THE EFFECT OF TWO TUBE-FEEDING PROTOCOLS ON BACTERIAL CONTAMINATION AND DIARRHEA IN ICU PATIENTS

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Abstract

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Diarrhea, a serious outcome for patients, commonly occurs following institution of enteral feeding. One suggested etiology for the problem is bacterial contamination of the enteral feeding solution. The purpose of this study was to extend previous pilot research on the occurrence of bacterial contamination and diarrhea in tube-fed ICU patients by comparing two enteral feeding protocols. The protocols compared were the routine hospital protocol vs an aseptic protocol for the preparation and maintenance of enteral nutrition. A convenience sample of 63 ICU patients, who met the inclusion criteria, were followed from the first day of enteral feeding to the fourth day. All subjects received the same isotonic formula (Osmolite^{R}).

Twenty-seven percent (n=17) of subjects developed diarrhea. There were no significant differences in the incidence of diarrhea between the two protocol groups. Bacterial contamination was low (n=9, 14%), and was not significantly different between protocol groups. Women had a significantly higher incidence of diarrhea (p=0.02) as did subjects whose primary medical diagnosis was respiratory (p=0.02). Subjects with a neurologic medical diagnosis had significantly less diarrhea (p=0.05). Also, subjects receiving aminoglycosides (p=0.02) or penicillin (p=0.03) had a higher incidence of diarrhea. Serum albumin was significantly lower in patients with diarrhea (p=0.05). This study indicates that the development of diarrhea in enterally fed patients is multifactorial.

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CHAPTER I

Introduction and Statement of the Problem

Enteral nutrition, a common and preferred modality for providing nutritional support to critically ill patients in the Intensive Care Unit (ICU), is frequently associated with diarrhea. Although the mechanism for this effect is not well understood, one plausible hypothesis is bacterial contamination of the enteral feeding. Because the gastrointestinal (GI) system is not viewed as a sterile system, enteral feedings are not routinely prepared under aseptic conditions. However, seriously ill or injured ICU patients who are immunocompromised and/or have altered GI flora may be unable to adequately resist microorganisms introduced via enteral feedings. These agents may potentially serve as opportunistic pathogens in the GI tract, producing diarrhea.

The specific aim of this study was to compare the use of two enteral feeding protocols with respect to the incidence of bacterial contamination and diarrhea in ICU patients. The independent variable was the enteral nutrition feeding protocol and the dependent variables were bacterial contamination and diarrhea. In addition to bacterial contamination, other factors that may have affected the development of diarrhea in enterally fed ICU

patients were nutritional status, gastric pH, osmotic load, and medication (Coale & Robson, 1980; Rombeau & Barot, 1981; Anderson, et al., 1984; de Leuuw & Vanderwoude, 1986; Drude & Hines, 1980; McDonald et al., 1982). For this study, formula type and rate were controlled; the same formula type was delivered approximately at the same rate to all patients. Data on nutritional status, medications, osmotic load, gastric pH, and days without food were collected because of their association to diarrhea. The proposed relationship for all these variables is shown in Figure 1.

The research questions for the study were:

1. Is there a difference in the incidence of bacterial contamination between ICU patients whose enteral feeding is prepared using aseptic technique and those whose enteral feeding is prepared using standard hospital procedure when both groups receive the same enteral formula?

2. Is there a difference in the incidence of diarrhea between ICU patients whose enteral feeding is prepared using aseptic technique and ICU patients who receive enteral feeding prepared using standard hospital procedure when both groups receive the same enteral formula?

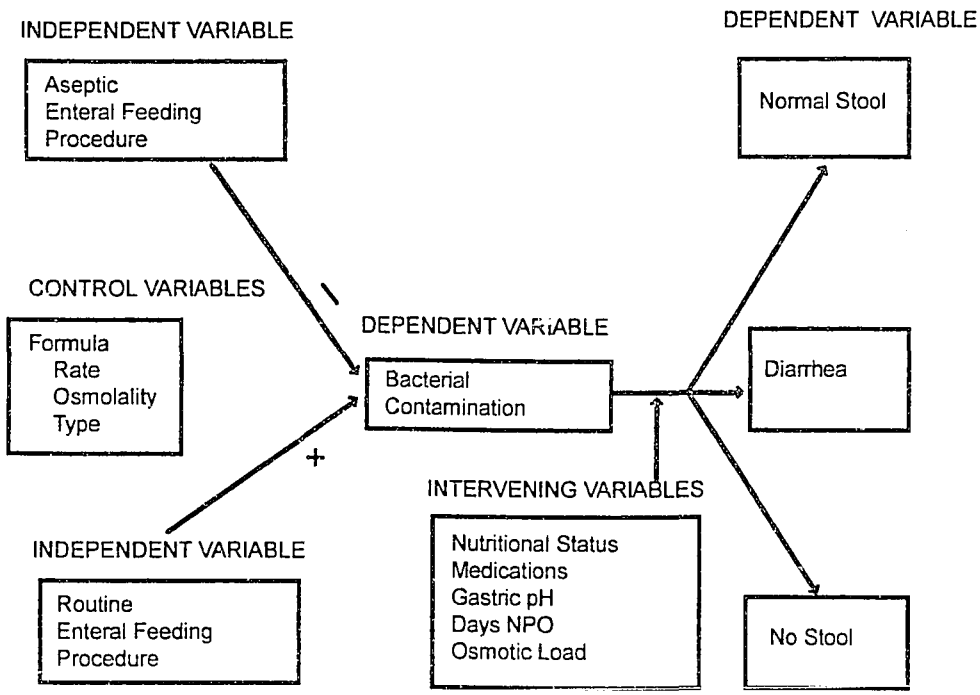

Figure 1. Relationship of Study Variables

3. If bacterial contamination occurs, is there a difference in the incidence of diarrhea between ICU patients who receive contaminated enteral feedings and those who do not when both groups receive the same enteral formula?

4. Which of the following variables are the best predictors of diarrhea in enterally fed ICU patients: bacterial contamination, osmotic load, gastric pH, protocol group membership, medications, nutritional status, and days without food?

For ICU patients, diarrhea is a serious and costly outcome. Its occurrence may contribute to malnutrition, electrolyte imbalance, and skin breakdown (Zimmaro, 1986), and lead to local or systemic infection (Anliker, 1988; Levy, 1989). The resulting cycle significantly increases morbidity and mortality. Kelly, Patrick, and Hillman (1983) studied all patients (n=81) admitted to the ICU for more than 48 hours over a 12-month period and reported the occurrence of diarrhea to be 41%. In that study, 25 patients received nasogastric feeding, with 17 developing diarrhea (68%). The average length of stay for patients with diarrhea was 11.9 days as opposed to 4 days for patients without diarrhea.

These data suggest that diarrhea may contribute to increased length of stay and therefore an increased cost

of hospitalization. While other factors are also related to length of stay in ICU, it is reasonable to believe that occurrence of diarrhea could be important. In addition, diarrhea is associated with psychologic and emotional upset in patients and requires a significant amount of nursing time (Smith, Faust-Wilson, Lohr, Kallenberger, & Marien, 1992).

One factor commonly associated with the onset of diarrhea in the ICU population is the initiation of enteral feedings. In seriously ill patients with functioning gastrointestinal (GI) tracts, enteral nutrition is the preferred modality for providing nutritional support. However, the initiation of enteral nutrition has been associated with a number of untoward GI effects. These side effects include gastric distention, abdominal cramping, nausea, vomiting, and diarrhea (Flynn, Celentano, & Fisher, 1987; Heymsfield, Bethel, & Ansley, 1979).

Diarrhea, occurring in 15% to 68% of hospitalized, enterally fed patients (Kelly et al., 1983; Flynn et al., 1987; Hayashi, Wolfe, & Calvert, 1985; Keohane, Attrill, Love et al., 1983; Gottschlich, Warden, Michel et al., 1988; Hart & Dobb, 1988; Smith, Marien, Brogdon, Faust-Wilson, Lohr, Gerald, & Pingleton, 1990), is a complication which is multifactorial in etiology with

poorly understood causal mechanisms. Suggested etiologies include malnutrition and malabsorption (Coale & Robson, 1980), hyperosmolar formulas (Rombeau & Barot, 1981), rapid administration of high osmolar drugs (Niemiec, Vanderveen, Morrison, & Hohenwarter, 1983), lactose intolerance (Walike & Walike, 1973), low serum albumin (Brinson & Kilts, 1987), altered stool flora due to antibiotic administration (McDonald, Ward, & Harvey, 1982), and bacterial contamination of formulas (de Leuuw & Vanderwoude, 1986; Anderson, Norris, Godfrey, Avent, & Butterworth, 1984).

While physicians order enteral nutritional therapy, nurses are responsible for the administration of the feeding, monitoring for intolerance and other adverse effects, teaching, and psychological support of the patient (Morrissey, 1984; Perry & Potter, 1986; Luckmann & Sorensen, 1987; Heitkemper & Shaver, 1989). Management of factors influencing human responses to feeding fall within the domain of nursing practice, and inquiry into these factors is necessary to provide scientific rationale for nursing practice. Nurses are also concerned about the increased nursing time required to care for patients with numerous episodes of diarrhea.

Keeping enteral feedings free from bacterial contamination is a nursing responsibility. Except for

kitchen prepared formula, nurses control the preparation and maintenance of enteral feedings. Nurses need research based information about the appropriate methods of handling formula to prevent untoward patient outcomes such as diarrhea. A Delphi study, which focused on the priority areas for critical care nursing research, identified causes of diarrhea and administration effects of nutritional alimentation on patient comfort as two areas where nursing research was needed (Lewandowski & Kositsky, 1983). Linquist, et al. (1993) included nutritional support modalities and patient outcomes as a priority for the 90s in their priority identification for critical care nursing research. The current tube-feeding study provides nurses with a basis for making decisions about the care of ICU patients receiving enteral feedings.

Conceptual Framework

This study was based on the physiological theory of normal digestion, absorption, and motility of nutrients through the GI tract. Introduction of microorganisms through enteral feedings may alter the normal functioning of these processes, particularly in the compromised host, and diarrhea may follow. For this study bacterial contamination of enteral nutrition was examined as a reflection of ingested microorganisms. However, other

microorganisms, such as viruses, fungi, and parasites have been associated with diarrhea.

Under normal conditions, food and fluid are cyclically introduced into the mouth to begin the ingestion process. This mixture is chewed and combined with saliva to mix and break food into smaller particles. Saliva provides both protective and digestive functions. The protective functions are related to the presence of antibacterial agents, lactoferrin and muramidase (Granger, Barrowman, & Kvietys, 1985).

Digestion is the process by which the large molecules are broken into smaller ones which can be absorbed by the enterocytes (epithelial cells of the intestine). Digestion is initiated in the mouth and stomach but occurs primarily in the small intestine where pancreatic enzymes hydrolyze carbohydrates, fats, and proteins into simpler substances (Moran & Greene, 1984).

Absorption of the products of digestion, amino acids, small and long chain fatty acids, monosaccharides, glycerol, vitamins, and minerals, takes place mainly in the small intestine, specifically the duodenum and jejunum (Moran & Greene, 1984; Granger et al., 1985). The small intestine is lined with villi that greatly increase the surface area available for absorption. During prolonged starvation or disuse, these villi

atrophy related to disuse, and malabsorption occurs (Coale & Robson, 1980; Love, 1986). Malabsorption of nutrients may then contribute to osmotic diarrhea.

In enterally fed patients, the ingestion phase begins in the stomach or the duodenum. The liquid nutrient formula is delivered via a tube which bypasses the protective and digestive functions of saliva. In ICU patients, the feeding procedure often provides continuous rather than intermittent ingestion to allow for a greater amount of calories and to prevent gastric distention commonly associated with large feedings given at one time.

Major host defense mechanisms which limit bacterial growth include gastric acidity and intestinal motility (Drasar, Shiner & McLeod, 1969; DuMoulin, Paterson, Hedley-Whyte & Lisbon, 1982; Simon & Gorbach, 1986). ICU patients often have compromised defense mechanisms. The danger of stress ulcers dictates the use of histamine receptor antagonists in many of these patients. Such agents raise the gastric pH, thus eliminating an effective barrier to bacterial entry into the small intestine (Ruddell, Axon, Bartholomew, et al., 1980; Hillman, Riordan, O'Farrell & Tabaqchali, 1982). Also, ICU patients often receive antibiotics that may alter the normal bowel flora leading to bacterial overgrowth (Smith

& Goulston, 1975). Therefore, at least three normal defense mechanisms are altered in ICU patients, which may make them more vulnerable to ingested bacteria: 1) no saliva, 2) pH alteration, and 3) antibiotic therapy. Under such conditions, even relatively small amounts of ingested bacteria may then contribute to the development of diarrhea (see Figure 2).

The purpose of this study was to compare the effect of two enteral feeding protocols with respect to the incidence of bacterial contamination and diarrhea among ICU patients. These results provide a research basis for nurses making choices about the care of ICU patients receiving enteral nutrition.

Research Hypotheses

H 1. There will be a significantly greater incidence of bacterial contamination in ICU patients who receive enteral feeding that is prepared using standard hospital procedure when compared to ICU patients who receive enteral feeding that is prepared using an aseptic procedure when both groups receive the same enteral formula.

H2. There will be a significantly greater incidence of diarrhea in ICU patients who receive enteral feeding that is prepared using standard hospital procedure when compared to those ICU patients who receive enteral

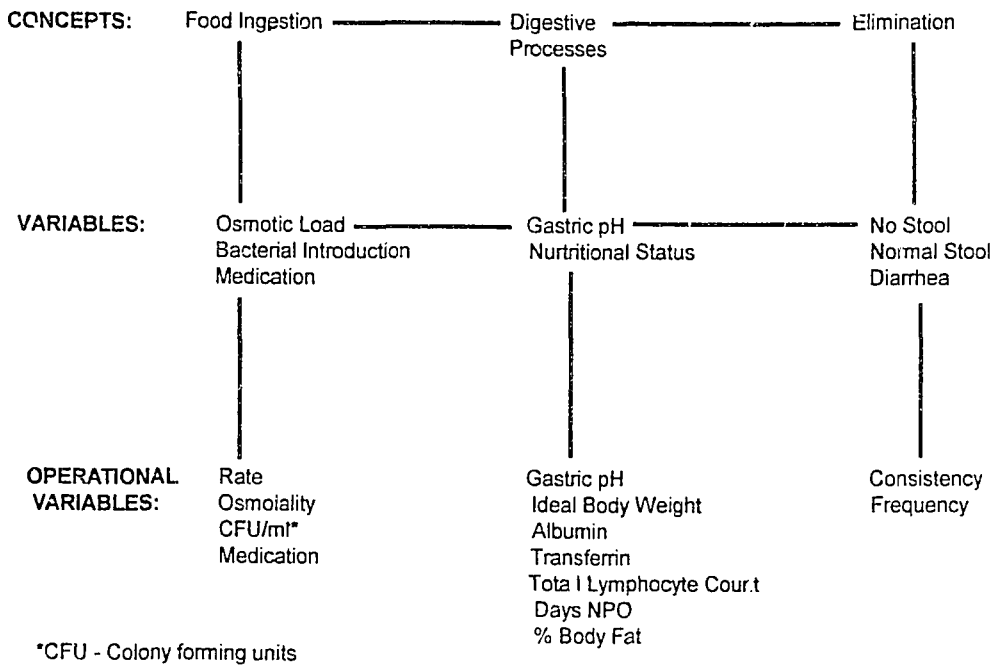

Figure 2. Model of Concepts

feeding that is prepared using aseptic procedure when both groups receive the same enteral formula.

