastrostomy : a prospective, randomised, double-blind trial. Aliment Pharmacol Ther 2003;18:209–15.
20. (71) Akkersdijk WL, van Bergeijk JD, van Egmond T, et al. Percutaneous endoscopic gastrostomy (PEG): comparison of push and pull methods and evaluation of antibiotic prophylaxis. Endoscopy 1995;27:313–6.
21. (72) Dormann AJ, Wigginghaus B, Risius H, et al. A single dose of ceftriaxone adminstered 30 minutes before percutaneous endoscopic gastrostomy significantly reduces local and systemic infective complications. Am J Gastroenterol 1999;94:3220–4.
22. (73) Gossner I, Keymling J, Hahn EG, Ell C. Antibiotic prophylaxis in percutaneous endoscopic gastrostomy (PEG): A prospective randomized clinical trial. Endoscopy 1999;31:119–24.
23. (74) Jain NK, Larson DE, Schroeder KW, et al. Antibiotic prophylaxis in percutaneous endoscopic gastrostomy Ann Int Med 1987;107:824–8.
24. (75) Preclik G, Gru¨ne S, Leser HG, et al. Prospective, randomised, double blind trial of prophylaxis with single dose of co-amoxiclav before percutaneous endoscopic gastrostomy. BMJ 1999;319:881–4.
25. (76) Jonas SK, Neimark S, Panwalker AP. Effect of antibiotic prophylaxis in percutaneous endoscopic gastrostomy. Am J Gastroenterol 1985;80:438–41.
26. (77) Sturgis TM, Yancy W, Cole JC, Proctor DD, Minhas BS, Marcuard SP. Antibiotic prophylaxis in percutaneous endoscopic gastrostomy. Am J Gastroenterol 1996;91: 2301–4.

SAFE PRACTICE OF PARENTERAL NUTRITION

SECTION I: INTRODUCTION

Over the past three decades, parenteral nutrition (PN) has become an important adjunctive therapy in a variety of disease states. Parenteral nutrition formulations are extremely complex admixtures containing amino acids, dextrose, lipids, water, electrolytes, trace elements, and vitamins & 40 or more components. Parenteral nutrition refers to all PN formulations; total nutrient admixtures (TNA) are PN formulations that include intravenous fat emulsions (IFE); and 2 in 1 formulations are PN formulations that do not include IFE. Early PN programs focused on minimizing the frequency, severity, and type of complications that could result from this therapy.

The interdisciplinary approach was found to improve efficacy, reduce complications, and facilitate efficient, cost-effective PN therapy. Despite the highly successful use of PN for many years, the following adverse events demonstrate that errors in managing this complicated therapy can result in serious harm and even death:

- two deaths related to errors in PN compounding led to a Safety Alert being issued by the US Food and Drug Administration (FDA) (1). Autopsy of the patients involved found diffuse microvascular pulmonary emboli. There were also at least two other cases of respiratory distress occurring in patients at the same institution. These patients had received total nutrient admixtures (TNA) thought to contain a precipitate of calcium phosphate that resulted from improper admixture practices in the pharmacy.
- hospital personnel misinterpreted the dextrose content on the label of a PN formulation used in home care, which resulted in a pediatric patient's death.2 The home care label read: "300 mL of 50% dextrose." The hospital pharmacy interpreted this as a final concentration of dextrose 50% (more than twice the maximal concentration normally or typically used in PN therapy). The patient died after 2 days of receiving infusion of the incorrect formula.
- two other fatal incidents have been reported involving pharmacy compounding operations for pediatric dextrose solutions.3 One infant was overdosed with dextrose when the PN was prepared with amino acids and two bags of 50% dextrose in place of one bag of 50% dextrose and one bag of sterile water. The other infant was underdosed with dextrose while receiving a 1.75% final concentration of dextrose solution rather than a 17.5% concentration.
- another PN formulation was compounded with no dextrose, resulting in irreversible brain damage when administered to a neonate.(4)
- an incident involving the misinterpretation of a label resulted in iron overload and liver toxicity in a child receiving PN with iron dextran.5 In this case, the PN label read, "iron dextran 1 mL," the intention being to use a 1-mg/mL concentration prediluted by the pharmacy. However, the solution containing the undiluted, 50-mg/mL concentration was used in compounding and resulted in a 50-fold error in the dose administered.
- four children were infected, two of whom died as a result of receiving contaminated PN admixtures.6 *Enterobacter cloacae* was cultured from disposable tubing that was used in the automated compounding of these PN admixtures.

As a result of these events, in 1995 A.S.P.E.N. established the National Advisory Group (NAG) on Standards and Practice Guidelines for Parenteral Nutrition. The purpose of this group was to identify problem areas in PN therapy specifically related to pharmacy practice and to make recommendations and guidelines that foster safe practices based on experience and the literature. It is realized that these recommendations may result in significant changes in practice related to

prescribing, compounding, labeling, and administering PN, but these examples prove that inconsistent practices within hospitals and other health care environments have the potential to cause harm. Pharmaceutical problem areas identified by the group were as follows: PN labeling, compounding, formulas, stability, and filtering. Guidelines will be presented in a format similar to the A.S.P.E.N. *Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients,*(7) beginning with a background of the issue, then rationales of various methods to address the issue, followed by a list of practice guidelines based on consensus of the NAG members, and concluding with a summary of areas in which further research is needed and references supporting the evidence presented.

References

1. Food and Drug Administration. Safety Alert: Hazards of precipitation associated with parenteral nutrition. Am J Hosp Pharm 1994;51:1427-8.
2. Carey LC, Haffey M. Incident: Home TPN formula order misinterpreted after hospital admission. Home Care Highlights 1995(spring):7.
3. Cobel MR. Compounding pediatric dextrose solutions. Medication error alert. ASHP Newsletter 1995(Aug):3.
4. Gebbart F. Test hyperal solutions? Florida mom says yes. Hosp Pharm Report 1992(Feb):35.
5. Iron overdose due to miscommunication of TPN order. Error alert. Pharmacy Today. 1995(Sep).
6. Two children die after receiving infected TPN solutions. Pharm J 1994(Aug):3.
7. A.S.P.E.N. Board of Directors. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. JPEN 1993; 17 (Suppl):4SA

SECTION II: LABELING PARENTERAL NUTRITION FORMULATIONS

Background

The manner in which PN ingredients are labeled varies considerably. PN base components (dextrose, amino acids, and IFE) are labeled as:
- the volume of the percent of original concentration added (250 ml of 50% dextrose),
- the percent of final concentration after admixture (25% dextrose), and
- the grams per liter or grams in the total volume of PN admixed (250 g per liter or 375 g per total volume).

Additives, especially electrolytes, are labeled as millimoles or millequivalents per liter or per volume. For example, sodium chloride (NaCl) in a dose of 80 mEq/L admixed in a PN with a volume of 2 liters may be labeled as follows:
- NaCl 80 mEq/L
- NaCl 160 mEq per total volume
- Na 80 mEq/L, Cl 80 mEq/L
- Na 160 mEq and Cl 160 mEq per total volume.

This lack of standardization causes a great deal of confusion when patients are transferred between healthcare environments. As such, an essential component of a patient transfer between healthcare environments is a pharmacist-to-pharmacist interaction to resolve potential problems with transfer of the prescription. Misinterpretation of a PN label that led to a patient death (1) exemplifies what may occur if this interaction is not performed. To avoid misinterpretation, the

labels for PN admixtures should be standardized. All PN labels in any health care environment must express clearly and accurately what the patient is receiving at any time.

Each method of labeling has distinct advantages and disadvantages. The use of the percent of original dextrose or amino acid concentration is specific for the product used by the pharmacy in compounding the PN admixture. However, interpretation of this label requires a knowledge of pharmaceutical calculations in order to determine the nutrient value of the PN admixture. This requires training professionals in several health care disciplines to determine the nutrient value of the PN admixture being administered. Using the percent of final concentration of dextrose, amino acids, or fat still requires calculations to determine the caloric value or dose being administered, but it is traditionally the most accepted type of label because it is consistent with the label of the original products as shipped from the manufacturer. To minimize calculation errors and provide a label more consistent with dispensing a PN admixture as a nutrient, some programs have used grams of base components per liter. This simplifies the conversion of the nutrients to calorie and gram doses being provided, but still must be converted to daily doses. This label also supports those programs that only compound PN admixtures in liter quantities so that prescriptions may be written as quantity per liter and thus consistent with the additive as it appears on the label.

Finally, grams per total volume, with use of a 24-hour nutrient infusion system is most consistent with that of a nutrient label, requiring the least number of calculations to determine the calorie or gram dose per day. It also supports the most cost-effective system of PN compounding and delivery, which is the 24-hour nutrient infusion system.2 This system has been determined to decrease PN wastage and to reduce personnel time in compounding and administering PN. Conceptually, this system is successful when acute electrolyte disorders are managed separately from the PN until the time that electrolyte changes in the PN go into effect. This system also requires the use of automated compounding devices, which have been shown to be more accurate and faster than gravity-fill PN admixture systems.

PN Label Template

The sample PN label templates provide a format to standardize labels for adult, pediatric and neonatal patients. A supplemental label template for IFE is also provided for those instances when IFEs are administered separate from the PN admixture. Due to the complex nature of the label, there are several points that should be clarified:

- The amount per day is the only column required on the label, but some programs accustomed to amounts per liter may supplement the label by adding a second column reflecting quantities per liter in parenthesis. The components are labeled as amount per day to facilitate review of the order for appropriate nutrient doses. However, certain additives expressed as quantity per liter and as labeled in parenthesis in the PN label template may be useful to the clinician in determining whether the PN may be infused via peripheral or central vein. Those familiar with ordering PN electrolytes (similar to other intravenous fluids) as mEq/L, will be able to interpret the mEq/L electrolyte content easier if provided in this format on the PN label. Finally, many programs order additives as quantity/liter. Labeling as such allows for the final check of the PN by the nurse versus the physician s order prior to its administration. This final check to confirm that the PN content is the same as the physician s order is an essential component of the PN system. Care should be taken in developing a label that is clear and concise and of a size that fits neatly on the PN admixture. Accordingly, some may chose to dispense the PN with a supplemental form providing these optional details that may also be used for documenting PN administration in the patient s chart.

- The PN label specifies the route of administration.
- The administration date and time and expiration date and time are expressed clearly on the label. The administration date, as the term denotes, is the date and time the PN is scheduled to be administered to the patient. This may be the same day as compounding and is different than the date and time of admixture which should be included on the compounding worksheet but is not necessary on the label.
- The dosing weight is provided so that anyone evaluating the contents of the label may determine if the doses of nutrients are appropriate. Dosing weight refers to the weight used in calculating nutrient doses and may be the patient s actual, ideal, dry or adjusted body weight.
- The phosphorus content is provided as both the mmol quantity of phosphorus as well as the milliequivalent quantity of the additive salt s cation; potassium or sodium.
- If the PN admixture includes overfill, it is clearly stated on the label.
- Rate is expressed in mL/hr over 24 hours. If the PN admixture is cycled, the infusion duration and rates are to be expressed on the label.
- For home care, additives to be admixed at home are labeled as Patient Additives.
- An auxillary label may also be desired that would list the individual electrolytes as milliequivalents, and the phosphorus content as millimoles provided per day. The auxillary label could also express the amount of total and nonprotein calories provided per day, as well as the percent of total and nonprotein calories provided by carbohydrate and fat.
- Notation of who prepared and checked the PN admixture is not required on the label if this is done on a compounding worksheet maintained in the pharmacy.
- If IFE are not included in the PN admixture, this line may be omitted from the label.

Practice Guidelines

1. The labels for PN admixtures should be standardized.

   - The amount per day is the only column required on the label for the base formula, electrolyte additives, micronutrients and medications. This supports the use of the 24-hour nutrient infusion system.
   - Using the quantity per liter option in parentheses supports those programs that continue to admix PN in 1 liter volumes.
   - The dosing weight is required on the label.
2. Auxillary labels or information may be used, especially when PN orders are written in a different format than the label.
3. Patient transfer between healthcare environments requires pharmacist-to-pharmacist communication regarding the accurate transfer of the PN prescription.
4. The PN label is compared to the physician s order and for expiration date prior to administration.

Areas Requiring Further Work

The concepts used in developing the practice guidelines were developed for hospitalized patients and for institutions and organizations having a consistent number of patients receiving PN therapy. It is assumed that these concepts apply to alternative health care settings, as well as those hospitals having only a few patients receiving PN. It may be that the cost of implementing a once-per-day nutrient infusion system that includes automated compounding would be excessive for pharmacies with small numbers of patients receiving PN. Various alternatives to achieving the

concepts for labeling in these circumstances may be successful but have not yet been determined objectively.

References

1. Carey LC, Haffey M. Incident: Home TPN formula order misinterpreted after hospital admission. Home Care Highlights 1995(spring) 7.
2. Mirtallo JM, Jozefzcyck KG, Hale KM, et al. Providing 24-hour nutrient infusions to critically ill patients. Am J Hosp Pharm 1986;43:2205-8.

Standard PN Label Template
Adult Patient

Institution/Pharmacy Name, Address and Pharmacy Phone number		
Name	Dosing Weight	Location
Administration Date/Time	Expiration Date/time	

Base Formula	Amount/day	(Amount/L)
Dextrose	**g**	(g/L)
Amino acids[a]	**g**	(g/L)
Lipid[a]	**g**	(g/L)

Electrolytes		
Sodium chloride	**mEq**	(mEq/L)
Sodium acetate	**mEq**	(mEq/L)
Potassium chloride	**mEq**	(mEq/L)
Potassium acetate	**mEq**	(mEq/L)
Potassium phosphate	**mmol of P**	(mmol/L)
	(mEq of K)	(mEq/L)
Sodium phosphate	**mmol of P**	(mmol/L)
	(mEq of Na)	(mEq/L)
Calcium gluconate	**mEq**	mEq/L)
Magnesium sulfate	**mEq**	(mEq/L)

Vitamins, trace elements and medications		
Multiple vitamins[a]	**mL**	
Multiple trace elements[a]	**mL**	
Insulin	**Units**	(Units/L)
H$_2$ - antagonists[a]	**mg**	

Rate _____ mL/hr   Volume _____ mL   Infuse over 24 hours

Admixture contains_____ mL plus _____mL overfill

Central Line Use Only

[a] Specify product name.

g = gram.

Standard PN Label Template
Neonate or Pediatric Patient

Institution/Pharmacy Name, Address and Pharmacy Phone number		
Name	Dosing Weight	Location
Administration Date/Time	Expiration Date/time	

Base Formula	Amount/kg /day	Amount/day
Dextrose	g/kg	g
Amino acids[a]	g/kg	g

Electrolytes

Sodium chloride[b]	mEq/kg	mEq
Sodium acetate[b]	mEq/kg	mEq
Potassium chloride[b]	mEq/kg	mEq
Potassium acetate[b]	mEq/kg	mEq
Potassium phosphate[b]	mmol of P/kg	mmol of P
	(mEq of K)/kg	(mEq of K)
Sodium phosphate[b]	mmol of P/kg	mmol of P
	(mEq of Na)/kg	(mEq of Na)
Calcium gluconate	mEq/kg	mEq
Magnesium sulfate	mEq/kg	mEq

Vitamins, trace elements and medications

Multiple vitamins[a]	mL/kg	mL
Multiple trace elements[a]	mL/kg	mL
L-cysteine	mg/kg	mg
H_2 antagonists[a]	mg/kg	mg

Rate _____ mL/hr   Volume _____ mL   Infuse over 24 hours

Admixture contains _____ mL plus _____mL overfill

Central Line Use Only

[a] Specify product name.