H 3. If bacterial contamination occurs, there will be a significantly greater incidence of diarrhea between ICU patients who receive contaminated enteral feedings compared with those who do not.

H 4. There will be significant relationships between diarrhea and bacterial contamination, osmotic load, gastric pH, protocol group membership, medications, nutritional status, or days without food.

CHAPTER II

Review of Literature

Diarrhea in the enterally fed patient may be related to the preparation and maintenance of enteral nutrition by nurses. The contamination of feeding formula with bacteria and/or yeast may contribute to the development of diarrhea. To understand the relationship between bacterial contamination and diarrhea requires an understanding of the normal processing of dietary intake. This chapter reviews the normal physiologic mechanisms of digestion, absorption, and motility through the gastrointestinal tract. Then, the normal microflora of the gastrointestinal tract will be presented with the mechanisms of how bacterial overgrowth can occur. Next, the literature related to diarrhea will be reviewed and finally, bacterial contamination and enteral nutrition will be discussed focusing on patient related factors and feeding related factors that contribute to diarrhea.

Normal Processing of Nutrition

The gastrointestinal tract functions to transfer nutrients from the bowel lumen to the body. To accomplish this task, the various chemical and physical forms of food must be converted into simpler molecules that can be easily moved across cell membranes. Under normal conditions, food and fluid are cyclically

introduced into the mouth. The mixture is chewed and combined with saliva to break the food into smaller particles. Saliva also functions as a protective agent, containing antibacterial agents, bicarbonate, and mucins (Granger et al., 1985).

The antibacterial agents in saliva include lactoferrin and muramidase. Lactoferrin inhibits bacterial growth by depriving the microorganism of iron. Muramidase hydrolyzes the bacterial cell wall polysaccharides, thereby destroying the microorganism (Granger et al., 1985).

The food bolus enters the stomach after traveling down the esophagus. Here the food mixes with gastric secretions and is further processed into a semifluid consistency. The two main functions of the stomach are related to motor activity and the secretion of substances that aid in digestion (Moran & Greene, 1984).

Gastric secretions include sodium, potassium, hydrochloric acid, pepsinogen, intrinsic factor, and mucus. The acid secretions assist in dissolving soluble food and making the osmolality of the mixture closer to that of plasma which is 280 mOsm (Moran & Greene, 1984). Most oral bacteria are destroyed by gastric acid and the gastric concentration of bacteria is usually less than 1 x 10^3 colony forming units/ml (cfu/ml) (Drasar, Shiner, &

Mcleod, 1969). Only the more acid-resistant species, such as lactobacilli, streptococci, fungi and large numbers of Escherichia coli, Shigella, Salmonella, and Campylobacter survive the acid environment of the stomach (Simon & Gorbach, 1984).

The motor function of the stomach muscle allows for relaxation to accept the food bolus and for peristaltic activity to mix and empty the food into the small intestine. The distal portion of the stomach has a membrane that depolarizes and repolarizes rhythmically. Mechanical contractions are related to this electrical activity. Gastric emptying is dependent on several factors including fluid and fat content of the food, mechanical stretch and release of gastrin, osmolality of the food, posture during ingestion, and drugs (Moran & Greene, 1984).

Digestible solids empty more slowly than liquids and isotonic solutions empty faster than solutions which are either hypo or hypertonic. Carbohydrates empty faster than proteins and proteins empty faster than fats. Receptors in the proximal small intestine sense the pH, fatty acid content, and osmolality of the chyme (semi-fluid paste food mixture) and regulate gastric emptying through neural and hormonal mechanisms (Granger et al., 1985; Moran & Greene, 1984).

Most nutrients are completely hydrolyzed and absorbed in the small intestine. Throughout the walls of the small intestine are fingerlike projections called villi. These villi are covered with a layer of epithelial cells (enterocytes) containing microvilli which form the brush border. This arrangement greatly increases the surface area of the small intestine, and thereby, the available absorptive surface (Granger, et al., 1985; Moran & Greene, 1984). Factors affecting absorption include osmolality and blood supply to the small intestine. A high osmolality meal is absorbed more distally than one of lower osmolality (Fordtran & Locklear, 1966). Shock and exercise shunt blood away from the gut and impair absorption (Moran & Greene, 1984).

Motility in the small intestine is dependent on the presence or absence of food. The fed pattern is characterized by random bursts of spike and motor activity. The interdigestive period contains well defined phases, one of which is the interdigestive migrating motor complex (MMC) (Fleckstein, 1978). The MMC is a normal motion pattern that acts as an "interdigestive housekeeper" because it sweeps up remnants of food and prevent stagnation and bacterial growth. Vantrappen, Janssens, Hellemans and Ghoos

(1977), found that patients with absent or markedly decreased MMC had small intestinal bacterial overgrowth.

Large quantities of fluid and electrolytes are absorbed in the colon as movement through the colon is slower than through the small intestine. Here the food is exposed to large numbers of bacteria which further metabolize complex molecules of fat, protein, and carbohydrate (Granger et al., 1985; Rowlands & Miller, 1984). Water soluble dietary fiber is fermented by the colon and affects the consistency of the stool (Granger et al., 1985).

The microflora of the colon consist of anaerobic and aerobic bacteria, with anaerobes predominating. The most prevalent anaerobes are Bacteroides and Eubacterium, with E. coli, enterococci, and Lactobacillus, the most common aerobes (Granger et al., 1985; Hill & Drasar, 1975; Simon & Gorbach, 1986). A major factor contributing to large bacterial growth is the low level of peristaltic activity.

Elimination occurs as the feces enters the rectum, the internal and external sphincters relax, and the increased rectal pressure moves the stool through the anal orifice. Many people defecate once per day, although twice per day or once every two days are within the normal range. Stool weight is influenced by the

fiber content of the diet and may vary from one bowel movement to the next. Bacteria and fiber compose 70% of the total solids in the stool (Granger et al., 1985).

If these normal processes are altered, either iatrogenically or through disease, the host can be vulnerable to untoward effects such as bacterial overgrowth and diarrhea. For example, diseases which alter gastrointestinal motility affect the removal of bacteria from the small bowel.

Normal Microflora

The normal gastrointestinal tract contains a large number of aerobic and anaerobic bacteria. There are more than 400 bacterial species which make up this complex ecosystem (Moore & Holdeman, 1975). Most oral bacteria are swallowed and destroyed by gastric acid (Drasar, Shiner & Mclead, 1969). The microflora of the stomach are mostly aerobic and gram positive in a concentration of less than 10^3 CFU/ml. The most common species found are streptococci, staphylococci, lactobacilli, and various fungi (Gorbach, Plaut, Nahas & Weinstein, 1967).

The small intestine is an area of transition. The microflora of the proximal small intestine is similar to the stomach. In the distal ileum, the gram negative bacteria outnumber the gram positive organisms with coliforms present and anaerobic bacteria in large

quantities (Drasar et al., 1969; Gorbach et al., 1967).

The bacterial concentrations in the colon increase sharply to 10^{11} - 10^{12} CFU/ml. Anaerobes greatly outnumber aerobes by 1000 fold (Simon & Gorbach, 1986). The most common anaerobic species colonizing the colon are Bacteroides. The large number of anaerobic bacteria keeps growth of aerobic bacteria under control and limits their ability to act as pathogens (Vollaard, Clasener, van Saene & Muller, 1990).

The major host defense mechanisms against bacterial overgrowth in the small bowel are gastric pH and normal motility. The high acidity of the stomach due to hydrochloric acid has been shown to effectively kill most bacteria in the stomach within 60 minutes. However, in persons with a higher pH (>4) there was no decrease in bacteria even after two hours of exposure to stomach contents (Giannella, Broitman & Zamcheck, 1972; Drasar et al., 1969).

Motility is also important in preventing bacterial overgrowth. The interdigestive motor complex acts as a sweeper to rapidly clear bacteria from the small bowel and prevent colonization from occurring (Simon & Gorbach, 1986). Persons with absent or markedly decreased interdigestive motor complexes are more likely to have bacterial overgrowth in the small intestine (Vantrappen

et al., 1977).

Bacterial overgrowth in the small intestine acts on bile acids and inhibits their normal absorption. As a result, bile acids pass into the colon where they can act as potent stimulators of colonic secretion and propulsive motor activity (Hart, 1988; Read, 1984), common triggers of diarrhea.

Diarrhea

The term diarrhea originates from Greek, dia (through) and rhein (to flow). Diarrhea occurs when there are abnormalities in absorption, secretion, and/or intestinal motility. Lack of absorption from the intestinal lumen or excessive secretion into the intestinal lumen results in excessive amounts of fluid. Normally, 1.5 to 2.0 liters of fluid are ingested per day. This amount, together with endogenous sources of fluid, salivary, gastric biliary and pancreatic secretions, makes the total fluid delivered to the intestines about 9 liters per day. Normally, fecal output is less than 300 milliliters. Fluid absorption is regulated by the movement of solute and the intestine acts as a relatively leaky epithelial membrane between the plasma and the lumen. When net fluid absorption is disrupted related to enteric infection, the balance is disturbed and large amounts of fluid may remain in the

lumen. This excess fluid overwhelms the large and small intestinal capacity for reabsorption and diarrhea occurs.

In addition, intestinal motility is a factor in the development of diarrhea (Banwell, 1986; Read, 1984). Increased intestinal motor activity may stimulate the intestinal wall to contract, with less epithelial surface area for absorption. Also, increased motor activity decreases the time which food can be absorbed, from both the small and the large intestine (Read, 1984).

Bruckstein (1988) identifies four major mechanisms, either alone or in combination, which result in diarrhea. These four mechanisms are osmotic, exudative, secretory, and transit alterations.

Osmotic diarrhea occurs when solutes are poorly absorbed. These solutes create an osmotic gradient attracting water to them which results in increases in water in the lumen. Examples of these solutes include lactose, carbohydrates, antacids, saline laxatives, and substances containing magnesium, phosphate, and sulfate. Medicinal elixirs containing sorbitol have also been associated with osmotic diarrhea (Edes, Walk & Austin, 1990). Hypoalbuminemia also has been linked to osmotic diarrhea (Brinson & Kilts, 1987).

Albumin is the main contributor to the plasma oncotic pressure. A decrease in the plasma oncotic

pressure results in inadequate reabsorption of fluid from the interstitial spaces and edema. The interstitial edema may contribute to poor motility and poor gastrointestinal absorption of nutrients. These intraluminal nutrients may draw water from the bowel wall and diarrhea may result (Moss, 1988).

Exudative diarrhea results when inflamed or ulcerated lesions of the bowel release plasma, blood, serum proteins, or mucus. Causes of exudative diarrhea include shigellosis, amebiasis, inflammatory bowel disease and infiltrative diseases of the small and large bowel.

Secretory diarrhea results when bowel mucosa releases excessive amounts of fluid. Fluid is released in response to enterotoxins (pathogenic Escherichia coli or Vibrio cholerae), or hydroxy fatty acids (bacterial overgrowth). Bacterial overgrowth occurs when those diarrhea causing bacteria that are normally held in check are allowed to multiply. It is bacterial overgrowth that is thought to cause diarrhea in patients receiving broad spectrum antibiotics. Secretory diarrhea is also the result of bacterial contamination in some people. There are several bacterial genera known to cause diarrhea such as Shigella, Salmonella, and Campylobacter. It is believed that normally non-pathogenic bacterial genera

may cause secretory diarrhea in favorable circumstances, such as in the malnourished, immunosuppressed patient (Remington & Schrimpff, 1981; Anderson et al., 1984).

Finally, altered intestinal transit can cause diarrhea by either increased or decreased contact between chyme and mucosa. These problems occur among people who have postgastrectomy, scleroderma, and visceral diabetic neuropathy.

Definitions of diarrhea vary widely. All definitions include varying combinations of consistency, frequency, and amount. Consistency has been described as watery, liquid, creamy, very loose, mushy, semiliquid, and/or different from the patient's usual consistency (Ament, 1985; Keohane et al., 1983; Petrusko, 1979; Walike & Walike, 1973).

Definitions of diarrhea based on stool frequency ranged from one or more stools per day to 20 bowel actions in 24 hours (Ament, 1985; McDonald, Ward, & Harvey, 1982). The most commonly cited frequency was three to five liquid stools in 24 hours (Anderson et al. 1984; Banwell, 1986; Brinson, Curtis, & Singh 1987; Brown, Powers, & Luther, 1988; Dobb, 1986; Gottschlich, Warden, Michel, Havens et al., 1988; Guenter, Settle, Perlmutter, et al., 1990; Keighley et al., 1978; Kelly et al., 1983).

Volume of stool has been reported in weight, ranging from greater than 200 g/day to greater than 300 g/day for 48 consecutive hours (Benya, Layden & Mobarhan, 1991; Brinson & Kolts, 1987; Bruckstein, 1988; Gottschlich et al., 1988; Pietrusko, 1979). There is little agreement in defining diarrhea. Few articles in which the definition of diarrhea was related to weight provided an explanation of the procedure for weighing diarrhea and, in general, sample sizes in these studies were small. The accuracy and feasibility of such a procedure was questionable in the ICU where patients were often incontinent of stool. Most agreement was found in defining diarrhea in terms of the frequency and consistency of stool. The most common definitions included liquid stool occurring three to five times in 24 hours (Anderson et al., 1984; Dobb et al., 1986; Kelly et al., 1983;).