[b] Since the admixture usually contains multiple sources of sodium, potassium, chloride, acetate, and phosphorus, the amount of each electrolyte/kg provided by the PN admixture is determined by adding the amount of electrolyte provided by each salt.

```
                    Standard IFE Label Template
                   Adult, Neonate or Pediatric Patient

    ┌──────────────────────────────────────────────────────────┐
    │ Institution/Pharmacy  Name, Address and Pharmacy Phone Number │
    Name                          Dosing Weight          Location
    Administration Date/Time                   Expiration  Date/time



                              Volume            Amt/kg /day   Amt/day

    Intravenous fat emulsion(%)      _____ mL          g/kg          g



                 Infusion rate _____mL/hr   Infuse over _____ hours

              Contains overfill - Discard any unused volume after 24 hours

                 ***For peripheral or central line administration***
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SECTION III: STANDARD NUTRIENT RANGES & SAMPLE PN FORMULATIONS

Background

Parenteral nutrition formulations should be designed to meet the estimated nutrition requirements for each individual patient. However, the pharmacist needs to be able to recognize when the amount of nutrient ordered for a patient is not within an acceptable standard range. The ordered quantity of protein, carbohydrate, fat, electrolytes, fluid, vitamins, and trace elements should all be assessed for appropriateness before compounding. Acceptable ranges for each of these nutrients should be based on compatibility, stability, and normal clinical requirements. It is not the intent of this document to provide guidelines on the nutrient requirements in various disease states and
conditions. Rather, the purpose of providing standard nutrient ranges is to serve as a reference point and guide the pharmacist in safe practice. The standard nutrient ranges apply to adult and pediatric patients with normal organ function.

Sample PN formulations are provided to illustrate use of the standard PN label template in the adult and pediatric patient. The sample formulations have been designed to provide nutrients within the standard ranges established. Some institutions may find it helpful to develop order forms for standard PN formulations that apply to specific patient populations with normal organ function. This may aid the prescriber in designing a complete, balanced, and physically compatible PN formulation that adequately meets the estimated daily nutritional requirements in that patient population.

Standard Nutrient Ranges

Standard ranges for protein and calories for adults should be based on actual body weight, or an estimated dosing weight if actual weight is >120% of ideal body weight. Various published guidelines are available that attempt to estimate dosing weight in obese patients.(1) See Table 1 for general guidelines for protein, calorie, and fluid requirements in adult patients. The standard distribution of nonprotein calories is 70-85% as carbohydrate and 15-30% as fat. This distribution may be adjusted based on tolerance; however, there is limited clinical benefit when fat content exceeds 30% of nonprotein calories.2 In adult patients, it is recommended that the fat content of the PN formulation not exceed 2.5 g/kg/day and carbohydrate content not exceed approximately 7 g/kg/day.

Standard ranges for electrolytes, vitamins, and trace elements in adult patients with normal organ function are provided in Tables 2 through 4. Sodium and potassium requirements for a given patient are highly variable and generally not limited by compatibility restraints. In general, sodium and potassium requirements in the PN formulation are 1-2 mEq/kg/day, but should be customized to meet individual patient needs. Chloride and acetate content should be adjusted to maintain acid-base balance. In general, acid-base balance can be maintained by using approximately equal amounts of chloride and acetate, but may require adjustment based on the clinical situation. Amino acid solutions themselves contain various amounts of chloride and acetate, depending on the individual product, for buffering purposes.3 For this reason, it is necessary to state the specific amino acid product name used in compounding on the PN label. It is not necessary, however, to list the amount of chloride, phosphorus, and acetate from the amino acid solution on the PN label as this may lead to confusion.

Guidelines for parenteral vitamin requirements in adults have been established by the Nutrition Advisory Group (NAG) of the Department of Foods and Nutrition, American Medical Association (AMA).(4) The AMA-NAG does not include vitamin K as part of the multivitamin formulation in order to avoid interactions in patients receiving oral anticoagulants. However, patients receiving PN, especially those also receiving antibiotic therapy, may require vitamin K supplementation. The AMA-NAG suggests the parenteral vitamin K supplementation of 2-4 mg/week in PN patients not receiving oral anticoagulation therapy. The patient s prothrombin time (PT) or international normalized ratio (INR) should be monitored for signs of vitamin K deficiency to determine the need for vitamin K supplementation.

The AMA-NAG also published recommendations for the parenteral administration of chromium, copper, manganese, and zinc.(5) The guidelines should be considered approximations, and it should be recognized that variations among individual patients may exist. For example, supplementation of selenium 20-60 mcg/day is recommended in patients receiving long-term PN. Routine iron supplementation to PN formulations is not recommended.

Table 1. Daily Protein & Calorie Requirements for the Adult. [a]

Protein	
Maintenance	0.8-1.0 g/kg
Catabolic patients	1.2-2 g/kg
Energy	
Total calories	25-30 kcal/kg
Volume	20-40 mL/kg

[a] Assumes normal organ function.

Table 2. Daily Electrolyte Additions to Adult PN Formulations. [a]

Electrolyte	Parenteral Equivalent of Recommended Dietary Allowance	Standard Intake
Calcium	10 mEq	10-15 mEq [b]
Magnesium	10 mEq	8-20 mEq
Phosphate	30 mmol	20-40 mmol [b]
Sodium	N/A	1-2 mEq/kg + replacement
Potassium	N/A	1-2 mEq/kg
Acetate	N/A	As needed to maintain acid-base balance
Chloride	N/A	As needed to maintain acid-base balance

[a] Assumes normal organ function.
[b] See Section V for compatibility guidelines.
N/A = non-applicable

Table 4. Daily Trace Element Supplementation to Adult PN Formulations. [a]

Trace Element	Intake [5,6]
Chromium	10-15 mcg
Copper	0.3-0.5 mg
Manganese	60-100 mcg
Zinc	2.5-5 mg

[a] Assumes normal organ function.

Table 3. Daily Vitamin Supplementation to Adult PN Formulations.[a, b]

Vitamin	Intake
Thiamin (B1)	3 mg
Riboflavin (B2)	3.6 mg
Niacin (B3)	40 mg
Folic acid	400 mcg
Pantothenic acid	15 mg
Pyrodoxine (B6)	4 mg
Cyanocobalmin (B12)	5 mcg
Biotin	60 mcg
Ascorbic Acid (C)	100 mg
Vitamin A	3300 IU
Vitamin D	200 IU
Vitamin E	10 IU

[a] Assumes normal organ function.

[b] Vitamin K supplementation 2-4 mg/week in PN patients not receiving oral anticoagulation therapy.

Standard nutrient ranges for infants and children receiving PN have been established. Rapidly changing organ function, metabolic immaturity, and normal but rapid weight gain, particularly in neonates and infants, result in age-related descriptors of nutrient need. Therefore, each table characterizes ranges for neonates, infants, children, and occasionally, adolescents (Tables 5 through 7). As can be readily appreciated, requirements for fluids, protein, and energy are substantially higher on a unit-of-weight basis for children than for the adult. The addition of Lcysteine HCl as an admixture just prior to PN administration is recommended by manufacturers of neonatal/infant amino acid formulations. The most commonly recommended dose is 40 mg Lcysteine HCl per gram amino acids. Current practice suggests supplementation with L-cysteine HCl for the first year of life, although practice varies widely. The distribution of PN nonprotein calories for pediatric patients does not vary significantly from that for the adult receiving PN; however, it is worth noting that the typical enteral diet of the neonate or infant derives approximately 50% of nonprotein calories from fat. Therefore, a PN solution appears less physiologically similar to standard enteral feedings in the neonate or infant than in the older child and adult. For the purposes of this document, calories will be non-protein calories when referring to the pediatric population, particularly the neonatal/infant population. Because of rapid growth with associated increase in lean body mass, it is desirable to consider protein for its protein synthetic role and not merely as a calorie source. Ranges for calories and protein for adults should be used for an individual >18 years of age.