In summary, diarrhea has been associated with bacterial infection and bacterial overgrowth. The mechanisms for diarrhea caused by infectious agents such as Shigella or Salmonella are well known. Less well understood are the mechanisms for diarrhea caused by overgrowth of usually nonpathogenic bacteria. Definitions of diarrhea are varied but the most consistently identified criteria found in the literature

were frequency and consistency. Liquid stools occurring at least three times in 24 hours appears as the most commonly used definition.

Enteral Nutrition

Enteral nutrition involves the delivery of nutrients through a tube placed in the stomach or small intestine. The nutritional regimen is liquid and may consist of blenderized food or commercially available formulas. For patients who are unable to take nutrition orally but have a functioning GI tract, enteral nutrition is generally preferred over parenteral nutrition (MacBurney & Young, 1984).

Formulas may be composed of crystalline amino acids, simple sugars, and/or low fat (elemental, chemically defined), or they may contain complete proteins, complex carbohydrates, and long chain triglycerides (polymeric, chemically defined), or they may be blenderized food (milk, eggs). Also, modular formulas (incomplete supplements) may be added to a maintenance formula to supplement protein intake.

Formula characteristics are believed to influence the patient's tolerance of the feeding. For example, protein may be intact, in its complete and original form. While intact protein does not add to formula osmolality, it does require normal pancreatic enzymes for digestion.

Protein may also be hydrolyzed to smaller peptide fragments and free amino acids. This form of protein contributes more to osmolality but is useful when there is a decrease in absorptive intestinal surface. Finally, protein may be given as crystalline amino acids which contribute greatly to osmolality but may be necessary for patients with hepatic or renal disease (MacBurney & Young, 1984).

Patient Factors Related to Diarrhea

Nutritional Status

Persons experiencing acute stresses are often malnourished. In acute injury or infection, reduction of protein stores occurs due to increased metabolic demand and the need to provide amino acids for gluconeogenesis and new protein synthesis. If nutritional support is delayed, changes in the GI tract may affect the adequate processing of protein, carbohydrates, and fats.

Chronic malnutrition alters GI digestive and protective functions by decreasing cell proliferation, migration, and maturation within the crypt villous unit. Malabsorption of sugar, starch, fat, and protein results from a decreased absorptive surface (Coale et al., 1980; Love, 1986). Bacterial proliferation and catabolism of unabsorbed carbohydrates may lead to diarrhea (Coello-Ramirez & Lifshitz, 1972). Also, bacterial

endotoxins may play a primary role in the pathogenesis of diarrhea by stimulating water and electrolyte secretion in the intestine (Banwell, 1986).

Nutritional status can be measured using a variety of sources including history, anthropometric measurements, and biochemical analysis of blood. Since any one of these parameters can be affected by other factors, it is best to use multiple sources to determine nutritional status (Bergstrom, 1988).

Historical data includes determination of past weight, recent history of weight loss, and usual dietary intake. Medication history, disease history, and age may also be important to consider. Obtaining a complete dietary history from critically ill patients, however, is difficult (Gianino & St. John, 1993).

Anthropometric measurement is another method to clinically assess nutritional status. Information about fat stores, skeletal muscle, and visceral protein can be obtained from these measurements. The most commonly used measurements are body weight, height, triceps skin fold thickness, and midarm circumference. Areas of concern regarding anthropometric measurement include instrument reliability (calipers), personnel training and supervision, and replication to maintain adequate interrater reliability (Bergstrom, 1988).

Body weight is an important measure which may reflect a loss of lean muscle mass in the critically ill patient. However, fluid retention or dehydration can occur which may also affect weight measurement. Often, percent ideal body weight is calculated. This measurement is the actual weight compared to ideal body weight. The Metropolitan Life Weight-Height Chart is often used as the standard for this measurement. Many problems are associated with the use of this chart as the standard. The information is organized by gender and body frame size, with ideal weights reported in ranges. Therefore, determination of frame size must be done to use the chart and, to calculate percent ideal weight, a value must be selected from the range. Also, the data used for the chart was collected from healthy individuals ages 18 to 59 which limits usefulness in elderly, critically ill patients.

Standard weight and body composition by frame size and height was also reported by Frisancho (1984) using data from NHANES I and II (National Health and Nutrition Examination Survey), in which 21,752 adults aged 25 to 74 years were studied. Tables were constructed for male and female aged 25 to 54 and aged 55 to 74. Percentiles of weight, skinfolds, and bone-free upper arm muscle area by height, sex, and frame size were established. Advantages

of this method for determination of ideal weight are the large data base, extended age range, and percentiles of weight reported instead of ranges.

Triceps skinfold thickness is a measure reflecting body fat stores since 50% of total body fat is stored subcutaneously. This measurement is usually taken with the subject standing, arms hanging freely at the side. Guidelines for measuring tricep skinfold in the supine elderly subject has been reported (Chumlea, Roche & Mukherjee, 1984). However, in the critically ill subject who is often bedridden with multiple tubes and dressings, the measure is more difficult to obtain. Errors in this measurement may occur from poor measurement technique, inaccurate instruments, limited patient position, or altered patient fluid status.

Midarm circumference (MAC) is used to calculate midarm muscle area (MAMC). This measurement in combination with tricep skinfold is derived from the formula:

$$\text{MAMC (cm)} = \frac{\text{MAC(cm)} - \pi\text{TSF(mm)}}{10}$$

Problems with this measurement include potentially large measurement variance and questionable accuracy as a measure of total body protein (Buzby & Mullen, 1984).

Percent body fat can also be measured using infrared spectrometry. Interactance with known wavelengths of

infrared beams is measured. The infrared penetration is modest and measures the same subcutaneous layer as the tricep skinfold technique. Mclean & Skinner (1992) report good correlation (r=.81) between infrared spectrometry and the gold standard, underwater weighing. However, the reliability of this measure in critically ill patients has not been reported.

Laboratory tests which have been asscciated with nutritional status include serum albumin, serum transferrin, and absolute lymphocyte count. However, no single test is specific for nutrition and therefore, several factors must be considered to accurately determine nutritional status.

Serum albumin, an indicator of visceral protein stores, is correlated with nutritional status (Moss, 1988). In sudden acute catabolic states such as burns, sepsis, trauma, or major surgery, serum albumin may drop 1 to 1.5 g/dl in 3-7 days (Tayek & Blackburn, 1984).

Rapid depletion of serum albumin may alter plasma osmotic pressure contributing to decreased absorption from the bowel and an osmotic catharsis (Moss, 1988). Several clinical studies (Cobb, Cartmill, & Gilsdorff, 1981; Zagoren et al., 1984; Andrassey, 1985; Brinson & Kolts, 1988; Brown, Powers, & Luther, 1988) have demonstrated an association between low serum albumin

levels and enteral feeding intolerance (abdominal distention and diarrhea). Brinson et al. (1987) found that serum albumin below 2.6 g/dl was associated with unexplained diarrhea and that diarrhea subsided when albumin levels rose above 2.5 g/dl. Brown et al. (1988) also found that 75% of the patients who developed diarrhea had serum albumin levels below 2.5 g/dl. Ford, Jennings, and Andrassy (1987) noted enteral feeding intolerance in patients with serum albumin below 3.0 g/dl while no signs of intolerance occurred when the serum albumin level was above 4.0 g/dl. However, in a retrospective study of 88 enterally fed, hospitalized patients, no association was found between serum albumin and diarrhea (Patterson, Dominguez, Lyman, et al., 1990).

Transferrin, a beta globulin which aids in the transport of iron in the plasma, has a shorter half-life than albumin (18-20 days vs 8-10 days) and may be a better indicator of protein depletion than serum albumin (Gianino & St. John, 1993). In a small study of 16 patients, serum transferrin was correlated ($p=0.001$) with prealbumin levels, indicating usefulness as an indicator of nutritional status (Fletcher, Little & Guest, 1987).

Absolute lymphocyte count is an indicator of cellular immune status, which is often compromised in malnutrition. Since many factors can affect the absolute

lymphocyte count, other measures are considered in measuring nutritional status.

Determination of nutritional status is difficult because many individual variables (albumin, lymphocyte count, transferrin) can be decreased for reasons other than poor nutrition. Also, often laboratory and anthropometric measures are divided into levels of severity (normal, mild, moderate, and severe) making assessment difficult. Therefore, an index that combined these values in a meaningful way would be useful.

Some attempts have been made to combine nutritional factors in formulas which can be used to identify patients at risk for malnutrition. Buzby, Mullen, Matthews, Hobb & Rosato (1980) tested the PNI (Prognostic Nutritional Index), which combined albumin, triceps skinfold, transferrin, and delayed hypersensitivity reactivity, on 145 surgical patients. Values were inserted into an equation which yielded a predicted risk of complications as a percent. Their findings suggest the usefulness of this tool in identifying at-risk patients preoperatively so appropriate nutrition could be instituted prior to surgery, thus preventing post op complications. Limitations of this tool include cost, accuracy of delayed hypersensitivity testing, and testing of the index in a limited patient population.

Medications

Diarrhea has been associated with antibiotic therapy (Keighley, Burdon, Arabi et al., 1976; Keohane, Attrill, Love, et al., 1984; Freedland, Roller, Wolfe, et al., 1989). However, studies relating antibiotics with diarrhea are conflicting. Overgrowth of Clostridium difficile (Keighley, Burdon, Arabi, Alexander-Williams, et al., 1978) and methicillin-resistant Staphylococcus aureus (McDonald, Ward, & Harvey, 1982) have been linked to diarrhea. However, Kelly and Patrick (1983), Dobb (1986), and Byers, Wiggins, & Morrelli (1988), reported that antibiotic therapy was not a significant factor in diarrhea among hospitalized patients.

In a pilot study conducted prior to the current study, antibiotic therapy was not found to be a significant factor in the occurrence of diarrhea among ICU patients (Mickschl, Davidson, Flournoy & Parker, 1990). The difference in these studies may have been related to the type of antibiotics used and the small sample sizes. Certain antibiotics such as clindamycin and ampicillin have been associated with diarrhea (Kelly, et al., 1983). Also, in the studies finding no association between antibiotics and diarrhea, the number of patients receiving any one type of antibiotic was small, making it difficult to find differences.

Histamine receptor antagonists or antacids are often given to ICU patients to prevent stress ulcers (Hillman, Riordan, O'Farrell, et al., 1982; Garvey, McCambley & Tuxen, 1989). However, these medications also increase gastric pH. Several investigators have reported a direct relationship between gastric alkalinization and bacterial overgrowth (Ruddell, Axon, Bartholomew, et al., 1980; Hillman, et al., 1982; DuMoulin, Paterson, Hedley-Whyte, et al., 1982; Garvey, et al., 1989). Therefore, ICU patients receiving histamine receptor antagonists or antacids and bacterially contaminated enteral feeding may be at high risk for developing bacterial overgrowth.

Feeding Factors Related to Diarrhea

Bacterial Contamination

The method of enteral nutrition preparation has been linked to bacterial contamination of the feeding. Enteral feeding mixed by nursing staff on the unit is significantly more contaminated compared to enteral feeding prepared under sterile conditions of the pharmacy or diet kitchen (Anderson et al., 1984; Beyer, Parrish-Zepeda, & Furtado, 1983; Gibbs, 1983; Iannini, Mumford, & Buckalew, 1983; Public Health Service, Food and Drug Administration, 1985). Organisms isolated from the feeding formula were similar in all of these studies: facultative gram-negative bacilli, staphylococci, and

yeast. These opportunistic organisms are typically endemic in the environment (Iannini et al., 1983) or are normal flora of skin, oral mucosa, or intestinal tract.

Although a relationship between contamination of feedings and diarrhea frequently is hypothesized, only a few studies have looked at the relationship between those variables and the results have been conflicting. Of the studies that measured diarrhea as an outcome variable, Keohane, Attrill, Love, Frost, and Silk (1983) found that contamination of feeding formula did not increase the incidence of diarrhea. They studied three groups, one group received blenderized formula (n=30), one group received aseptically prepared formula (n=29), and one group received sterile prepackaged formula in 2 liter bags (n=27). In that study, diarrhea was defined as whatever the nurse or patient reported as diarrhea and only 15% (n=13) of the sample experienced diarrhea. The incidence of diarrhea appears particularly low given that the formula used was Clinifeed 400 which has a milk base and therefore contains lactose. Also, subjects were eliminated if they were fluid restricted to less than 2000 cc/day. No information on medical diagnoses or severity of illness was provided. There was no difference between the groups in the number of patients who had diarrhea (4 of 30, 5 of 29, 4 of 27). However,

subjects were not drawn from an ICU population but included all patients who required nasogastric feeding as determined by the nutritional support service.

Also, in that study, there was no information regarding the collection of samples or how soon after collection samples were plated onto the culture media. In addition, the procedure for sampling the formula was reported as random but no information was given about how many samples were done for each patient. Keohane et al. (1983) suggested that the reason contamination was not found to increase the incidence of diarrhea may be related to low gastric pH which kills many bacterial organisms. Their study did not look at gastric pH nor was there any information concerning the use of histamine antagonists or antacids. Further study is needed to examine that hypothesis.

Freeland, Roller, Wolfe, and Flynn (1989) also found no relationship between liquid stool and feeding formula contamination (n=33; 16 ICU patients). Cultures were obtained just after initial filling of the reservoir bag (baseline), 24 hours later, just prior to completing a feeding, and 48 hours later. Twenty cultures were estimated to be sufficient for baseline and for 48 hours later, but the authors do not state if they were randomly selected. In this study, diarrhea was not defined but

referred to as "liquid stool" or "watery stool." No information about the types of formula, osmolality, or nutritional status of the patients was reported.

Anecdotal reports from Iannini et al. (1983) and Schroeder, Fisher, Volz, and Paloucek (1983) also indicated no apparent relationship between bacterial contamination and diarrhea. However, Anderson et al., (1984) studied 35 tube fed patients during two separate 24 hour periods one month apart and found a significant association between the extent of contamination of enteral feeding and the presence of diarrhea ($p=0.027$). In that study, specimens were refrigerated and held overnight for varying periods (0 - 24 hours) prior to inoculation on microbiological media. Since many organisms can multiply in the cold (Flournoy, 1984), those specimens may have reflected false positives. In addition, medical records were used to determine diarrhea (4 or more liquid stools in 24 hours). If no information could be found in the medical record regarding stools, the patient was classified as having no diarrhea. That was the case for 31% ($n=11$) of their sample.

While bacterial contamination is often listed as a contributing cause of diarrhea in the enterally fed patient, research based supportive evidence is controversial. Four studies were found that examined

bacterial contamination and diarrhea. (Anderson, Norris, Godfrey, et al., 1984; Freedland, Roller, Wolfe, et al., 1989; Keohane, Attrill, Love, et al., 19983; Michschl, Davidson, Flournoy, et al., 1989). These studies were limited in that several enteral formulas were used, both bolus and continuous, starting at various rates and formula strengths. Better control of these variables is necessary to examine the effect of bacterial contamination on the development of diarrhea in enterally fed ICU patients.

Also, it is possible that the level of bacterial contamination necessary to cause diarrhea in ICU patients is lower than that necessary for a healthy individual. Some researchers have suggested that critically ill patients may colonize potentially harmful bacteria at lower levels (Remington & Schimpff, 1981 Anderson et al., 1984). It is also possible that diarrhea may be a result of viral contamination. By controlling or measuring other causes of diarrhea, further study will add to nursing knowledge required to safely administer enteral nutrition to the critically ill.

Delivery Method

Diarrhea has often been associated with enteral feeding delivery procedure, comprised of feeding rate and formula osmolality (Broom & Jones, 1981; Del Rio,

Williams, & Miller, 1982; Cataldi-Betcher, Seltzer, Slocum, et al., 1982; Heymsfield, Bethel, Ansley, Nixon, & Rudman, 1979). Prior to commercially available, isotonic, lactose free formula, enteral feedings were started at slow rates and diluted strengths. These "starter regimens" were thought to decrease bloating, nausea, and diarrhea through reduction of osmotic load (Keohane, Attrill, Love, Frost, & Silk, 1984). However, in a study by Keohane et al., (1984) with 118 subjects who had normal gastrointestinal function, there was no difference in GI symptoms between randomly assigned patients who received diluted hypotonic starter regimens, isotonic, or hypertonic formulas.

While it is still common practice to start enteral feedings at dilute hypotonic strengths and slow rates, other studies have shown that this may not be necessary (Kaminski & Freed, 1981; Rees, Keohane, Grimble, Frost, Attrill, & Silk, 1985, Pesola, Hogg, Yonnios, McConnell & Carlon, 1989; Pesola, Hogg, Eissa, Matthews & Carlon, 1990; Edes et al., 1990). Other factors, such as type of illness or length of time without nutrition, may be related to the ability of the intestines to handle the solute load of enteral nutrition.

Formula Content

Many enteral formulas are low residue and it is

thought that patients may develop diarrhea related to the change from high residue to low residue diets (Cataldi-Betcher et al., 1982; Kelly et al., 1983). Therefore, one method of counteracting diarrhea may be to administer high fiber enteral feeding (Del Rio et al., 1982; Raizman & Braunschweig, 1986). One study which examined the addition of pectin to isotonic tube feeding formula reported a significant decrease in diarrhea (Zimmaro, Rolandelli, Koruda, Settle, Stein, & Rombeau, 1989). That study was conducted on 14 healthy volunteers. Other studies of fiber in tube fed patients have found conflicting results (Fischer, Adkins, Hall, Scamen, Hsi, & Marlett, 1985; Frank & Green, 1979; Hart & Dobb, 1988; Frankenfield & Beyer, 1989; Guenter, Perlmutter, Settle, Marino, Nimir & Rolandelli, 1990) Most of these studies were limited by small sample size, low fiber intake, and/or nonrandomization. Further studies on patient populations are necessary before any conclusions can be claimed.

Liquid medications containing sorbitol have also been implicated in onset of diarrhea (Edes, Walk & Austin, 1990). Sorbitol is often added to elixirs to improve palatability. Edes, et al (1990) found an association between consumption of a elixirs containing sorbitol and diarrhea in 13 tube feed patients. In all

cases, diarrhea persisted until the elixir was stopped. The relationship of sorbitol and diarrhea warrants further study.

In summary, a variety of factors have been studied as possibly contributing to diarrhea in enterally fed patients. Contamination is an area where nursing may have a significant influence. Administration of enteral feedings requires knowledge and judgment that is within the realm of independent nursing practice. Further study is needed to compare the procedures for the preparation and maintenance of enteral nutrition on the outcome of diarrhea in ICU patients. Although a relationship between contamination of enteral feedings and diarrhea is frequently hypothesized, only a few researchers have studied this problem. These researchers have reported conflicting conclusions.

Preliminary Work

Mickschl, Davidson, Flournoy, and Parker (1990) conducted a pilot study to investigate the incidence of bacterial contamination and diarrhea in enterally fed ICU patients. The subjects were randomly assigned to the control (n=18) or experimental group (n=18). The experimental group received their enteral feeding using aseptic technique including the use of Entrition in an Entri-pak, a sterile, closed system for delivery of

enteral nutrition. The control group received a variety of commercially available enteral formulas, based on physician or dietitian preference, using the usual, standard protocol for administration of enteral feedings. The standard protocol was defined as the procedure in the hospital procedure manual. This procedure was based on current nursing procedure manuals. Dependent variables of bacterial contamination and diarrhea were assessed for four days. Intervening variables of severity of illness, medications, nutritional status, and immune status were also measured. Of these 36 ICU patients, 41.6% (n=15) developed diarrhea and 22% (n=8) received contaminated feedings. Within the two protocol groups, there was significantly less contamination of feedings in the aseptic group than in the routine group (Fisher's exact test, p=.04). The incidence of diarrhea between protocol groups approached significance (Mann-Whitney U test, p=.06), with more days of diarrhea occurring in the routine group.

While there was no statistically significant relationship between the development of diarrhea and the receipt of contaminated feedings, the sample size was small (n=8, 1 in the aseptic group and 7 in the routine group). Based on a power analysis, the power in that study was .33, with the alpha at .05 and an effect size

of .40 (medium). Therefore, there was a decreased chance of finding a significant difference.

Also, in the pilot study, there were methodological problems which favored less contamination of the routine protocol group. For example, the investigators changed the enteral feeding system every 24 hours for each group. This action may have decreased the contamination of the routine group. In addition, the aseptic group received Entrition and the routine group received a variety of commercially prepared formulas. Thus, it is possible that differences may have been related to the type of formula the routine group received.

In the pilot study, patients were randomly assigned to a protocol group, with the same nurses caring for patients from each group. This method of assignment reduced control of the study protocols and allowed bias to occur. No attempt was made to measure this effect.

In the pilot study, there were no differences in rate or osmolality between those patients who developed diarrhea and those who did not. However, no record was kept of how much formula patients actually received each day regardless of stated rate.

To summarize, the reported research findings are controversial concerning the association of bacterial contamination and diarrhea in enterally fed patients.

Previously conducted studies have been small with poorly defined variables and methodological problems. The results of the pilot study showed a significant difference in bacterial contamination in the two protocol groups. Also, the difference in diarrhea between the two protocol groups approached significance. While there was no significant relationship between those patients with bacterial contamination and those patients who developed diarrhea, the sample size was small and there were methodological problems. Clearly, further study is warranted.

CHAPTER III

Method

In this chapter the methodology of the study is discussed, beginning with the study design, sample, and setting. Following this discussion, the study protocol and data collection procedures are reviewed. Next, instrumentation and measurement issues are presented. Finally, data analysis and protection of human subjects are discussed.

Design

A quasi-experimental, non-equivalent control group design was used for this study (Campbell & Stanley, 1963). There were two groups, one receiving the experimental treatment (n=30), and one acting as the control (n=33). The experimental group received the aseptic procedure for preparation and maintenance of enteral feedings and the control group received the usual routine enteral feeding procedure. The independent variable was the enteral feeding procedure, aseptic or routine. The dependent variables were the presence or absence of bacterial contamination and the presence or absence of diarrhea. Both groups were checked daily for formula contamination and diarrhea on four consecutive days after the initiation of enteral nutrition. The control group data were collected first and then the

experimental group data since the same nurses carried out the protocol for both groups.

The non-random assignment of subjects does affect external validity. However, data collection in this order prevented contamination of the group protocols and provided greater control of the independent variable.

Setting

The study settings were ICUs from the Veteran's Administration Medical Center (15-bed Surgical Intensive Care Unit, 7-bed Medical Intensive Care Unit, and an 8-bed Coronary Care Unit), and Oklahoma Memorial Hospital (12-bed Intensive Care Unit, 8-bed Coronary Care Unit). Both are large (>250 beds), not for profit, teaching hospitals on the campus of the Oklahoma City Health Science Center complex. Two hospitals were chosen so that data collection could be expedited.

The Veterans Administration Medical Center is a 389-bed acute care hospital serving approximately 9,800 adult male veterans in the last fiscal year. There is an average of nine patients per month who receive enteral nutrition in the critical care units.

Oklahoma Memorial Hospital is a 283-bed acute care hospital serving 12,600 patients in the last fiscal year. Approximately 15 patients per month receive enteral nutrition in the critical care units.

Sampling

The sampling frame was convenience, with all patients who fit the criteria approached for inclusion in the study. Each patient accepted into the study was assigned to the control group (the first 33 patients) or the experimental group (the next 30 patients).

The study sample included patients aged 18 or older, of either gender, who had orders to receive enteral feeding. These patients had a variety of illnesses, acute and chronic. Patient illnesses included trauma, acute cardiovascular, pulmonary, and neurologic illnesses, and various other conditions. Because of the severity of the illness, many of these patients were unable to eat and required enteral nutrition.

Patients were excluded from the study if there was evidence of 1) hepatic dysfunction (Protime > 1.3 x control, and/or total bilirubin > 1.5 mg/100 ml), 2) bowel disease (Crohn's, ulcerative colitis), 3) gastric disease (active bleeding ulcers, diverticulitis, ileus), or 4) diarrhea within the previous 2 days. Patients were also excluded if they had a previous feeding tube placement/feeding within the last 48 hours or if they were receiving laxatives.

Patients with hepatic disease were excluded because they required enteral feeding formulas that were low in

protein. Bowel disease may influence the occurrence of diarrhea and, therefore, those patients were also excluded. Finally, it would be difficult to know if diarrhea was related to enteral feedings in patients who have had diarrhea in the preceding 48 hours or who have received laxatives prior to beginning the enteral feeding and they were also excluded.

The desired sample size was estimated using data from the pilot study (Mickschl et al., 1990). For the research question comparing diarrhea in experimental and control protocol groups in the pilot study, the effect size was calculated to be .41 for the Chi square statistic (Cohen, 1988, p 216).

	Aseptic Group	Routine Group	
No Diarrhea	13	8	21
Diarrhea	5	10	15
	18	18	36

A computer program developed by Bernstein and Cohen on power analysis was used to determine the appropriate number of subjects (Bernstein & Cohen, 1988). Using an effect size of .41 with an alpha of .05 and a power of .75, a sample of at least 33 subjects per group was required for the research question comparing diarrhea and

protocol. Because of difficulty in obtaining the necessary number of subjects in a timely manner, data collection was stopped after 26 months with 33 subjects in the routine group and 30 subjects in the aseptic group. With that sample size, power was .70.

Definition of Terms

Diarrhea - ≥ 3 liquid stools within a 24 hour period or ≥ 2 liquid stools on consecutive days, not including any stool which was formed or semi-formed.

Bacterial Contamination - The presence of microorganisms in locations where they normally are not found or are not intended to be found. Contamination was categorized according to the presence or absence of at least 1×10^3 colony forming units/ml of bacteria or yeast in the feeding formula. Bacteria categories used were gram negative bacilli, gram positive cocci, yeast, and other.

Culture - The application of an enteral feeding specimen to microbiological media in order to determine the presence and identity of microorganisms.

Enteral Feeding - Any commercial solution made for the purpose of providing nutrition through direct entrance into the GI system via indwelling feeding tube. For this study, Osmolite^R (Ross Laboratories, Columbus, Ohio), an isotonic, polymeric formula, was used for both

groups.

Stomach aspirate - The liquid in the stomach at the time of aspiration. For the study, a 5 ml sample of stomach fluid drawn from the enteral feeding tube with a syringe after discarding a 3-5 ml sample drawn to clear the tubing.

Routine Enteral Feeding Procedure - The usual procedure for preparation and maintenance of enteral feeding solutions in the study hospitals. This procedure was based on protocols described in nursing journals and textbooks and included direct handling of the enteral solution to replenish the supply, breaking the system to give medications, checking for placement, and irrigating the feeding tube (Appendix B).

Aseptic Enteral Feeding Procedure - The use of a closed system for delivery of enteral feeding with minimal interruption. This system included an in-line stopcock used for giving medications, checking for placement, and irrigation; sterile water or normal saline for irrigation; and a pre-packaged enteral feeding bag (Appendix B).

Aseptic Technique - Methods which destroy or prevent the entrance of microorganisms into the body. For this study, aseptic technique included hand washing and handling equipment and ingested substances (medications,

feeding formula) to prevent the introduction of microorganisms to patients.

Medication - A substance prescribed by the physician for healing, curing, or easing pain. For this study medications were substances which patients received according to the nurses' medication record. Medications were recorded each day of the study and were divided into categories according to their general classification. Antimicrobials, antacids, elixirs containing sorbitol, and histamine antagonists were analyzed for their relationship to diarrhea.

Nutritional Status - The degree to which persons have adequate calories and protein to maintain anabolism. For this study, a combination of serum albumin, serum transferrin, percent ideal body weight and absolute lymphocyte count were analyzed individually and measured as an index (See Appendix J). In addition, percent ideal body weight, tricep skinfold thickness, and percent body fat was analyzed for their relationship to diarrhea.

Days Without Food - The number of days since the subject last ate solid food as reported by the patient or close family member.

Osmotic Load - The product of the concentration of particles in solution and the amount of solution ingested in 24 hours. For this study, osmotic load was the

combination of feeding rate, amount ingested, and osmolality over a 24 hour period. Feeding rate was taken from the nursing flowsheet. Osmolality was reported by the product manufacturer. Osmotic load was calculated each 24 hours for four days. For example, a patient who was on full strength Osmolite with an osmolality of 300 mOsm/1000 ml who received 1000 ml of formula in 24 hours would have an osmotic load of 300 mOsm/day.