There is growing evidence that the 20% IFE is the preferred product for use in the neonate and infant. In addition to its greater calorie content per unit volume, the lower content of surface active agents (egg phosphatides) per gram fat results in more normal concentrations of components of circulating lipoproteins, especially low density lipoproteins8. In the very low birth weight infant, the use of the 20% IFE does require accurate and low flow pump delivery systems. Currently the American Academy of Pediatrics (AAP) recommends the delivery of IFE over 20 to 24 hours per day with a limit of 4 g/kg/day9. In general, 3 g/kg/day is the accepted limit for IFE administration in the small for gestational age neonates and preterm neonates less than 32 weeks gestational age.

Standard ranges for electrolytes, minerals, vitamins, and trace elements for infants and children with normal organ function are found in Tables 8 through 10. Calcium and phosphate requirements of the neonate and infant are substantially different from those of the older child and are dramatically different from the requirements for the adult (Table 8). These differences in mineral needs are reflected in the composition of neonatal and infant formulas and human milk. When one attempts to meet these increased requirements in pediatric PN solutions, problems can arise because of incompatibility of calcium and phosphate salts in aqueous solution (addressed in greater detail in Section V). In general, adult doses of electrolytes should be used for a child who weighs more than 50 kg.

Guidelines for vitamin and trace element additions to PN solutions for pediatric patients up to age 11 have been published (10). Adult multivitamins should be used for a child who weighs more than 40 kg. As for adults, the guidelines should be considered approximations of need, with individual patient variation to be expected. The long-term use (home PN) of multi-trace element products at recommended doses is associated with excessive blood concentrations of chromium(11). The ratio of trace elements in commercially available products for pediatric use result in excessive intake of manganese if recommended doses of zinc are given. It is clear that micronutrient requirements for children receiving TPN is a fertile area for research and an area in which further commercial product development is required.

Table 5. Daily Fluid Requirements for Pediatric Patients [7]

Body Weight	Amount
<1500 g	130–150 mL/kg
1500–2000 g	110–130 mL/kg
2.5–10 kg	100 mL/kg
>10 kg–20 kg	1000 mL for 10 kg + 50 mL/kg for each kg >10
>20 kg	1500 mL for 20 kg + 20 mL/kg for each kg >20

Table 6. Daily Protein Requirements (g/kg) for Pediatric Patients[a]

Neonates	2.5–3.0
Infants	2.0–2.5
Children	1.5–2.0
Adolescents	0.8–2.0

[a] assume normal age-related organ function

Table 7. Daily Energy Requirements (nonprotein kcal/kg) for Pediatric Patients

Preterm neonate	120–140
<6 months	90–120
6–12 months	80–100
1–7 yr	75–90
7–12 yr	60–75
>12 - 18 yr	30–60

Table 8. Daily Electrolyte and Mineral Requirements for Pediatric Patients[a]

Electrolyte	Neonates	Infants/Children	Adolescents
Sodium	2–5 mEq/kg	2–6 mEq/kg	individualized
Chloride	1–5 mEq/kg	2–5 mEq/kg	individualized
Potassium	1–4 mEq/kg	2–3 mEq/kg	individualized
Calcium	3–4 mEq/kg	1–2.5 mEq/kg	10–20 mEq
Phosphorus	1–2 mmol/kg	0.5–1 mmol/kg	10–40 mmol
Magnesium	0.3–0.5 mEq/kg	0.3–0.5 mEq/kg	10–30 mEq

[a] assumes normal age-related organ function

Table 9. Daily Dose Recommendations for Pediatric Multiple Vitamins[a,b]

Manufacturer		NAG AMA	
Weight (kg)	Dose (mL)	Weight (kg)	Dose
1	2	<2.5	2 mL/kg
1–3	3.5	> 2.5	5 mL
> 3	5	—	—

Table 10. Trace Element Daily Requirements for Pediatrics[a,c]

Trace Element	Preterm Neonates (mcg/kg)	Term Neonates (mcg/kg)	<5 Years Old (mcg/kg)	Older Children and Adolescents
Zinc	400	300	100	2–5 mg
Copper	20	20	20	200–500 mcg
Manganese	1	1	2–10	50–150 mcg
Chromium	0.2	0.2	0.14–0.2	5–15 mcg
Selenium	2–3	2–3	2–3*	30–40 mcg
Iodide	1**	1**	1**	—

*Limit = 40 mcg/kg.
**Percutaneous absorption from protein-bound iodine may be adequate.

a	assumes normal age-related organ function
b	Pediatric multiple vitamin formulation (5 mL): A (IU) 2300, D (IU) 400, E (IU) 7, K (mcg) 200, C (mg) 80, B-1 (mg) 1.2, B-2 (mg) 1.4, B-3 (mg) 17, B-5 (mg) 1, B-12 (mcg) 1, Biotin (mcg) 20, Folic acid (mcg) 140.
c	Recommended intakes of trace elements cannot be achieved through the use of a single pediatric multi-trace product. Only through the use of individualized trace element products can recommended intakes of trace elements be reproduced. [6]

Sample PN Formulation
Adult Patient

Institution/Pharmacy Name, Address and Pharmacy Phone number

...ation

	Amount/day	(Amount/L)
	400 g	(166.7 g/L)
100 g		(41.7 g/L)
65 g		(27.1 g/L)

Electrolytes

	80 mEq	(33.3 mEq/L)
80 mEq		(33.3 mEq/L)
40 mEq		(16.7 mEq/L)
30 mmol of P		(12.5 mmol/L)
...5 mEq of K)		(18.8 mEq/L)
10 mEq		(4.2 mEq/L)
10 mEq		(4.2 mEq/L)

Vitamins, trace elements and medications

Multiple vitamins [a]	10 mL
Multiple trace elements [a]	1-3 mL [b]

Infuse over 24 hours

...dmixture contains 2400 mL plus 100 mL overfill

Central Line Use Only

[a] Specify product name.
[b] Volume dependent on specific product used.

Sample PN Formulation
Pediatric Patient

Patient Name	Dosing Weight	Location
Administration Date/Time		Expiration Date/Time
Base Formula	Amount/kg/day	Amount/day
Dextrose	20 g	300g
Amino Acids	2 g	30g
Electrolytes		
Sodium chloride	3mEq	45mEq
Sodium phosphate	0.7 mmol	10.5 mmol
	(0.9 mEq of Na)	(14 mEq of Na)
Potassium Chloride	1 mEq	15 mEq
Potassium acetate	0.7 mEq	10 mEq
Calcium gluconate	1 mEq	15 mEq
Magnesium sulfate	0.3 mEq	4.5 mEq
Vitamins, trace elements and medications		
Pediatric multivitamins	5mL	
Pediatric multiple trace	0.1mL	1.5mL
Infusion rate 50 mL/hr	Volume 1200 mL	Infuse over 24 hours

Admixture contains 1200 mL plus 100 mL overfill
Central Line Use Only

[a]   Specify product name
[b]   MVI-Pediatric^R
[c]   PTE-5^R

Sample Supplemental IFE Label:

Institution/Pharmacy Name, Address and Pharmacy Phone Number

Name	Dosing Weight 15 kg		Location	
Administration date/time			Expiration date/time	
	Volume	Amt/kg/day		Amt/day
IFE 20%	144 mL	1.9 g		28.8 g

Infusion rate: 6 mL/hr   Infuse over 24 hours

Combines with Pediatric PN formulation to provide 90 mL/kg/day and 87kcal/kg/day.

For peripheral or central line administration

Pediatric Patient

Sample PN Formulations:
Infant Patient

Institution Name, Address and Pharmacy Phone Number

Patient Name	Dosing Weight	Location
Administration Date/Time		Expiration Date/Time

Base Formula	Amount/kg/day	Amount/day
Dextrose	25 g	125g
Amino Acids	2.5 g	12.5g

Electrolytes		
Sodium chloride	2.5mEq	12.5mEq
Sodium phosphate	1.0 mmol	5.3 mmol
	(1.49 mEq of Na)	(7 mEq of Na)
Potassium Chloride	1 mEq	5 mEq
Potassium acetate	1 mEq	5 mEq
Calcium gluconate	2 mEq	10 mEq
Magnesium sulfate	0.4 mEq	2 mEq

Vitamins, trace elements and medications		
Pediatric multivitamins	0.25 mL	
Pediatric multiple trace	100 mg	500 mg

Infusion rate 21 mL/hr   Volume 504 mL   Infuse over 24 hours

Admixture contains 504 mL plus 50 mL overfill
Central Line Use Only

a	Specify product name
b	MVI-Pediatric[R]
c	PTE-5[R]