Protocol

Once the enteral feeding was ordered, the patients were assigned to one of two groups, the first 33 patients were the routine enteral feeding group, then next 30 patients were the aseptic enteral feeding group. All patients admitted to the identified intensive care units who met the criteria were asked to participate. The physicians were notified of the study at the beginning of each month. Each critical care unit had a binder with information concerning the study. This information included physician responsibilities (Appendix A), protocol (Appendix B), nursing procedure for aseptic and routine groups (Appendix C & D), and aseptic and routine checklist (Appendix K). As study patients were identified, each physician was contacted personally so the appropriate orders could be written.

Data Collection

Data collection lasted 26 months. This extended time period was required to recruit the number of subjects who fit the study criteria. While the estimated number of enterally fed patients for both hospitals was 24 per month, some patients were ineligible, some refused to participate and some physicians refused to participate. Also, some patients expired or had their tube feeding stopped before data collection was complete.

Once the investigator was notified of a potential subject, the chart was checked for exclusion criteria. The physician was contacted and permission to enroll the patient was received. Next, patient consent was obtained, preferably from the patient. However, patients who were critically ill were often not able to give consent, in which case the legal guardian was asked for consent. The enteral tube was inserted by the physician or nurse, using clean technique.

Samples of the enteral feeding, taken from the feeding bag, and of the stomach aspirate, taken from the end of the enteral tube, were obtained by the investigator, using aseptic technique. These samples were obtained each morning for a total of four days. Number and consistency (normal or diarrhea) of stool were recorded by the nurses or the investigator each day up

through four days.

Prior to the beginning of the study, a review of the study was presented for the nurses in each unit, with an emphasis on the established routine protocol for the study and the nurses' role in data collection (Appendix D). At the time of the protocol change (routine to aseptic), another inservice was done in all study units, emphasizing staff nurses' tasks and responsibilities in maintaining the aseptic protocol and collecting data. Also, instructions for the nurses were placed at the bedside of each study patient for each protocol group (Appendix C and D).

Group A (experimental group) received Osmolite in a 1000 cc plastic bottle using a closed system of delivery. Osmolite^{R} was chosen for this study because it came packaged in one liter sterile bottles that allowed for minimal handling and potential contamination of the formula. Osmolite was a nutritionally balanced isotonic, 1 kilo-calorie per milliliter, formula. It was very similar in composition to Isocal^{R} and Nutren 1.0^{R}. The nurses or the investigator hung a prefilled bottle of formula in which the only contact with the formula was in placing the tubing spike in the bag. This procedure was done using aseptic technique. Bags were changed at least every 24 hours by the investigator or the nurse using

aseptic technique. Feedings were delivered by continuous infusion pump. Any time the system was entered, aseptic technique was followed. The investigator changed the tubing each day. The nurses provided written information on the enteral feeding flow sheet which was kept at the bedside (Appendix E). The investigator also used this form to record information. The time spent by the nurses to record information was minimal.

Group B (control group) received the standard procedure for administering and maintaining enteral feedings as defined by a combination of the two hospitals procedure policies (Appendix F and G). If conflict existed between the policies, the most conservative approach was chosen. The guidelines can be found in Appendix D. These patients received canned Osmolite^{R} that the nurses prepared on the unit. This formula was packaged in cans and required the nurses to transfer the formula to the feeding bag. All feedings were delivered by continuous infusion pump. The investigator obtained samples from the enteral feeding bag for culture and the stomach for pH.

For each group, the feeding formula samples were delivered to the hospital laboratory where the cultures were done. All specimens were inoculated onto 5% sheep blood and MacConkey agars with a 0.001 ml calibrated loop

within two hours of sample collection. Plates were incubated at 35°C for four days. Organisms present in the concentrations ≥ 1 x 10^3 cfu/ml were identified by conventional methods. The investigator paid for the cost of those cultures.

The investigator had a data sheet which was used to record demographic data, laboratory values, and medications. This information was used to examine the intervening variables (Appendix H). A schedule of laboratory and sample collection is found in Appendix I. Many of the laboratory tests (WBC, Chem 19) were routinely ordered for ICU patients and therefore, were not paid for by the study investigator. The feeding formula cultures and transferrins were not routinely ordered for ICU patients and were paid for by the investigator.

Instrumentation and Measurement

Dependent Variable

Diarrhea. For the study, diarrhea was defined as ≥ 3 liquid stools per day or ≥ 2 liquid stools on consecutive days, not including any stool that was formed or semi-formed. The staff nurse counted each liquid or watery stool and noted it on the patient data collection form. Also, each normal stool was recorded on the patient flow sheet. If there appeared to be missing

data, the investigator checked the patient flow sheet and the nurses narrative notes. Also, the nurses were verbally questioned each day about the occurrence of diarrhea in the patient. The selection of the definition for this study was based on research findings, practice knowledge, and clinical feasibility. Diarrhea was recorded both as a dichotomous variable, present or absent, for each subject and as the total number of liquid stools. The number of days of diarrhea in those subjects who develop diarrhea was also collected.

The content validity of this measurement was addressed by the investigator in a survey of ICU nurses which asked them to define diarrhea (Davidson, 1989, unpublished data). Liquid or loose stool were terms used by 13 out of 15 surveyed nurses to describe diarrhea. Also, 13 out of 15 nurses stated they were rarely uncertain about whether or not the patient had diarrhea.

Reliability of the measure was strengthened by training sessions with the nurses to describe the study and reinforce the definition of diarrhea. Also, narrative descriptions of diarrhea were examined in the nurses notes.

Bacterial Contamination. The other dependent variable was bacterial contamination. Agreement was not found among researchers about the definition of bacterial

contamination. The FDA has identified a standard for acceptable bacterial growth in milk products which is 2 x 10^4CFU/ml on culture plates of 5% sheep blood and MacConkey agar (Public Health Service, Food and Drug Administration, 1985). Several studies used this value as the critical indicator of bacterial contamination (Anderson et al., 1984; Beyer et al., 1983; Gibbs, 1983; Schroeder et al., 1983). Iannini et al. (1983) and Meijer, Van Saene and Hill (1990) used 1 x 10^3/ml and Keohane et al. (1983) used 1 x 10^2/ml. Since there are no definite guidelines for what constitutes bacterial contamination, this study used a conservative approach and $\geq$ 1 x 10^3 cfu/ml of bacteria or yeast was used to identify the presence or absence of bacterial contamination in the feeding formula. For this study, only aerobic bacteria were identified. Although anaerobic organisms may also contaminate the GI system, particularly Bacteroides, numerous species makes it costly and time consuming to culture for these organisms. Aerobic organisms were identified as yeast, gram positive cocci, gram negative bacilli, or other.

All bacterial cultures were sent to one laboratory and interpreted by the same microbiologist. This laboratory had daily quality assurance routines designed to ensure accurate measurement. For example, the culture

media were routinely tested for pH and appropriate test bacteria results. The laboratory was approved by the American College of Pathology. Content validity of the techniques for plating and counting bacteria was established by agreement of three microbiology experts. Intrarater reliability was established by using split random samples for at least 10% of the culture samples. Reliability of 100% was obtained.

Independent Variable

Enteral Nutrition Feeding Protocol. The independent variable was the treatment of aseptic or routine enteral feeding protocol. The routine protocol group was studied first. The investigator met with the staff nurses in all five units to explain the study and to review the routine protocol. After collection of the first 33 patients, the investigator again met with the staff nurses to explain the aseptic enteral feeding protocol (Appendix C and D).

The investigator observed the nurses adherence to the both the routine and aseptic protocol randomly during the study for 10% of the patients. The first random check occurred within the first five study patients for both protocols. Then, any problems were rectified. During these observations, the investigator checked for such issues as proper use of the stopcock, use of clean

syringes when entering the system, and appropriate handwashing prior to manipulation of the enteral system. A checklist was used to determine if breaks in protocol were major and if the patient data should be discarded (Appendix K).

In addition, the investigator checked daily for any breaks in the protocol. If major breaks were found, the patient data was discarded from the study and the reason for the break determined (Appendix K).

Control of the protocols was enhanced by the initial explanation of the study, instructions at the bedside, and the daily observance of the protocol by the investigator. Reliability of the protocol was formally assessed by random protocol checks for 10% of the patients. No major breaks in technique were found.

Intervening Variables.

The intervening variables for the study were severity of illness, medications, gastric pH, nutritional status, days without food, and osmotic load. These variables, because of their potential relationship to diarrhea, were measured but not controlled. These data were used to answer the question of what variable or variables might be the best predictor of diarrhea. Also, these variables were used to determine the equality of the groups.

Severity of Illness. Apache II is an established point score based upon weighted values of 12 routine physiological variables (Appendix M). The validity of Apache II was tested in association with hospital mortality in 5812 carefully described ICU patients admitted to 13 hospitals. Interobserver reliability testing revealed 96% agreement for all physiologic data (Knaus, Draper, Wagner & Zimmerman, 1985).

Medications. Medications were defined as all current medications being administered according to the nurses medication record during the time of the study. Medications were recorded each day of the study on a data collection sheet and were divided into categories according to their general classification. Medications have been linked to diarrhea, particularly antimicrobials (related to overgrowth of bacteria in the small bowel), sorbitol (laxative found in elixirs), and histamine receptor antagonists (related to an increased gastric pH), although the evidence is controversial (Dobb, 1986; Edes, et al., 1990; Kelly et al., 1983; Ruddell & Losowsky, 1980). Antimicrobials were divided into general groups for analysis. Since histamine receptor antagonists alter gastric pH and most ICU patients receive them to prevent stress ulcers, pH was measured daily for four days using gastric aspirate samples. All

gastric pH samples were measured with a Model 701A pH meter (Orion Research, Cambridge, Mass) to the nearest 0.1 pH unit. The 701A pH meter was reported by the manufacturer to have a relative accuracy equal to ±0.1 mv, ±0.002 pH, or 0.05% of a reading, which ever is greater. The meter was calibrated daily against a known standard.

Nutritional Status. Nutritional status was determined using serum albumin, serum transferrin, percent ideal body weight, and absolute lymphocyte count as an index. These variables have been used in varying combinations and have successfully predicted mortality and morbidity (Seltzer, Fletcher, Slocum, & Engler, 1981; Rainey-MacDonald, Holliday, Wells, et al., 1983). Using the index, the subjects were categorized by degree of malnutrition: none (0 - 2), mild (3 - 5), moderate (5 - 9), or severe (10 - 12) (Cerra, 1984). Each variable was assigned a number based on the degree of abnormality. The scores of each variable were summed and the degree of malnutrition assigned for each patient. For example, the normal range of albumin is 3.5 - 5.5 g/dl and any patient values in this range were assigned zero. If the patient value was 2.8 to 3.4 g/dl, one was assigned; 2.1 - 2.7, two was assigned; <2.1 received a three. Each variable was divided into four categories and the sum of the

scores for the four variables comprised the total score. The assigned values for each variable can be found in Appendix J. Intrarater reliability was determined on 10% of the patient indexes with a reliability of 100%.

Content validity of the nutritional index was established by a panel of experts (three dietitians). Other methods of measuring nutrition such as underwater weight and some anthropometric measurement are not feasible for an ICU population.

The nutritional index was used in the pilot study (Mickschl, et al., 1990). None of the individual index measures were significantly correlated to diarrhea. However, 67% of those with moderate or severe malnutrition had diarrhea and 67% of those with mild or no malnutrition had no diarrhea. Intrarater reliability of the index was established by reexamining 12 (33%) of the pilot study charts with a reliability of 96%.

Each of the index variables were also examined individually for any relationship to diarrhea. Several previous studies reported a relationship between low albumin and diarrhea (Brinson & Kilts, 1987; Brinson, Curtis & Singh, 1987; Brown & Jones, 1989).

Serum albumin was measured with a Kodak ectochem analyzer and an SMA II instrument using the bromocresol green dye-binding method. Reliability checks were made

using split samples every eight hours in both labs. Sensitivity/precision was ±0.1 mg/dl for both machines.

Serum transferrin was measured with a rate nephelometry procedure using a Beckman Array automated rate nephelometer and a Cobas Bio Atlantic nephelometer. Reliability checks using split samples were done three times per week with sensitivity reported as ±12 mg/dl for both labs.

Percent ideal body weight was measured using data from NHANES I and II (Frisancho, 1984). Tables based on height, gender, age (separate tables for ages 25 to 54 and 55 to 74) and frame size (small, medium, and large) were used with the 50% value chosen for comparison. Frame size was determined by measurement of the circumference of the ankle as prescribed in the procedure for measuring percent body fat. While Frisancho (1984) used elbow breadth to determine frame size, ankle measurement was used in this study to provide consistency between the two measures (ideal body weight and percent body fat). Accuracy of elbow breadth measurement in supine, unconscious patients may be questioned. However, no data was found which compared ankle measurement to elbow breadth or wrist measure and no information was found on how ankle norms were determined.

Lymphocyte count was measured using a Coulter

Counter in both labs. Split samples were run every two hours or every 20 specimens, whichever came first in each lab.

Percent body fat was measured using near-infrared spectroscopy (Futrex-5000™, Futrex, Inc., Gaithersburg, Maryland). This technology uses Near Infrared Interactance for determining body composition. First, weight, height, and frame size are measured. For this study, weight was obtained by the staff nurses using bed scales on the first day of the study. Height was measured by the investigator using a fiberglass tape measure. Frame size was determined by measuring the ankle circumference just above the tibiotalar joint.

The Futrex-5000™ is a hand held unit which includes an optical light wand. Measurements are made by placing the light wand on the anterior midline of the biceps halfway between the antecubital fossa and acromion of the prominent arm. The instrument provides a direct digital readout of percent fat approximately two seconds after the wand is placed on the biceps. The measurement is based on a calibration equation built into the unit. Based on this value, percent lean mass can be determined. Intrarater reliability was done on 10% of the study patients (r=.95).

Test-retest reliability was done on ten healthy

subjects with a correlation of 0.94 reported (Davis & Paynter, 1988). Concurrent validity was reported using hydrostatic weighing as r=0.83. However, no data was found which compared other methods of measuring body fat in critically ill patients.

Triceps skinfold thickness was also used to measure percent bodyfat using a Lange caliper. Prior to the study, the investigator attended training sessions with an expert in anthropometric measurement technique. After practice on several normal subjects, 90 percent agreement was achieved with the expert. Then, the technique was adapted for supine patients with more practice until 90 percent agreement was once again achieved (Chumlea, Roche & Mukherjee, 1984).

Days without food was the number of days since the patient last ate solid food. Since some subjects were unconscious or heavily medicated, family members were asked for this information in some cases. If unable to obtain the information from the family, the subject was not included in that part of the analysis.

Osmotic load. Osmotic load was calculated by multiplying the osmolality of the formula times the amount of the formula ingested in 24 hours. For example, a patient who was on full strength Osmolite with an osmolality of 300 mOsm/1000 ml who received 1000 ml of

formula in 24 hours would have an osmotic load of 300 mOsm/day. Often critically ill patients have their enteral feeding stopped for surgery or diagnostic tests. Osmotic load accounted for variations in total daily intake. This information was recorded from the nurses flow sheet at the bedside.

Osmotic load has been identified as potentially contributing to diarrhea (Silk, 1988). Prior studies have reported rate and osmolality but not daily intake of feeding formula. The reliability of this measure was dependent on the nurses accurately recording the running time of the feeding formula. The use of an infusion pump for all patients helped to insure greater reliability in that a running total of amount infused could be recorded from the machine.

Control Variables

The control variables included formula type, rate, and osmolality. Both groups received the same formula, Osmolite^{R} at full strength (isotonic). The aseptic group received Osmolite^{R} in the sterile liter bottles and the routine group received Osmolite^{R} in the can. Preparation of the canned Osmolite^{R} required the nurses to fill the open bag initially and at intervals throughout the day.

The rate of feeding was started at 25 ml/hour

initially. At two hours, the gastric residual was checked. If there was less than 50 ml, the feeding continued. At four hours the gastric residual was checked again. If there was less than 50 ml, the feeding continued. The same procedure occurred at six hours. Finally, at eight hours the gastric residual was checked again. If there was less than 50 ml, the feeding rate was increased to 50 ml. If there was gastric residual in excess of 50 ml, the tube feeding was stopped for one hour and the residual checked again. When the gastric residual was less than 50 ml, the feeding was resumed. The same procedure was instituted for the next 8 hours, with the amount of gastric residual increased to 100 ml. This procedure continued until the tube feeding was at the desired infusion level for calorie requirements of the subject. Then, residuals were checked every 4 hours, according to routine policy (Mayo Clinic Diet Manual, 1988).

Data Analysis

The dependent variables of bacterial contamination and diarrhea were nominal level measures. The intervening variables of liquid stools, gastric pH, nutritional status, and osmotic load were interval level measures. Medications and sex were nominal level measurement. The data analysis was descriptive and

inferential and was divided into three parts: 1) description, 2) preliminary analysis, and 3) hypothesis testing. A significance level of .05 was used for all tests. Statistical analyses were performed using SPSS 6.0 for Windows^{R}. A p value of ≤ 0.05 was considered the *a priori level* of significance.

Description of the Sample

Means, standard deviations and percentages were computed on all interval level intervening variables. The sample was also described by age, gender, and diagnoses. Chi square and student t-tests were performed to determine if groups (hospital, protocol, and diarrhea) were equal. If expected frequencies were less than five in any cell, the Fisher's exact test was used. Stool patterns were described by frequencies of normal, none, or diarrhea.

Preliminary Analysis

Student t-tests were done as the significance test to determine any pretest differences between the two groups (both diarrhea and procedure groups) on the intervening variables of gastric pH, nutritional status, and osmotic load.

Hypotheses Testing

Hypothesis 1: There will be a significantly greater incidence of bacterial contamination in ICU patients who

receive enteral feeding which is prepared using standard hospital procedure when compared to ICU patients who receive enteral feeding which is prepared using an aseptic procedure when both groups receive the same enteral formula. The Chi square test was used to compare the difference in bacterial contamination between enteral feeding protocols. Bacterial contamination was dichotomous, ($<1 \times 10^3$ or $\geq 1 \times 10^3$ organisms).

Hypotheses 2: There will be a significantly greater incidence of diarrhea in ICU patients who receive enteral feeding which is prepared using standard hospital procedure when compared to ICU patients who receive enteral feeding which is prepared using aseptic procedure when both groups receive the same enteral formula. The Chi square test was used to compare the difference in diarrhea between enteral feeding protocols. Diarrhea was treated as a dichotomous variable. Diarrhea was also measured as the number of liquid stools and examined with the student t-test.

Hypothesis 3: If bacterial contamination occurs, there will be a significantly greater incidence of diarrhea in ICU patients who receive contaminated enteral feedings than those who do not. The Chi square test was done to compare the relationship between bacterial contamination and diarrhea in both protocol groups. A

Chi square was also done for each protocol group with contamination and diarrhea. If the expected value in any cell was less than 5, a Fisher's exact test was done. A two by four Chi square test was done to compare diarrhea group with organism group (yeast, gram negative bacilli, gram positive cocci, other).

Hypothesis 4: There will be significant relationships between diarrhea and bacterial contamination, protocol group membership, gastric pH, medications, osmotic load, nutritional status, and days without food.

To address this hypothesis, logistic regression was done, with all subjects combined, to see which of the intervening variables best predicted membership in the diarrhea group. Variables entered into the regression were chosen based on univariate testing. In this case, gender, respiratory diagnosis (yes, no), penicillin (yes, no), aminoglycoside (yes, no), and albumin (≤ 3.4, ≥ 3.5) were entered in a stepwise (forward) manner.

Human Subjects

Human subjects were protected by application and review of the proposal by the Institutional Review Board (IRB) at the Health Sciences Complex in Oklahoma and by the IRB at Case Western Reserve. All subjects had the study explained to them or their legal guardian and a

copy of the consent form was given to them (see Appendix L). The consent form was written in lay language with the benefits and risks clearly defined. Confidentiality and the right to withdraw at any time without penalty was explained. Any identifying data sheets were kept in a locked drawer at the hospital or a locked file cabinet in the investigator's office.

CHAPTER IV

Results

The purpose of this study was to compare the use of two enteral feeding protocols with respect to the incidence of bacterial contamination and diarrhea in ICU patients. This chapter describes the sample, and presents the results of the data analysis undertaken to confirm or dispute the hypotheses. Data analysis was performed using the Statistical Program for the Social Sciences (SPSS for Windows V6.0, 1993). Descriptive statistics such as frequency distributions, histograms, measures of central tendency, and skewness were used to examine variables for normal distribution. There was a minimum of missing data in this study and no substitutions for data were made.

Descriptive Characteristics

Sample. Over a 26 month period, 108 subjects were approached, 3 subjects (or their guardian) refused consent, and 9 subject's physician refused to participate. Ninety-six subjects met the inclusion criteria. The total number of subjects who completed the study was 63. Thirty-three subjects were dropped from the study for a variety of reasons: (a) expired (seven subjects), (b) unable to tolerate enteral feeding as measured by high residuals (17 subjects), (c) changed to

an oral diet (four subjects), (d) tube feeding orders changed (four subjects), and (e) unable to replace feeding tube (one subject).

Subjects were recruited from five intensive care units in two large university-affiliated hospitals on a health science center in central Oklahoma. There were 44 subjects from Oklahoma Memorial Hospital and 19 subjects from Veteran's Hospital. The age of subjects ranged from 18 to 97 years (M=55.5, SD=17.7). There were 16 women and 47 men. Table 1 lists the variety of medical diagnoses which were represented.

Table 1. Comparison of Diarrhea by Diagnosis

Diagnosis	Diarrhea (n)	No Diarrhea (n)	Total	p
Neurologic	3	16	19	0.05*
Cardiovascular	1	5	6	N.S.
Respiratory	7	12	19	0.02*
Gastrointestinal	0	1	1	N.S.
Musculoskeletal	0	2	2	N.S.
Otorhinolaryngeal	3	9	12	N.S.
Cancer	2	0	2	N.S.
Multiple Trauma	1	1	2	N.S.
	17	46	63	

*p ≤ .05
N.S.=Not Significant

Subjects had been patients in the ICU an average of 7.6 days (range 1 to 33 days) before enteral feeding was begun.

Hospital Groups. There were significant differences between subjects in the two hospitals in age, gender, and APACHE scores, both on the first day of ICU admission (APACHE) and the first day of the study (APACHE2). The VA patients were older, all male, and had higher APACHE scores (Table 2). However, except for gender, there were no significant differences in incidence of contamination or diarrhea, and the data were combined for analysis.

Table 2. Comparison of Patients by Hospital

Variable	OMH (N = 44) (Mean ± SD)	VA (N = 19) (Mean ± SD)	p
Age	49.5 ± 16.3	69.4 ± 11.9	0.000*
APACHE	11.5 ± 5.6	15.3 ± 6.0	0.018*
APACHE2	9.4 ± 4.4	15.5 ± 7.0	0.002*

*significant at ≤0.05

Comparisons between Protocol Groups

Contamination. Six subjects in the routine group and three subjects in the aseptic group received enteral formula that contained bacterial contaminants. There was not a significantly greater incidence of bacterial contamination in ICU patients who received enteral

feeding prepared using the standard hospital procedure when compared to ICU patients who received enteral feeding which was prepared using an aseptic procedure (Fisher's exact, p=0.29). Each of the nine subjects received contaminated formula for one day. Contaminants from these formulas included gram negative rods; Enterobacter aerogenes (n=1), Enterobacter agglomerans (n=2), Escherichia coli (n=1) Acinetobacter calcoaceticus van lwoffi (n=1), Pseudomonas sp (n=2), and gram positive cocci; Gamma streptococcus (n=1) and coagulase negative Staphylococcus (n=1).

Diarrhea. Diarrhea was measured as a dichotomous variable and as the number of liquid stools. When diarrhea was measured as a dichotomous variable, (three or more liquid stools/day or two or more liquid stools/day on successive days), 17 subjects developed diarrhea. Of those subjects, 7 (4 women, 3 men) were in the routine group and 10 (4 women, 6 men) were in the aseptic group for an incidence of 27%. There was not a significantly greater incidence in diarrhea in ICU patients who received enteral feeding which was prepared using standard hospital procedure when compared to those ICU patients who received enteral feeding which was prepared using aseptic procedure (Chi square=1.17, p=0.28). The number of subjects with diarrhea steadily

increased over the four study days [Day 1 = 5, (8%); Day 2 = 9, (14%); Day 3 = 13, (21%); Day 4 = 16, (25%)].

There was a significant difference in gender and the development of diarrhea (Fisher's Exact, p=0.02), with women having a greater frequency of diarrhea (women=8, 50%; men=9, 20%). Also, there was a significant difference in medical diagnosis (respiratory vs all others) and the development of diarrhea (Chi square=5.7, p=0.02) and a significant difference in neurologic diagnoses (vs all others) and the development of diarrhea (Chi square=3.74, p=0.05).

When the number of liquid stools, normal stools, or total stools was compared by protocol group, no difference was found (Table 3). Of those subjects with no diarrhea (n=47), 45% (n=21) had no stools over the four days of the study and 55% (n=26) had normal stools.

Table 3. Comparison of Protocol and Number of Stools.

Number of Stools	Routine (N=33) (Mean ± SD)	Aseptic (N=30) (Mean ± SD)	p
Normal	.94 ± 1.54	1.10 ± 1.69	0.69
Liquid	2.00 ± 4.50	2.43 ± 3.17	0.66
Total	2.94 ± 4.76	3.53 ± 4.11	0.60

Contamination and Diarrhea. Of the nine subjects who received contaminated enteral formula, two developed

diarrhea. There was not a significantly greater incidence of diarrhea between ICU patients who received contaminated enteral feedings compared with those who did not (Fisher's Exact=0.32, p=0.58). Those subjects who developed diarrhea had formula contaminated with Acinetobacter calcoaceticus van lwoffi and coagulase negative staphylococcus on one day only.

Nutritional Variables. Subjects had been hospitalized an average of 7.6 days (S.D.= 7.98, range 1-33) before receiving enteral feeding. Nutritional status was measured using an index which included albumin, transferrin, total lymphocyte count, and percent of ideal body weight. Cronbach's alpha for the index was 0.15, with a standardized alpha of 0.39. No difference was found in the nutrition index between those subjects who did and did not develop diarrhea. The only significant difference between those subjects who did and did not develop diarrhea in any of the nutritional variables was in the level of serum albumin (p=0.05). Ten percent of the subjects had either no malnutrition or were severely malnourished. The other 90% were mildly or moderately malnourished (Table 4).

Antimicrobials. A total of 30 different antimicrobials and antifungals were received by 57 of the 63 subjects in this sample.

Table 4. Nutritional Variables

Variable	Diarrhea (N=35) (Mean ± SD)	No Diarrhea (N=25) (Mean ± SD)	t	p
% Ideal Body Wt	96.62 ± 23.53	94.32 ± 24.15	0.33	0.74
Bodyfat % (Infra-red)	19.71 ± 9.43	15.89 ± 8.52	1.52	0.13
Albumin (gm/dl)	2.66 ± .73	3.13 ± .88	-1.97	0.05*
Trans-ferrin	145.06 ± 42.12	162.59 ± 37.80	-1.55	0.13
Total Lymph Count	1.06 ± 0.61	1.24 ± 1.20	-0.62	0.54
Hospital days NPO	9.24 ± 9.84	6.96 ± 7.20	1.01	0.32
Index Nutrition Score	2.59 ± .71	2.28 ± .62	1.67	0.10

*Significant at $p \leq 0.05$

Of the 57 subjects, 25 received one antimicrobial, 25 received 2 antimicrobials, and 6 received 3 antimicrobials. There was no relationship between number of antimicrobials received and number of liquid stools ($F=2.4$, $p=0.07$). Because individual drug groups were very small, antimicrobials and antifungals were collapsed into six general categories (Table 5). There was a

significant relationship between receipt of penicillin and diarrhea (Chi square=4.83, p=0.03) and aminoglycosides and diarrhea (Chi square=5.73, p=0.02).

Other Medications. Eight subjects were receiving metoclopramide (Reglan). Those subjects receiving histamine antagonists were divided between ranitidine (Zantac=37) and cimetidine (Tagamet=8). There was no significant relationship between receipt of any of these medications and the development of diarrhea.

Five subjects received elixirs (theophylline=4, cimetidine=1) which are reported to contain sorbitol. There was no significant relationship between receipt of those elixirs and diarrhea.

Osmotic Load. All subjects were started on Osmolite at 25cc per hour. Rates were increased by the nurses every eight hours as tolerated, up to target rates ranging from 75 to 150cc per hour. Mean osmotic load increased daily until the fourth day when it decreased. There was no significant difference in osmotic load between those subjects who did and did not have diarrhea on any day (p=0.32-0.93).

Other Variables. Most subjects had small bore feeding tubes (n=49, 78%), with a few Salem sumps (n=9, 14%) and gastrostomy tubes (n=4, 6%), and a Levine tube (n=1, 2%).