```
Sample Supplemental IFE Label:

┌─────────────────────────────────────────────────────────────────┐
│ Institution/Pharmacy Name, Address and Pharmacy Phone Number      │
└─────────────────────────────────────────────────────────────────┘

Name                 Dosing Weight 5 kg            Location
Administration date/time                           Expiration date/time

                     Volume        Amt/kg/day              Amt/day
IFE 20%              48 mL          1.9 g                   9 g


Infusion rate: 2 mL/hr               Infuse over 24 hours

Combines with infant PN formulation to provide 110 mL/kg/day and 104 kcal/kg/day.

        ***For peripheral or central line administration***

                        Infant Patient
```

Practice Guidelines

1. The development of order forms for standard adult and pediatric PN formulations may be a useful tool to aid the prescriber in designing a complete, balanced, and physically compatible formulation that adequately meets the estimated daily nutritional requirements in patients with normal organ function.
2. The pharmacist should assess the PN formulation to determine whether its contents are within an acceptable standard range based on the specific patient population (i.e. adult or
3. pediatric patient) or if a clinical disease state or condition warrants a dose outside of the standard range.

Areas Requiring Further Work

Further work is required to determine optimal parenteral trace element requirements in adult and pediatric patients and develop commercially available multi-trace element solutions which better meet these requirements. The use of currently available multi-trace element solutions may result in toxicity of certain trace elements in certain disease states. This problem may be compounded by trace element contamination, particularly aluminum, found in large volume parenterals and additives.

References

1. Ireton-Jones CS, Francis C. Obesity: nutrition support practice and application to critical care. Nutr Clin Pract 1995;10:144-149.
2. Delafosse B, Viale JP, Tissot S, et al. Effects of glucose-to-lipid ratio and type of lipid on substrate oxidation rate in patients. Am J Physiol 1994;267(5 Part 1): E775-80.
3. McEvoy, GK (ed). American Hospital Formulary Service (AHFS) Drug Information. American Society of Health-System Pharmacists Inc, Bethesda, MD, 1996.

4. American Medical Association Department of Foods and Nutrition, 1975. Multivitamin preparations for parenteral use: a statement by the Nutrition Advisory Group. JPEN 1979; 3:258-62.
5. American Medical Association Department of Foods and Nutrition. Guidelines for essential trace element preparations for parenteral use. A statement by an expert panel. JAMA 1979;241:2051-4.
6. Shils ME. Parenteral Nutrition. In: Shils ME, Olson JA, Shike M (eds). Modern Nutrition in Health an
7. Holliday MA, Seger WE. The maintenance need for water in parenteral fluid therapy. Pediatrics 1957;19:823%32.
8. Haumont D, Deckelbaum RJ, Richelle M, et al. Plasma lipid concentration in low birth weight infants given parenteral nutrition with twenty or ten percent lipid emulsion. J Pediatr 1989; 115:787-93.
9. Committee on Nutrition, American Acadamy of Pediatrics, Commentary on parenteral nutrition. Pediatrics 1983;71:547-52.
10. Green HL, Hambidge KM, Schanler R, et al. Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: Report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice Issues of the American Society for Clinical Nutrition. Am J Clin Nutr 1988;48:1324%42.
11. Moukarel AA, Song MK, Buchman AL, et al. Excessive chromium intake in children receiving total parenteral nutrition. Lancet 1992;339:385-8.

SECTION IV: EXTEMPORANEOUS COMPOUNDING OF PARENTERAL NUTRITION FORMULATIONS

Screening the Nutrient Prescription

Background

Serious disorders and death have been attributed to PN formulations having inappropriate nutrient compositions. Deficiencies of trace elements and essential fatty acids have been reported in both pediatric and adult patient populations.(1,2) The most dramatic, yet insidious, example of the dangers associated with the omission of micronutrients occurred during the national parenteral multivitamin shortage during the summer of 1988 (3) and throughout 1997. (4) At that time, omission of parenteral multivitamins resulted in three deaths of patients predisposed to vitamin deficiencies. Specifically, a refractory lactic acidosis led to the death of three patients associated with thiamin deficiency that was accentuated by the administration of dextrose in the PN admixture. Similarly, a death related to the omission of dextrose from a neonatal PN caused irreversible brain damage. Finally, life-threatening deficiencies have resulted when patients received phosphate-free PN.(5) Overdoses of nutrients included in PN may also be harmful. As explained in Section I, the incorrect admixture of PN resulting in excessive dextrose infusions led to a patient's death, and a 50-fold error in an iron dextran admixture caused serious liver damage in a child. In all these cases, there was inadequate review of the PN prescription for appropriateness of dose and adequacy of nutrient composition. It is the responsibility of the pharmacist to review each prescription for appropriate indication, dose, and route of administration, and the potential for drug-drug, drug-nutrient and drug-laboratory interactions.(5)

For those systems requiring that the PN prescription be rewritten each day, the potential exists for transcription errors that omit or significantly increase nutrient doses. In this regard, it is important

when refilling the day's order for PN therapy that the pharmacist review the contents of the PN for consistency with the previous day's prescription. Major deviations should be questioned to avoid nutrition-related complications. For example, the pharmacist should clarify with the prescribing physician a prescription for a patient if insulin was present in the previous day's order at a dose of 20 units and the present order is for 100 units without a change in the quantity of dextrose received between the two days. In this case, it is both appropriate and reasonable to question the order. Other orders that might be appropriately questioned are drug and nutrient quantities; other large-scale changes including omissions, dramatic increases, or decreases; and other types of extreme day-to-day fluctuations.

Practice Guidelines

1. The energy, protein, fluid, electrolyte, vitamin, trace element and medication content is reviewed for all PN prescriptions to assure that a complete and balanced nutrient formulation is provided. *Balanced* is defined as the presence of the proper proportion of calories, protein, electrolytes, trace elements, and vitamins to assure adequate use by and assimilation into the body.
2. Each of the PN components should be assessed for adequacy of dose and for the potential of a compatibility or stability problem. Any dose of a nutrient outside a normal range, that is *not* explained by an unusual patient condition or history, should be questioned and clarified before the PN is compounded.

Areas Requiring Further Work

Traditionally, the pharmacist is assigned the responsibility of verifying the indication, dose, and use of a drug or nutrient, as is the case with PN. It is recognized that because of the variety in the organization of nutrition support teams, this responsibility may be reassigned to other team members in addition to the pharmacist. Also, some computer programs for TPN admixture may be programmed to cue the pharmacist that the PN admixture is inappropriate when nutrient doses are outside an acceptable range.

PN Compounding

Background

The 1994 FDA Safety Alert (referred to in Section I) highlights the serious consequences that are possible when quality compounding practices are not in place. The responsibility of the dispensing pharmacist is to ensure that the PN is prepared, labeled, controlled, stored, dispensed, and distributed properly.(7) PN formulations are sometimes considered high-risk sterile products because of the large umber of chemical entities found in the admixture process and the complex nature of PN admixing, hether with gravimetric or automated compounding.(7,8,9) Serious harm may come to patients receiving a PN formulation that has precipitates resulting from a chemical interaction between nutrients that are present in too high a dose, exposed to extremes of temperature, or admixed in an improper sequence. Automated or manual methods of PN compounding are available. The compounding of the PN admixture can be accomplished manually through the separate addition of nutrients via syringe or needle delivery or with the aid of sterile solution transfer sets. The manual method allows the pharmacist to decide the order of mixing and should be carefully undertaken to avoid potentially lethal incompatibilities. Alternatively, automated compounding devices are widely available that admix PN under computer-assisted commands connected to special hardware housed with sterile, disposable compounding sets. Assistance in optimizing the compounding order for automated compounding

devices should be obtained through consultation with the manufacturer of macronutrients currently used at the institution because brand-specific issues might influence compatibility of the final formulation, as well as the manufacturer of the compounding device. Finally, there are premixed parenteral nutrition products that come in a variety of forms that include, for example, crystalline amino acids with electrolytes, amino acids/dextrose kits as either separate entities or in the same container separated by a divider that can be released or activated to produce the final admixture, or even an empty container as a dual-chamber bag. However, even these preassembled units of use packaging require some level of pharmaceutical compounding in an aseptic environment prior to use.

Observing the physical appearance of the final admixture is one of the most fundamental quality assurance measures that pharmacists routinely apply. Although it represents a crude measure of compatibility, it does identify gross particulate matter that likely represents the greatest clinical risk of embolic syndrome if infused to the patient. The process generally includes a detailed assessment of the final formulation against a dark background under high-intensity illumination. For translucent intravenous solutions, the highly trained eye is searching for the presence of insoluble particulate matter, such as "cores" from elastomeric vial enclosures, cotton fibers from alcohol wipes, etc, as well as characteristic indicators of incompatible formulation such as gas formation, turbidity or haziness, and crystal formation. It is important to remember that in the absence of any obvious physical signs of incompatibility, visual clarity does not equate with safety. Subvisible particulate matter may exist, yet still be capable of inducing an embolic syndrome that originates at the level of the capillaries. However, visual assessments are valuable and necessary in the routine quality assurance process, but they should be supplemented with other safety-enhancing measures that include sufficient documentation of the concentrations of nutrients prepared, use of filters in the manufacturing process or during the infusion, and possibly particle-size analysis when available. Documentation of the daily compounding activities for PN, irrespective of the products or procedures used, should exist that includes batch records for all formulations prepared, that are consistent with institutional policies and procedures.

For opaque parenteral dispersions such as total nutrient admixtures, visual assessments can still be performed. The principal aim of these assessments is focused on signs of phase separation, in which the unstable emulsion is manifested by the presence of free oil either as individually discernible fat droplets or a continuous layer at the surface of the formulation. In general, creaming is a common occurrence and not a significant determinant of infusion safety except in extreme cases.

Practice Guidelines

1. The additive sequence in compounding should be optimized and validated as a safe and efficacious method.
2. If the manual method currently in use at an institution has not been recently reviewed, or if the contract with a particular manufacturer of macronutrients is about to change, then a review of the compounding method is strongly recommended. This review should include an evaluation of the most current literature as well as consultation with the manufacturer when necessary.
3. Manufacturers of automated methods of PN compounding should provide an additive sequence that ensures the safety of the compounding device. This compounding sequence should be reviewed with the manufacturer of the parenteral nutrient products used by the institution. As most institutions in the U.S. are represented by buying groups with many participants, such buying groups should not only ensure the safety and support of the automated compounding device, but should avoid splitting PN contracts (mixing brands of

amino acids, dextrose and IFE) unless such combinations have adequate physiochemical data that ensures the stability, compatibility and safety of the final formulations commensurate with the data for single source PN products.

4. Each PN formulation compounded should be visually inspected for signs of gross particulate contamination, particulate formation and/or phase separation of TNAs.

Quality Assurance of the Compounding Process

Background

Numerous cases have been reported of adverse events associated with erroneous final concentrations of dextrose in parenteral fluids. Also, infectious events have occurred from microbial contamination of pharmacy-prepared PN formulations.(10) In-process or end-product testing of PN should be performed in accordance with USP standards and ASHP recommendations for sterile product admixture. (7-9) Because of the complex nature of PN formulations, these processes may be modified to accommodate the special physiochemical characteristics of PN with use of the methodologies for gravimetric, chemical, or refractometric analysis and in-process testing.

Gravimetric Analysis

Weight-based delivery of PN additives is the principal method by which automated compounders manufacture PN admixtures. These devices provide a high degree of accuracy and accomplish it in afraction of the time it takes with use of manual, gravity-fed compounding techniques. In general, as a final check of the admixture, the PN formulation is weighed and is expected to be within an acceptable margin of error. However, this evaluates only the accuracy of the total contents, and not individual additives. To ensure that certain additives having a narrow margin of safety are assessed individually, pharmacists can apply gravimetric techniques similar to those used by the compounding device. This is particularly important for additives such as potassium chloride and highly interactive salts such as phosphates. In the case of potassium chloride, a 2000-mL final PN volume with a 5% compounding error acceptance means that a 100-mL overfill would be tolerated. If the entire overfill came from the potassium chloride container(s), it could be lethal. Thus individual monitoring of certain PN additives is recommended, and this monitoring can be simply accomplished within the sterile compounding facility each day. The gravimetric method is preferred, with use of the analytical balance associated with the automated compounder.

Chemical Analysis

A random, but continuously applied assessment of the final glucose concentration is reasonable. One approach is through the use of glucose measuring devices that allow for *direct* assessment of the dextrose concentration. Although these instruments have a limited effective range of detection, appropriate dilutions may be made from a PN aliquot to measure the final concentrations of dextrose and to assure that they are in accordance with the prescribed quantities intended for the patient. When this quality assurance method is devised, it is important to outline a stepwise procedure, validate the findings against appropriate control glucose solutions, and apply the appropriate error analysis that
gauges an acceptable margin of error.

Refractometric Analysis

Refractometers have been used in pharmacy practice for determining dextrose content. However, they may require training and experience in order to obtain consistent and reliable results. In addition, because refractometry measures a physical characteristic of dextrose (ie, refractive index), it is an *indirect* determinant of dextrose concentration and is subject to interference by other components, as well as to variation in technique from one operator to another and in subsequent interpretation of the final results. As with direct measurement techniques of dextrose concentration, the procedures should be validated in a similar manner to ensure the integrity of the results. Refractometers are rendered inoperable with total nutrient admixtures, and therefore are of no use for these formulations.

In-Process Testing

There are three ways to test the integrity of the extemporaneous compounding process of PN formulations, and all three can be accomplished at any time before, during, or after the hours of operation for PN manufacturing. For purposes of this summary, "in-process" can include any one of the aforementioned periods. The amount of potassium chloride used after each stock bottle exchange, along with the appropriate density conversion for the additive tested, can be determined gravimetrically at multiple points during the day within the compounding facility. As long as the number of patients who received a portion of the stock from a container is properly recorded, the pharmacist can determine whether the delivery is accurate by analyzing a subset of the PN formulations and can take appropriate action for only those formulations affected, thereby reducing the costs associated with waste if they need to be remade. Similarly, individual PN containers can be analyzed for dextrose content during chemical or refractometric analysis, which can be applied in a cost-effective manner.

In addition to these assessments of hardware function, the software can be similarly challenged to see whether the response is appropriate to the command. For example, if an extraordinary amount of calcium and phosphorus are entered into the compounding program, does the software recognize a potential incompatibility? However, such challenges to the software program are best performed either before or after the PN admixtures are formulated, rather than during the time of operation. Such tests run the risk of an inadvertent compounding command that may be overlooked and could result in dispensing an incompatible and potentially dangerous formulation.

Practice Guidelines

1. Gravimetric analyses that indirectly assess the accuracy of the individual additives delivered or the final contents of the PN can be readily applied in the pharmacy practice setting. Particular attention should be focused on the most dangerous additives that tolerate the least margin of error such as the potassium salts.
2. Chemical analyses that directly measure the final content of the individual additives can be easily incorporated into the PN compounding operations of the pharmacy. The accuracy of the PN dextrose content is an example of an additive that may be associated with significant morbidity and mortality.
3. Refractometric analysis is an alternative, as well as an indirect measure of the final additive concentration. For example, dextrose concentration is frequently assessed by this technique. However, this method is limited to PN formulations that do not contain IFE.
4. In-process or end-product testing of PN formulations is recommended daily so as to ensure a safe, final formulation is dispensed to the patient.
5. The aseptic extemporaneous preparation of intravenous admixtures intended for patient administration should adhere to the ASHP Technical Assistance Bulletin on Quality Assurance for Sterile Products.(10)

References

1. Heller RM, Kirchner SA, O'Neill JA, et al. Skeletal changes of copper deficiency in infants receiving prolonged parenteral nutrition. J Pediatr 1978;93:847%51.
2. Riella MC, Broviac JW, Wells M, et al. Essential fatty acid deficiency in human adults during total parenteral nutrition. Ann Intern Med 1975;83:786%9.
3. Anonymous. Death associated with thiamine deficient total parenteral nutrition. MMWR 1987;38:43.
4. 4 Alliou M, Ehrinpreis MN. Shortage of intravenous multivitamin solution in the United States. [Letter]. NEJM 1997; 337(1):54-55.
5. Travis SF, Sugarman HJ, Ruberg RL, et al. Alterations of red-cell glycolytic intermediates and oxygen transport as a consequence of hypophosphatemia in patients receiving intravenous hyperalimentation. N Engl J Med 1971;285:763%8.
6. A.S.P.E.N. Board of Directors. Standards of Practice: Nutrition support pharmacists. Nutr Clin Pract 1993;8:124%7.
7. Sterile Drug Products for Home Use (1206). USP23/NF18. United States Pharmacopeial Convention Inc, Rockville, MD, 1995;1963%75.
8. Total parenteral nutrition/total nutrient admixture. USP DI Update, vol I and II. United States Pharmacopeial Convention Inc, Rockville, MD 1996;66%71.
9. ASHP Technical Assistance Bulletin on quality assurance for pharmacy-prepared sterile products. Am J Hosp Pharm 1993;50:2386%98.
10. Bozetti F, Bonfanti G, Regalia E, et al. Catheter sepsis from infusate contamination. Nutr Clin Pract 1990;5:156%9.

SECTION V. STABILITY AND COMPATIBILITY OF PARENTERAL NUTRITION FORMULATIONS

PN Stability

Background

The stability of PN formulations principally focuses on the degradation of nutritional components over time. The Maillard reaction ("the browning reaction") is well-known and involves the decomposition of carbohydrates by certain amino acids such as glycine, which is facilitated by temperatures used for sterilization of commercial products. Thus the combination of amino acids and dextrose must be compounded by the pharmacist rather than provided in a single commercial package. It is generally recognized that the extemporaneous compounding of any PN accelerates the rate of physiochemical destabilization. Presently, certain amino acids, multivitamins and lipids are most susceptible to instability. Except for an isolated case report, the discoloration of commercial amino acid products forming a bluish hue is not associated with adverse effects. However, the oxidation reaction involving tryptophan that produces the discoloration should be prevented by storage away from light and, preferably, keeping the manufacturer s protective packaging intact until the time of use.

From a clinical perspective, the physiochemical stability of PN formulations is largely focused on multivitamins, several of which are known to deteriorate substantially over time. For the most part, despite their degradation, very few produce clinically significant disturbances in the acute care setting. They tend to be more important in patients with marginal body stores and who are dependent on long-term parenteral nutrition support. The clearest example of this was demonstrated in a case report of a home PN patient who received weekly batches of parenteral

nutrition prepared by a hospital pharmacy in which the vitamins were added for a period of up to 7 days. Within 6 months, the patient had night blindness, was treated with a large intramuscular dose of vitamin A, and the symptoms resolved. Six months later, the patient had a relapse in symptoms, prompting an investigation into why the multivitamin supplement was insufficient in meeting the patient s needs. Because the vitamins were added up to a week before the solution was administered, substantial amounts of vitamin A were lost to degradation and adsorption into the plastic matrix of the infusion container. Adding the vitamins to the PN formulation daily just prior to infusion resolved the problem (1).

Similarly, when ascorbic acid was added in a batch fashion, it degraded and resulted in the formation of a large, discernible precipitate in the PN admixture. Careful analysis revealed that the precipitate was calcium oxalate. Oxalic acid is a degradation product of vitamin C that readily reacts with free calcium. Significant degradation can be avoided by adding vitamins just prior to infusion (2).

The extemporaneous preparation of L-glutamine for addition to PN poses several concerns. L-glutamine has limited stability in PN formulations, and it requires specialized parenteral manufacturing techniques not routinely available in most institutional pharmacies. The formulation needs to be evaluated to ensure that its final contents meet the desired concentration and that it is sterile and free of pyrogens. Assuming the sterile compounding facility is qualified to make such a product, it is the pharmacist s responsibility to quarantine the product and ensure that it passes the aforementioned tests prior to its infusion. In most cases, the quarantine period is at least 7 days in order to complete the microbiological analyses for the appearance of slow-growing pathogens. For products with limited stability, however, USP guidelines do allow for release of the product prior to the end of the quarantine period. Therefore, although less than ideal, quality control issues arising after quarantine can be dealt with retrospectively.

In addition to the above concerns for PN formulations, the stability of submicron lipid droplets must also be maintained in TNA dispersions during the period of infusion. Because the TNA dispersion is stabilized by an anionic emulsifier and numerous destabilizing cations are routinely included in the admixture, the risk of infusing an unstable and potentially dangerous admixture is present. Generally, when producing a TNA, the pharmacist is guided by the manufacturer of the lipid emulsion product as to its physiochemical limitations. The pharmacist is urged to use this brand-specific information and not to extrapolate to other products.