Table 5. Antimicrobial Comparisons

Category	Diarrhea (n)	No Diarrhea (n)	Total (n)	p
Amino-glycosides	9	10	19	0.02*
Misc@	8	18	26	0.57
Cephalo-sporins	7	18	25	0.88
Peni-cillins	9	11	20	0.03*
Anti-fungals	1	2	3	0.80
Sulfon-amides	0	4	4	0.21

@Includes Cleosin, Erythromycin, Vancomycin, Ciprofloxacin, Aztreonam
*Significant at $p \leq 0.05$

Eight subjects (13%) had pitting edema and seven subjects (11%) had septicemia. There was no significant difference in pitting edema or septicemia and the development of diarrhea. Mean gastric pH ranged from 4.38 on day 1 to 5.40 on day 4. There was no significant difference in the development of diarrhea and gastric pH on any of the four study days (Table 6).

Table 6. Comparison of Gastric pH and Diarrhea.

	Gastric pH			
	Diarrhea (N=12-15) (Mean ± SD)	No Diarrhea (N=31-38) (Mean ± SD)	t	p
Day 1	4.0 ± 2.3	4.5 ± 2.3	-.66	0.51
Day 2	5.4 ± 0.6	5.2 ± 1.6	.84	0.40
Day 3	5.5 ± 0.8	5.1 ± 1.3	1.20	0.24
Day 4	5.9 ± 0.8	5.2 ± 1.5	1.82	0.08

Multiple stepwise logistic regression analysis was used to determine the variables that best predicted the probability of diarrhea. Using logistic analysis, the predicted probability can be interpreted as the estimated percentage of subjects with that variable combination who will have diarrhea.

Six variables entered into the logistic regression analysis were albumin (greater or less than 3.5), penicillin (yes/no), aminoglycoside (yes/no), respiratory diagnosis (yes/no), and gender. These variables were chosen on the basis of univariate findings from the data.

Data on 63 subjects were complete on all six variables. Three variables were identified as significant predictors of diarrhea at the 0.05 level: aminoglycoside ingestion, serum albumin, and gender.

Gender was the first variable entered into the regression equation because it accounted for the greatest amount of variability in the incidence of diarrhea. Aminoglycoside entered next, with albumin entering last (Table 7). Using these three variables, 78% (n=49) of subjects were correctly classified.

Overall fit of the model was tested with a Chi square distribution (p=0.581). In this case, the large significance indicates that the model fits adequately. A model Chi square with a significant p value (p=.004) indicates the predictors do add to the model and the null hypothesis is rejected.

Table 7. Logistic regression predictor variables

	B	p	Odds Ratio	95% Confidence Intervals
Gender	2.0765	.0078**	7.9764	1.726 - 36.855
Amino-glycosides	1.5984	.0264*	4.9450	1.206 - 20.279
Albumin	2.2008	.0531*	9.0325	1.030 - 84.041

* p ≤ .05
**p ≤ .01

There were 14 subjects misclassified, most of whom were predicted as having no diarrhea. Influential cases were identified using Cook's test and DFBeta. Also, residuals were examined. One patient was found to be very influential with high residuals. This patient was a

forty year old female with a neurologic problem (subarachnoid hemorrhage) who had an albumin of 5.0, was not receiving aminoglycosides and developed diarrhea on the last day of the study. She had a very low transferrin and was moderately malnourished.

The limitation of this model is poor precision indicated by the wide confidence intervals. Also, prediction is better for who will not get diarrhea rather than who will.

CHAPTER V

Discussion

Many studies have suggested that bacterial contamination of feeding formula may contribute to diarrhea. A pilot study examining this hypothesis suggested this finding was true. However, the pilot study had few subjects, low power, and many intervening variables. This quasi-experimental study improved on the pilot study with a larger sample size, higher power, and greater control of many intervening variables.

The purpose of this study was to determine the differences in the incidence of contamination and diarrhea between subjects receiving routine and aseptic procedures in managing their enteral feeding systems. The objectives of this chapter are to discuss the results of the four hypotheses, the limitations of the study, and the implications for nursing practice and future nursing research.

The first hypothesis posited that there would be a difference in the incidence of bacterial contamination between ICU patients based on how the enteral feeding was prepared and delivered (routine or aseptic). This hypothesis was based on pilot

work (Mickschl et al., 1990) and was not supported in this study. The result may be explained, in part, because of very small numbers of subjects with contamination (routine=6, aseptic=3). Each subject who received contaminated formula received it on one day only. Those subjects receiving contaminated formula in the aseptic group were subjects who received food coloring (n=2) in the formula or who had documented manipulation of the system by staff nurses which was not part of the protocol (n=1).

Most reported studies found highest contamination rates in kitchen prepared or powdered formulas which were reconstituted (Anderson et al., 1984; Keohane et al., 1983). Oie (1993) found contamination of all residual solutions obtained immediately after administration (n=22). In that study, contamination was thought to be related to frequent reuse of bags and tubing, not manipulation of the formula. In this study, no bags or tubing were reused and equipment was changed every 24 hours with no formula reconstitution. This practice is generally recommended in current nursing texts (Potter & Perry, 1990; Flynn, 1993)

Another possible explanation of the low contamination rate may be practice related. ICU

nurses may be more conscientious about protecting their patients from nosocomial infections than other staff nurses, and therefore, use better technique in handling enteral feeding equipment. Also, since the nurses knew they were part of a study, they may have been more careful in caring for study patients.

The second hypothesis posited that there would be a difference in the incidence of diarrhea between ICU patients based on formula preparation and delivery. This hypothesis was not supported. There were approximately equal numbers of subjects between the two protocol groups with diarrhea (routine=7, aseptic=10). One explanation for this finding may be that there was not much variation between the protocols. Perhaps, if the nurses had not been given a strict protocol for the routine group, results may have been more reflective of actual practice. However, one would be concerned about too much variability between nurses confounding the results. Given the assumption that the protocol was followed in each group, it appears that other factors influenced the development of diarrhea in this study.

In this study, 27% of tube-fed critically ill patients developed diarrhea. This incidence is less

than the 32 to 63% reported in the literature (Flynn, et al., 1987; Hart, et al., 1988; Kelly et al., 1989; Mickschl et al., 1990; Smith, et al., 1990). Many factors may have affected the incidence of diarrhea in this population. First, the definition of diarrhea in the literature is quite varied, and accounts for some of the wide range reported (Bliss, et al., 1992). In this study, if the definition of diarrhea included any liquid stool, the incidence of diarrhea increased to 37%.

Another factor which may have contributed to the low incidence of diarrhea was the study formula. Osmolite^{R}, an isotonic formula, may have been better absorbed. Osmolality has been identified by some investigators as significantly contributing to diarrhea (Smith, et al., 1990; Silk, 1987). However, these investigators reported data on subjects receiving a variety of formulas. The current study subjects all received Osmolite^{R}, full strength, starting at 25cc per hour. Osmotic load was a computed variable which accounted for osmolality and amount of formula ingested in 24 hours. No significant differences in diarrhea were noted for subjects based on osmotic load.

Finally, of those subjects who had no diarrhea

(47), 21 (45%) had no recorded stools over the four day study period. It is not clear why these patients had no stools but one reason might be impaction. If the study had lasted longer, perhaps the incidence of diarrhea would have increased.

The most frequent diagnoses for these subjects was neurological (n=19), respiratory (n=19), and otorhinolaryngeal (n=12). There was a significant difference in those subjects with a neurologic diagnosis (vs all others) and diarrhea and a significant difference in those subjects with a respiratory diagnoses (vs all others) and diarrhea. Subjects with a neurological diagnosis were less likely to develop diarrhea while subjects with a respiratory diagnosis were more likely to develop diarrhea. There were no studies found which explained or offered a reason for a lower incidence of diarrhea in neurologic patients. However, the respiratory diagnosis has been linked to higher incidences of diarrhea by Smith (1990) who studied critically ill, ventilator dependent respiratory patients. Smith suggested that pulmonary disease patients may enter critical care units with intestinal atrophy related to malnutrition and therefore have a decreased ability to absorb

nutrients.

The third hypothesis posited that if contamination occurred, there would be a significant difference in the incidence of diarrhea between those subjects who received contaminated feedings and those who did not. There was a low number of subjects receiving contaminated formula (n=9), and the hypothesis was not supported. This finding is consistent with findings reported by Keohane (1983) and Freedland (1989) in which bacterial contamination as an etiology for diarrhea was not supported. Keohane suggested that stressed patients have high gastric acidity and therefore, effectively destroy gastric organisms. However, many critically ill patients are given H_2 receptor antagonists and antacids, which increase gastric pH. In this study, 45 subjects (71%) received H_2 receptor antagonists and 9 subjects (15%) received antacids. There was no significant relationship between receipt of H_2 receptor antagonists or antacids and diarrhea. Additionally, three subjects who received contaminated formula also received H_2 receptor antagonists or antacids. No significant relationship was found.

Also, continuous enteral feeding may contribute

to an increased gastric pH. Normal gastric pH is 1.0 - 3.5. In this study, the pH steadily increased, with a mean of 4.38 on day 1 to 5.40 on day 4. Again, no relationship was found between pH and the development of diarrhea.

The fourth hypothesis examined several other factors for association with diarrhea. These factors were nutritional variables, receipt of antibiotics, receipt of diarrhea causing medicines (sorbitol, cimetidine), osmotic load, and gender.

Clearly, the nutritional index used in this study was not predictive of diarrhea, with a Cronbach's alpha of 0.15. The nutritional variables included in the index were not found to be associated with diarrhea, with the exception of albumin. In addition, neither percent of body fat measured by infrared spectrometry or triceps skinfold were found to be associated with diarrhea.

Nutritional variables have been linked to diarrhea, particularly hypoalbuminemia. In this study, low serum albumin was significantly related to the development of diarrhea. These findings are consistent with those of several investigators (Brinson & Kolts, 1987; Cobb, Cartmill, & Gilsdorf, 1981; Brown, Powers & Luther, 1989). Low serum

albumin is thought to indicate malnutrition which contributes to an alteration in intestinal absorption, predisposing the patient to diarrhea. Acutely ill patients may experience a period of no enteral intake with resultant atrophy of colonic cells. When feeding is reinitiated, inadequate ion exchange occurs with decreased absorption (Pesola, Hogg, Yonnios, et al., 1989). Hypoalbuminemia may be the clinical sign indicating such a problem.

Serum transferrin was also examined for association to diarrhea. Although approaching significance ($p=0.13$), it was not found to be associated with the development of diarrhea.

In this study, all but five subjects were receiving at least one antimicrobial agent. Most antimicrobials were administered intravenously. Type of antimicrobial was associated with diarrhea. This finding gains strength in that all subjects were given the same formula, starting at the same rate. Receipt of aminoglycosides was associated with a higher incidence of diarrhea, as was penicillin. Several investigators report an association of diarrhea and antibiotic ingestion (Beyers, Wiggins & Morelli, 1988; Gottschlich, Warden, Michel, et al., 1988; Hart & Dobb, 1988;

Keohane, Attrill, Love, et al., 1984). However, several studies have found that antibiotic use did not significantly predict diarrhea occurrence (Kelly, Patrick, & Hillman, 1983; Smith, Marien, Grogdon, et al., 1990).

Problems with all studies looking at antibiotics and diarrhea include small sample size, failure to control confounding variables, and inconsistent definitions of diarrhea. Therefore, it is difficult to determine the association of diarrhea and antibiotics. In the current study, number and type of antimicrobial received prior to the study onset was not collected, and therefore, the potential influence on diarrhea is not known.

Other medicines found to be associated with diarrhea are histamine-2 receptor antagonists and sorbitol. No relationship was found in this study between receipt of histamine-2 receptor antagonists and diarrhea. Edes (1990) suggested that elixirs containing sorbitol are responsible for diarrhea in some patients. Sorbitol is a common ingredient in elixirs, serving as a sweetener, humectant (moistening agent), and/or vehicle. Liquid preparations may contain 5 to 65% sorbitol without the manufacturer's having to reveal the amount

(Estoup, 1994). In this study, sorbitol was not associated with diarrhea. However, since sorbitol is an inactive ingredient, it is difficult to determine which elixirs contain large enough amounts to be problematic. For this study, elixirs that were reported in the literature to contain sorbitol were identified.

To account for differences in rates over the four days, osmotic load was measured (amount of formula taken in each day times the osmolality divided by 100). Some studies compare rates of formula. Smith (1990) compared rates and found rates over 53cc/hour to be associated with diarrhea. A problem with measuring rates is that, in ICU patients, feedings are often stopped for diagnostic testing, high residuals, and medications administration, thereby altering the actual amount of formula given over a 24 hour period. In this study, diarrhea was not associated with osmotic load on any day ($p=0.32-0.93$).

One unexpected finding of this study was the significantly greater incidence of diarrhea in women. No studies were found which reported a similar finding. The women in this study were different from the men in that they were younger,

and, predictably, weighed less. No other variables were found which gave further explanation to this result. No data were recorded concerning menstrual cycle or menopausal status which may be important. Small sample size (N=16) limits one's confidence in the importance of this finding. One might suggest this unexpected result may simply represent many outliers and may not be replicable. However, if a real difference does exist, treatment modalities may need to be based on gender. Certainly, further research to examine this finding would be helpful.

The logistic regression produced a model with good prediction of subjects who were likely not to develop diarrhea but was not as good for predicting those who were likely to develop diarrhea. Based on the univariate analysis, receipt of aminoglycosides, gender, and albumin level combined to predict 78% of subjects correctly. Possibly other variables would improve that percentage but none were discovered. Again, perhaps menstrual cycle or menopausal status could be important.

Limitations

Several limitations of this study must be acknowledged. First, this was a clinical study with all the inherent problems of attempting to control a

practice setting. As such, one limitation was the assumption that the protocol was followed by the nurses in each unit on all shifts. Certainly it was not feasible to observe each nurse with each patient to ensure absolute conformance. However, several steps were taken to address this problem. The protocol was explained to the nurses several times for each shift, in each unit. Also, the investigator randomly observed nurses adherence to the protocol all during the data collection period. Of those behaviors listed as major, no deviations were observed (n=6). Also, the investigator reinforced the procedure on daily rounds to the units, occurring both on days or evenings.