The use of dual-chamber bags, whereby for example, the lipid is physically separated from the remaining admixture components, can enhance the shelf-life of extemporaneously prepared TNAs. It s greatest utility appears to be in the homecare setting where batch preparation of PN formulations is most common. Although TNAs have been formulated for use in the neonate/infant, stability of lipid particles within the admixture must be established for each combination of additives before use. The higher content of divalent cations can reduce particle zeta potential (negative surface charge), resulting in coalescence. Additionally, higher content of calcium and phosphate in neonatal/infant parenteral nutrition admixtures increases the risk of precipitation, which can go undetected because of TNA opacity.

PN Compatibility
The complex formulations typical of PN pose several possible physiochemical incompatibilities. Degradation of drugs or nutrients is always a possibility, yet little evidence exists that such reactions cause clinical harm. The most serious risk of incompatibility in PN formulations and thus the most imminent threat to the patient arises when macroprecipitates exceeding 5 to 7 microns form in the admixture and pass into the central circulation. Two forms of precipitates -

solid and liquid – may appear in an extemporaneously prepared admixture. Commonly, the existence of crystalline matter is most frequently cited in PN formulations, yet with the use of TNA emulsions, phase separation with the liberation of free oil constitutes the liquid precipitate.

Solid precipitates can develop when an incompatible combination of various salts is added to a PN formulation; this results in the formation of insoluble product. Calcium salts are one of the most reactive compounds and readily form insoluble products with a number of additives. Dibasic calcium phosphate (CaHPO4) is an example of one of the most dangerous incompatible combinations and has resulted in embolic deaths when infused in the clinical setting. This can be avoided through a variety of measures. First, calcium gluconate is the preferred form of calcium used in multicomponent PN formulations. Calcium chloride is far more reactive than an equivalent amount of calcium gluconate salt. Second, the order of compounding is extremely important in order to avoid the formation of an insoluble precipitate that would otherwise be soluble if added in the correct sequence. Generally, phosphate should be added first, and calcium should be added near the end of the compounding sequence to take advantage of the maximum volume of the PN formulation. Other risks of forming solid precipitates include the use of bicarbonate salts when indicated to correct a base deficit through the PN. Again, bicarbonate reacts with calcium to form the insoluble product calcium carbonate. If an alkalinizing salt is indicated, then sodium or potassium acetate should be used. The dose of the alkalinizing salt is the same for either bicarbonate or acetate (1 mEq of bicarbonate has the same alkalinizing power as 1 mEq of acetate). Finally, ascorbic acid is a highly unstable vitamin that has been suggested to be added in supraphysiologic quantities (up to 2000 mg per day) in the PN for its antioxidant effects. However, because of its unstable characteristics, it readily degrades to form oxalic acid, which is also highly reactive with calcium, forming the insoluble product calcium oxalate. Thus the use of this vitamin in supraphysiologic quantities should be given via separate infusion and not in the PN formulation.

Phase separation and the liberation of free oil from the destablization of TNAs can result when an excess of cations is added to a given admixture. The higher the cation valence, the greater the destablizing power; thus trivalent cations such as Fe^{+3} (from iron dextran) are more disruptive than divalent cations such as calcium and magnesium. Monovalent cations such as sodium and potassium are least disruptive to the emulsifier, yet when given in sufficiently high concentrations, they may also produce instability. There is no safe concentration of iron dextran in any TNA3. Of the divalent and monovalent cations, adult patients' clinical needs can usually be met without significant concern of producing an unstable and potentially dangerous formulation. Even the order of compounding can cause instability of TNAs, and the compounding sequence must not place destabilizing additives such as the cations or hypertonic dextrose in close sequence with a minimally diluted intravenous fat emulsion.

In general, the pharmacist should be guided by the instructions of the manufacturer for the macronutrients and the automated compounder in use to ensure that all parenteral nutrient formulations are compounded optimally, and that they are safe and compatible.

The presence of enlarged lipid globules can be successfully identified if the proper techniques are used. There are only two stages of emulsion destabilization that are visually detectable by the naked eye, namely creaming and coalescence. As visual observation is the most routinely applied quality assurance method employed by practicing pharmacists, an appreciation of the physical signs of TNA integrity is essential. The initial stage in emulsion breakdown is creaming which occurs almost immediately upon standing once fat emulsion has been mixed with the other chemical constituents (nutrients, electrolytes, vitamins, etc). The presence of a cream layer is visible at the surface of the emulsion as a translucent band separate from the remaining TNA

dispersion, although the lipid particles in the cream layer are destabilized, their individual droplet identities are generally preserved. As such, this phase (creaming) of emulsion breakdown is still safe for patient administration.

The terminal stage of emulsion destabilization is the coalescence of small lipid particles forming large droplets that may vary in size from 5-50+ microns that pose potential clinical danger, yet escape visual detection. The existence of coalesced lipid particles in a TNA formulation is characterized by the variable presence of yellow-brown oil droplets at or near the TNA surface. In its usual presentation, the free oil may exist as individual spherical droplets or as segmented (discontinuous) oil layers. Careful observation of each TNA admixture is required to detect the subtle appearance of coalescence. In its most extreme form, the oil presents as a continuous layer of yellow-brown liquid at the surface of the formulation that is readily discernible from the remaining dispersion, and can be accompanied by marbling or streaking of the oil throughout the admixture. In either case, the presence of free oil in any form in a TNA should be considered unsafe for parenteral administration (4). The danger associated with the infusion of unstable lipid droplets enlarged through electromechanical destabilization is unclear. However, the existence of fat globules >5 microns in diameter comprising >0.4% of the total fat present has been shown to be pharmaceutically unstable, and such admixtures are considered unfit for intravenous administration (3).

The manufacturers of lipid emulsions use a variety of stability assessment techniques; however, laser assessment is the most reliable and sensitive to the subtle, yet important physiochemical changes in emulsion stability that serve as a harbinger of possible dangers. There are currently three methods of laser analysis frequently used in the assessment of lipid emulsion stability&laser diffraction, photon correlation spectroscopy, and light obscuration or extinction. The first two techniques principally focus on the submicron globules and provide information about mean particle size. They are relatively
insensitive to the remote, yet potentially significant droplets that have been enlarged through electromechanical destabilization. Laser diffraction and photon correlation spectroscopy do not count individual particles, but through a variety of mathematical correlations, they construct the typical particle size distribution around the mean globule size. The principal benefit of these techniques is for the manufacturer during the homogenization of lipid droplets in the production process of the commercial emulsion.

Finally, standard PN formulations have been useful to organizations whereby the physiochemical stability and compatibility are assured via adequate documentation by the institution or the manufacturer of parenteral nutrient products. Such standardization limits the risk of compounding and dispensing potentially unstable or incompatible PN formulations. However, any change in the composition of standard formulations needs to be applied cautiously and with adequate assurance that the new or revised formula is stable and compatible.

Practice Guidelines

1. The dose, admixture preparation, packaging, delivery process, and storage and administration method should be confirmed to ensure that the PN is stable and all components are compatible.
2. The responsible pharmacist should verify that the coinfusion of drugs with PN either admixed in the PN or coinfused through the same intravenous tubing is safe, stable, and free from incompatibilities.
3. Decisions related to stability and compatibility are made according to the most reliable information available from the literature or manufacturer of intravenous nutrients. If no

information exists, stability and compatibility of the PN must be determined in consultation with the manufacturer before it is dispensed to the patient.

4. Given the limited amount of published stability information available, the use of a 2-in-1 formulation with separate administration of IFE is recommended for neonatal/infant patients.

References

1. Howard L, Chu R, Feman S el al. Vitamin A deficiency from long-term parenteral nutrition. Ann Intern Med 1980;93:576-7.
2. Gupta VD. Stability of vitamins in total parenteral nutrient solutions. Am J Hosp Pharm 1986;43:2132.
3. Driscoll DF, Bhargava HN, Li L et al. Physicochemical stability of total nutrient admixtures. Am J Hosp Pharm 1995;52:623-34.
4. Driscoll DF. Total nutrient admixtures: Theory and practice. Nutr Clin Prac 1995;10:114-9.

SECTION VI: IN-LINE FILTRATION OF PN ADMIXTURES

Background

Use of an in-line filter with PN can prevent the administration of particulate matter, air, and microorganisms to patients. The National Coordinating Committee on Large Volume Parenterals,(1) the Intravenous Nurses Society,(2) and the Food and Drug Administration (3) have recommended that inline filters be used during the administration of intravenous products such as PN.

Rationale for the Use of In-Line Filters

Particulates. It is known that both large-volume injectables and their containers contain minute amounts of particulate matter and that additional particulates may be introduced to solutions with multiple additives, such as PN. The entry of large numbers of particles of diverse sizes and composition into pulmonary capillaries and their dissemination into other organs, such as the renal medulla, brain, lungs, spleen, and liver, may lead to blockage of these vessels and harmful effects on the surrounding tissues. Particles of 5 to 20 microns and larger are capable of obstructing blood flow through the pulmonary capillaries, which could lead to complications such as pulmonary embolism.(6,7)

Phlebitis. Foreign particles can produce phlebitis at the injection site.(8) Although phlebitis is not a consideration when administering PN through a central vein, phlebitis can be a therapy-limiting problem when PN is administered peripherally. Use of an in-line filter has been shown to delay the development and reduce the incidence of phlebitis, and even reduced the length of stay in one study. (4,9,10) However, other studies have reported no benefit. (11,12)

Reasons for these mixed results may be related to differences in the pH and composition of the infused solutions, the compounding techniques used in their preparation, and study design differences. If pharmacists use a filter needle for incorporation of reconstituted solutions into large volume fluids or incorporate a final filtration step during compounding, the clinical benefit of a second filtration through an in-line filter in reducing phlebitis may be negligible.

Microprecipitates. Formation of microprecipitates in intravenous admixtures is principally dependent on concentration, pH and temperature. If no filter is used, microprecipitates can be infused, potentially causing catheter occlusion and loss of intravenous access, as well as patient

harm. Formation of microprecipitates due to concentrations of calcium and phosphate in excess of their solubility is a potentially harmful source of particulate matter. Factors that affect the solubility of calcium and phosphate in PN have been described.(14,15) Precipitation is more likely to occur at higher temperatures because the more insoluble dibasic calcium phosphate predominates at higher temperatures.(15) This is of particular concern with TNAs because the opacity of the emulsion prevents effective visual inspection. Precipitation may occur inside the catheter at body temperature even though a precipitate was not visible in the admixture on inspection.(16) Two deaths and at least two other cases of respiratory distress were recently attributed to microprecipitates of calcium and phosphate in TNAs.(4) Drug precipitates may also cause a crystalline occlusion similar to calcium phosphate. In-line filters are recommended as a means of removing these crystals and avoiding catheter occlusion.(17,18)

Initial visual inspection cannot be relied upon to detect formation of a precipitate. Unless a formulation is grossly incompatible, it is unlikely that a precipitate will form instantaneously.(7) In most situations, precipitates may take hours to develop, thus visual inspection at the time of compounding or dispensing may not detect a precipitate. Additionally, the limitations of visual detection should be recognized. The highly trained unaided human eye is capable of distinguishing particulate matter as small as 50 microns.(14) However, because of variations in visual acuity and the difficulty of paying close attention when inspecting large numbers of PN formulations on a daily basis, precipitates may escape detection by visual inspection. Even at best, visual detection is limited to particles with a diameter _50 microns, but particles in the range of 5 to 20 microns may lodge in the pulmonary capillaries and cause complications. (8,9) By the time a precipitate can be detected by visual inspection, the formulation is grossly incompatible and unsafe for administration.(19)

Filters have sometimes been criticized because they may clog, causing infusion pumps to alarm, and requiring nursing intervention. It should be recognized that a clogged filter is a potential sign of a precipitate. It is never appropriate to remove a clogged filter and allow the admixture to infuse without a filter.

Infection. PN can become contaminated during compounding or during setup for administration. PN formulations are at risk for contamination due to the multiple manipulations required for compounding and the ability of these solutions to support the growth of fungal and Gram-negative microorganisms.(20) Contaminated PN formulations have been linked to patient infections, and episodes of contamination have been reported with both PN formulations without IFE, TNAs and even in-use manufacturer s bottles of lipid emulsion.(21,22,24) Use of a 0.2-micron filter can remove microorganisms, either as a final step in the compounding process or used in-line during solution administration; however, use of a 0.22 micron filter for removal of microorganisms is limited to use with 2-in-1 formulations.

Use of a 0.2-micron filter is a reliable method of sterilization, but contamination can occur from exposure of solutions to the environment after filtration, or from touch contamination distal to the filter. Additionally, manipulation of the filter itself may provide an opportunity for contamination.(15)

Pyrogens. Once bacteria are trapped on the surface of a membrane filter, it is possible for pyrogen, or gram-negative endotoxin, to leak through the pores in the filter. Bacterial endotoxin can pass through standard membranes such as cellulose acetate or polysulfone.(25) However, filters are available with a positive charge on their surface that can retain the pyrogens by electromagnetic forces. A positively charged nylon membrane has been shown to produce a pyrogen-free effluent for 96 hours when used with 2-in-1 formulations.(25)

Air emboli. Air emboli can be prevented by the use of air-venting in-line filters to prevent air from being introduced into the patient. Although the chance of patient harm from air emboli is relatively remote in adults, it is much greater in infants.(15)

Limitations to the Use of Filters

A 0.22-micron filter is not appropriate for use with lipid emulsions. Stable lipid emulsions usually contain lipid droplets ranging in size from less than 0.1 micron to approximately 1.0 micron. Even though these particles are readily deformed and can be pumped through a 0.22-micron filter, it is not advisable to do so because the particles will shear, altering the emulsion's stability.(15) The manufacturers of lipid emulsions advise against passing them through a 0.22-micron filter either alone or in a TNA. Lipids or TNAs can be safely filtered through a pore size of 1.2 microns or greater.(6) A 1.2-micron filter is not a sterilizing filter, and it will not reliably remove common bacterial contaminants such as *Staphylococcus epidermidis or Escherichia coli.*(26) However, use of a 1.2-micron filter will remove large organisms such as *Candida albicans* that are approximately 3 to 6 microns in diameter.27 Additionally, a 1.2-micron filter will remove particulate matter from the administration line. (28) Since particles 5 microns and greater can lodge in the pulmonary capillaries, use of a 1.2 micron in-line filter has recently been recommended as a standard part of nutrition therapy.

Use of in-line filters can cause decreased flow rates, clog, or air lock. These problems can lead to increased manipulation of the intravenous administration set, creating a potential for the introduction of contamination. Many current pumps and controllers are equipped with air-in-line alarms that decrease the need for the air-eliminating filters. Although filters can dependably remove particulates that are present in the line proximal to the filter, what about those particulates which form or are introduced distal to the filter? In one case, a patient developed pulmonary deposition of calcium phosphate crystals while receiving a 2-in-1 formulation at home administered through intravenous tubing that used a 0.22-micron filter. The patient denied observing crystals in the solution, and solution bags stored in the refrigerator appeared clear. However, when the patient's solution bags were placed in a 37(C water bath, rapid precipitation and crystal formation occurred within 1 hour.(29)

Finally, in the current cost-conscious health care environment, the high cost of filters cannot be ignored.

Filter Selection

A number of types of filter membranes may be acceptable for use with PN formulations. Membrane filters composed of mixed esters of cellulose can be used for most PN formulations, but should not be used for fluids with a pH outside the range of 4.0 to 7.5. Polysulfone filters are chemically inert, and they are acceptable for a wider range of pH values. Specially processed nylon 66 filters are available with a positively charged surface that is used to adsorb negatively charged substances such as pyrogens, bacteria, and viruses.(15)

Most in-line filters should be used for no more than 24 hours because of the build up of trapped bacteria and subsequent potential for leakage of pyrogens through the filter membrane. Filter membranes made of positively charged nylon may be used for up to 96 hours for 2-in-1 formulations because of their ability to retain bacteria and pyrogens more reliably.28 By use of a positively charged nylon filter, the tubing change period can be extended to 72 to 96 hours, which can offset the additional cost of using an in-line filter.(31)

Consensus

In the current cost-constrained health care environment, it is difficult to assure complete control of the prescribing, compounding, delivery, and administration of PN formulations. The solubility of calcium and phosphate is not entirely predictable. Even following the best compounding practices, some risk of solution contamination exists. Use of a filter provides an additional safety check to prevent potential patient harm.

It should be noted that use of filters is not a complete cure for the potential problems of contamination or precipitation of PN formulations. Skill in prescribing and formulation, and careful aseptic technique during compounding and handling of solutions are required to minimize the risk of patient harm.

Practice Guidelines

1. A 0.2-micron filter should be used for 2-in-1 formulations. A 1.2- to 5-micron filter should be used for TNAs. Alternatively, a 1.2 micron filter may be used for all PN formulations.
2. A clogged filter during administration of PN is indicative of a problem and may be replaced, but should never be removed entirely.

Work to be done

Further work is needed to more clearly define the appropriate use of filters in clinical practice. For example:
- What patient and environmental factors lead to development of microprecipitates distal to the filter?
- Would use of a filter in line with an automated compounder be beneficial in removing contaminants and microprecipitates, and if so, could the filter be used for multiple patient containers, reducing the overall cost? Or would filtration during compounding be of little benefit because these products are initially sterile, and development of microprecipitates might occur after the filtration step?
- Is use of a one piece tubing and in-line filter unit advantageous compared to a separate add-on filter unit in reducing manipulation and potential contamination?
- What is the most appropriate replacement interval for filters, given the trend towards extending the duration of tubing use?
- Do pyrogen retentive filters have a role for TNAs, or is the positively charged filter membrane s performance affected by the negatively charged exterior of lipid droplets?

All these questions need to be answered.

References

1. National Coordinating Committee on Large Volume Parenterals. Recommendations to pharmacists for solving problems with large volume parenterals. Am J Hosp Pharm l980;37:663-7.
2. Anon. Intravenous nursing standards of practice. J Intraven Nurs. 1990; suppl: S56-7.
3. Food and Drug Administration. Safety Alert: Hazards of precipitation associated with parenteral nutrition. Am J Hosp Pharm l994;51:1427-8.
4. Falchuk KH, Peterson L, McNeil BJ. Microparticulate-induced phlebitis. Its prevention by inline filtration. N Engl J Med l985;312:78-82.

5. Turco S, Davis NM. Clinical significance of particulate matter: A review of the literature. Hosp Pharm l973;8:137-40.
6. Wells P. A guide to total nutrient admixtures. Precept, Chicago, l992.
7. Driscoll DF. Total nutrient admixtures: Theory and practice. Nutr Clin Pract. l995;10:114-9.
8. DeLuca D, Rapp RP, Bivins B, et al. Filtration and infusion phlebitis: A double-blind prospective clinical study. Am J Hosp Pharm l975;32:1001-7.
9. Allcutt DA, Lort D, McCollum CN. Final inline filtration for intravenous infusions: prospective hospital study. Br J Surg 1983; 70: 111-3.
10. Rusho WJ, Bair JN. Effect of filtration on complications of postoperative intravenous therapy. Am J Hosp Pharm 1979; 36: 1355-6.
11. Rypins EB, Johnson BH, Reder B, et al. Three-phase study of phlebitis in patients receiving peripheral intravenous hyperalimentation. Am J Surg l990;159:222-5.
12. Maddox RR, John JF Jr, Brown LL, et al. Effect of in-line filtration on postinfusion phlebitis. Clin Pharm l983;3:58-61.
13. Trissel LA. Handbook on injectable drugs, 8th ed. Bethesda, MD: American Society of Hospital Pharmacists, l994.
14. Driscoll DG, Newton DW, Bistrian BR. Precipitation of calcium phosphate from parenteral nutrition fluids. Am J Hosp Pharm l994;51:2834-6.
15. McKinnon BT, Avis KE. Membrane filtration of pharmaceutical solutions. Am J Hosp Pharm l993;50:1921-36.
16. Robinson LA, Wright BT. Central venous catheter occlusion caused by body-heat-mediated calcium-phosphorus precipitation. Am J Hosp Pharm l982;39:120-1.
17. Rubin M, Bilik R, Aserin A, et al. Catheter obstruction; analysis of filter content of total nutrient admixture. J Parenter Enteral Nutr l989;13:641-3.
18. Rubin M. Response to Dr Pennington's letter [letter]. J Parenter Enteral Nutr l990;14:551.
19. McKinnon BT. FDA Safety Alert: Hazards of precipitation associated with parenteral nutrition. Nutr Clin Pract l996;11:59-65.
20. Thompson B, Robinson LA. Infection control of parenteral nutrition solutions. Nutr Clin Pract l991;6:49-54.
21. Bozetti F, Bonfanti G, Regalia E, et al. Catheter sepsis from infusate contamination. Nutr Clin Pract 1990;5:156-9.
22. DeCicco M, Chiardaia V, Veronese A, et al. Source and route of microbial colonization of parenteral nutrition catheters. Lancet l989;2:1258-61.
23. Dolvin BJ, Davis PD, Holland TA. Contamination rates of 3-in-1 total parenteral nutrition in a clinical setting. J Parenter Enteral Nutr l987;11:403-5.
24. Ebbert ML, Farraj M, Hwang LT. The incidence and clinical significance of intravenous fat emulsion during infusion. J Parenter Enteral Nutr l987;11:42-5.
25. Baumgartner TG, Schmidt GL, Thakker KM, et al. Bacterial endotoxin retention by inline intravenous filters. Am J Hosp Pharm l986;43:681-4.
26. Mershon J, Nogami W, Williams JM, et al. Bacterial/fungal growth in a combined parenteral nutrition solution. J Parenter Enteral Nutr l986;10:498-502.
27. Warshawsky KY. Intravenous fat emulsions in clinical practice. Nutr Clin Pract 1992;7:187-96.
28. Driscoll DF, Bacon MN, Bistrian BR. Effects of in-line filtration on particle size distribution in total nutrient admixtures. J Parenter Enter Nutr 1996; 20: 296-301.
29. Knowles JB, Cusson G, Smith M, et al. Pulmonary deposition of calcium phosphate crystals as a complication of home total parenteral nutrition. J Parenter Enteral Nutr 1989;13:209-13.
30. Clarke R. A cost-effective system for TPN. Nursing Times 1990;86:65-7.
31. Robathan G, Woodger S, Meranta D. A prospective study evaluating the effects of extending total parenteral nutrition line changes to 72 hours. J Intraven Nurs 1995;18:84-7.