Also, history was a threat to the internal validity of the study, as data collection occurred over 26 months. For example, physician practice changed for the group of ORL patients between the routine and aseptic protocol data collection period resulting in fewer ORL patients in the aseptic group. If there had been a significant relationship between ORL diagnosis and diarrhea, this change could have been important. Over such a long period of data collection, other unrecognized events may have occurred which threatened internal validity. In

addition, turnover rates of ICU nurses could have affected the results although several mechanisms were used to diminish this problem (see above).

Data collection progressed slowly for several reasons. First, communication was sometimes difficult between the staff nurses and the investigator since the paging system did not function well outside of a 20 mile radius and the investigator lived 25 miles from the hospitals. This problem occurred on weekends when nurses tried to contact the investigator about a new patient. Also, float nurses or agency nurses did not always call the investigator when a potential study patient was to be started on enteral feeding.

Another problem with data collection was constant physician change. Each month a new group of physicians rotated through the units and sometimes they were not supportive of the study. For example, one month the physicians ordered another enteral feeding for most patients after talking with the company representative. Many physicians had little understanding of enteral formulas and what would be most appropriate. In addition, dietitians were often not consulted by physicians.

Contamination rates were low in this study. One explanation for these low rates may be that sampling was from the enteral nutrition bag. If sampling had occurred further down the tubing, more contamination may have been found.

Use of a nonrandom, convenience sample clearly limits the generalizability of this study. However, protocol contamination using a randomized sample would have rendered the results meaningless. In addition, since directional hypotheses were tested and the results were in the opposite direction, there was a greater chance for a Type II error to occur. The power calculated for the hypothesis regarding diarrhea and protocol was only 0.28 resulting in a large possibility of missing any treatment affect.

In this study, no attempt was made to measure emotional factors which may have contributed to diarrhea in some patients. It is reasonable to believe that critically ill patients may experience both acute and chronic stress which may contribute to the development of diarrhea. Also, among the women, menstrual cycle or menopause may affect stool consistency.

Implications

The results of this study indicate that for similar groups of patients, current practice for the maintenance of enteral feeding formula and equipment (as defined in current nursing literature) may be adequate. However, caution is advised in generalizing to all patients receiving continuous enteral feeding.

Current practice for handling enteral feeding formula and equipment should include good handwashing, capping feeding bags, and limiting solution hang time to 24 hours. Careful adherence to these practices may have contributed to the low rate of contamination found in this study. Also, sampling of formula from the bag rather than further down the tubing may have resulted in more contamination.

Certainly, further study is necessary in examining the relationship of antimicrobials and diarrhea. This study suggests that those patients receiving aminoglycosides and/or penicillin may be at greater risk for the development of diarrhea. But, as with other studies, small sample size limits generalizability. In addition, studies which examine use of antimicrobials prior to initiation of

enteral feeding may provide additional explanation.

Another direction for future research may be to examine another population such as nursing home patients and patients at home. Random testing of formula could be done to determine if clean technique is adequate to prevent problems with diarrhea. Routine care of nursing home patients is often done by aides who may be less concerned with proper system maintenance and adherence to procedural guidelines.

Finally, further examination of tube-feeding effects on women would be another direction for research. Perhaps menstrual cycle and menopause could be explored for any relationship to diarrhea in women receiving tube-feedings.

Conclusion

The original interest in this topic was prompted by experience in caring for ICU patients who often experienced diarrhea after the initiation of enteral feeding. If nurses could alter this occurrence by changing nursing practice, patients would benefit. Following the direction of a pilot study, this investigation used a larger sample size, more control of intervening variables, and measured confounding variables. In this population of

subjects, the results indicate that many factors may contribute to the development of diarrhea in critically ill patients. No change in current nursing practice for the preparation and maintenance of enteral feeding for ICU patients is recommended on the basis of these findings.

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APPENDIX A

Physician Responsibilities

1. Insert the feeding tube using sterile technique. Wash hands, use gloves and a sterile towel.

2. Write orders for **continuous** enteral feeding:

   a. Osmolite, full strength, to run at 25 cc/hour.

   b. Check for residual every two hours. If less than two times the hourly rate continue feeding until 8 hours. Then, increase the feeding by 25 cc/hour. Continue to increase every 8 hours until the desired rate is reached. If the residual is greater than two times the hourly rate, stop feeding and check residual hourly. When residual is less than two times the hourly rate, resume feeding using the previous protocol.

3. Write orders for transferrin on the 4th day of the study for all patients.

Dear ICU Physician:

I am currently conducting a research study involving ICU patients receiving enteral feedings. As you are aware, one of the untoward consequences of enteral feeding is diarrhea. Although several causal mechanisms have been suggested by the literature, empirical data is meager.

Therefore, I am investigating several potential influencing factors, including bacterial contamination, nutritional status, severity of illness, and gastric pH. The procedure entails assignment of patients to receive Osmolite using two protocols. Group I (the first 50 patients) will receive canned Osmolite using the regular, routine protocol. Group II (the next 50 patients) will receive Osmolite using a sterile, self contained system. Cultures of the feeding formula will be collected daily for 4 days and the occurrence of diarrhea will be noted. In addition, a CBC with diff and a transferrin will be drawn if not already ordered. If the patient is less than 40 years old and has a closed head injury, a UUN and pre-albumin will also be ordered. Consent to participate will be obtained from all patients (or family). Extra lab costs will be paid by me.

I request that you write or co-sign my written orders as follows:

1. Osmolite, full strength, at 25 cc/hr. Check residual q 2 hr and, if tolerated (residual less than 2 times the hourly rate), increase by 25 cc q 8 hr to desired rate of _____. If residual is greater than 2 times the hourly rate, stop feeding, check residual hourly, and resume when residual is less than 2 times the hourly rate, using the previous protocol.

2. Transferrin (CBC, Chem 19, pre-albumin, urine urea nitrogen for some patients) on the 4th study day if not already ordered.

Also, please use sterile technique, or as nearly as possible, to insert the feeding tube. If you have any questions, please do call me. There is an information notebook on each ICU unit and my phone number is posted prominently by the unit telephones. I also have a digital beeper [redacted]. This study has been approved by the OUHSC IRB, VAMC Research Committee, and Dr. Postier (for OMH).

Thank you for your cooperation.

Sincerely,

Lynda J. Davidson, RN, MN
Assistant Professor

APPENDIX B

ENTERAL FEEDING PROTOCOL

Before the sampling procedure begins, the feeding tube will be inserted by the nurse or physician. Placement will be checked radiographically.

FOR THE ROUTINE ENTERAL FEEDING GROUP:

Investigator: (Day 1)

1. Collect the following equipment and bring to the bedside:
   1 Sherwood Medical Kangaroo Pump Set
   1 Kangaroo 324 Feeding Pump
   2 10cc syringes
   2 red top tubes
   2 labels for sample identification
   2 20 gauge needles
   alcohol wipes
   1 can Osmolite
2. Wash hands with antimicrobial preparation.
3. Wipe top of Osmolite can with alcohol wipe and let dry.
4. Open can and aseptically transfer the contents of the can into the bag. If contamination occurs, obtain new materials and begin the process again.
5. Open the roller clamp and allow formula to fill the infusion set.
6. Place a needle at the end of the infusion set and insert into a red top tube to obtain the formula sample. Use this method of obtaining the formula sample on the first day only. Draw approximately 10 cc for this sample.
7. Replace the needle cap while the gastric sample is drawn.
8. Check feeding tube placement by auscultation of insufflated air.
9. Insert a 10 cc syringe into the feeding tube and slowly aspirate the gastric contents, approximately 1 cc every 5 seconds. If no sample is obtained, reposition the patient. If no sample is obtained, irrigate the feeding tube with 10 cc of sterile normal saline. Note irrigated samples on the data collection sheet. Obtain a 10 cc sample and insert into a red top tube.
10. Connect the feeding tube to the infusion set.
11. Start the formula infusion at the prescribed rate and notify the staff nurse.
12. Place proper identification labels on tubes. Date, Time, Hospital and Unit, Pt number, Sample Site
13. Collect demographic and laboratory data from chart.

Staff Nurse (All four days of the study):

1. Record the following information on the Enteral Feeding Flow Sheet for each shift. This sheet will be attached to the IV pole next to the feeding pump.

   Rate
   Bag change
   Tubing change
   Formula intake
   Stool frequency & consistency (normal or diarrhea)

2. Follow standard procedure as outlined by the investigator for hanging and maintaining enteral feeding, giving medications, and checking for residual. These instructions can be found at the patient bedside and in the enteral nutrition study manual at the desk in each unit.

3. Start the feeding at 25 cc/hour. Check for residual every two hours. If less than two times the hourly rate, continue feeding until 8 hours. Then, increase the feeding by 25 cc/hour up to 50 cc/hour. Continue to increase every 8 hours until the desired rate is reached (determined by the physician or dietitian). If the residual is greater than two times the hourly rate, stop the feeding and check the residual hourly. When the residual is less than two times the hourly rate, resume the feeding using the previous protocol. Any time the feeding is stopped, record the time, the reason, and the time resumed on the bedside flow sheet.

4. Change the bag and tubing according to standard procedure.

Investigator on Day 2-4, each morning between 9:00 & 12:00:

1. Collect the following equipment and bring to the bedside:
   2 10cc syringes
   2 red top tubes
   2 labels for sample identification
   2 20 gauge needles
   alcohol wipes

2. Wipe the top of the red-top tube with an alcohol wipe, let dry, and place on bedside stand.
3. Wash hands with antimicrobial preparation.
4. Open the top of the feeding bag and draw a 10cc formula sample with a 10 cc syringe and 20 gauge needle.

5. Transfer the sample into a red top tube.
6. Separate the feeding tube from the infusion set. Place a sterile needle on the end of the infusion set.
7. Insert a 10 cc syringe into the feeding tube and slowly aspirate gastric contents, approximately 1 cc every 5 sec @43 onds. Discard the first 5 cc. If no sample is obtained, reposition the patient. If no sample is obtained, irrigate the tube with 10 cc of sterile normal saline. Note irrigated samples on the data collection sheet. Insert a 10 cc sample into the red top tube.
8. Remove the sterile needle from the end of the infusion set and re-connect the feeding tube to the infusion set.
9. Start the formula infusion at the prescribed rate and notify the staff nurse.
10. Place proper identification labels on tubes. Date, Time, Hospital and Unit, Pt number, Sample Site
11. Collect demographic and laboratory data from chart.
12. Check flow sheet for missing data.

FOR THE ASEPTIC ENTERAL FEEDING GROUP:

Before the sampling procedure begins, the feeding tube will be inserted by the nurse or physician. Placement will be checked radiographically.

Investigator: (Day 1)

1. Collect the following equipment and bring to the bedside:
   - 1 Sherwood Medical Kangaroo Pump Set
   - 1 Kangaroo 324 Feeding Pump
   - 1 prefilled sterile bag of Osmolite
   - 2 10cc syringes
   - 2 red top tubes
   - 2 labels for identification
   - 1 20 gauge needles
   - 1 stopcock
   - alcohol wipes
2. Wash hands with antimicrobial preparation.
3. Wipe top of red-top tubes with alcohol, let dry, and place on bedside table.
4. Insert infusion set spike into Osmolite bag.
5. Open the roller clamp and allow formula to fill the infusion set.
6. Place a needle at the end of the infusion set and insert into a red top tube to obtain the formula sample. Use this method of obtaining the formula sample on the first day only. Draw approximately 10 cc for this sample.
7. Replace the needle cap while the gastric sample is drawn.
8. Check feeding tube placement by auscultation of insufflated air.
9. Insert a 10 cc syringe into the feeding tube and slowly aspirate the gastric contents, approximately 1 cc every 5 seconds. If no sample is obtained, reposition the patient. If no sample is obtained, irrigate the feeding tube with 10 cc of sterile normal saline. Note irrigated samples on the data collection sheet. Obtain a 10 cc sample and insert into a red top tube.
10. Aseptically place stopcock between infusion set and feeding tube.
11. Start the formula infusion at the prescribed rate and notify the staff nurse.
12. Place proper identification labels on tubes. Date, Time, Hospital and Unit, Pt number, Sample Site
13. Collect demographic and laboratory data from chart.

Staff Nurse: (All four days of the study)

1. Aseptically hang a bag of Osmolite if the bag hung by the investigator runs out. Wash hands before hanging the bag. Spike bag without touching any other surfaces.
2. When entering the system, use the stopcock. Each time the system is entered, use a new syringe. If stopcock covers become contaminated, replace them. Use sterile water or normal saline to flush the tubing after giving medications. Whenever possible, try to obtain the liquid or IV form for medications.
3. Start the feeding at 25 cc/hour. Check for residual every two hours. If less than two times the hourly rate, continue feeding until 8 hours. Then, increase the feeding by 25 cc/hour up to 50 cc/hour. Continue to increase every 8 hours until the desired rate is reached (determined by the physician or dietitian). If the residual is greater than two times the hourly rate, stop the feeding and check the residual hourly. When the residual is less than two times the hourly rate, resume the feeding using the previous protocol. Any time the feeding is stopped, record the time, the reason, and the time resumed on the bedside flow sheet.
4. Record the following information on the Enteral Feeding Flow Sheet for each shift. This sheet will be attached to the IV pole next to the feeding pump.
   - Rate
   - Bag change
   - Tubing change
   - Formula intake
   - Stool frequency & consistency (normal or diarrhea)

Investigator on Day 2-4, each morning between 9:00 & 12:00:

1. Collect the following equipment and bring to the bedside:
   - 1 prefilled sterile bag of Osmolite
   - 2 10cc syringes
   - 2 red top tubes
   - 2 labels for identification
   - 1 20 gauge needles
   - 1 stopcock
   - alcohol wipes
2. Wash hands with antimicrobial preparation.
3. Wipe top of red top tubes and place on bedside table.
4. Change tubing and stopcock every 24 hours between 9:00 am and 12:00 pm. If less than 250 cc Osmolite left in the bag, hang a new prefilled 1000 cc bag. If greater than 250 cc, aseptically change the

tubing and insert new tubing into the bag hanging. Draw the 10 cc formula sample from the bag with a 10cc syringe and a 20 gauge needle before connecting the bag to the new infusion tubing.

5. Place a sterile stopcock on the end of the infusion tubing. Leave sterile caps on all openings.
6. Open the roller clamp and allow formula to fill the infusion set.
7. Insert a 10 cc syringe into the feeding tube and slowly aspirate the gastric contents, approximately 1 cc every 5 seconds. If no sample is obtained, reposition the patient. If no sample is obtained, irrigate the feeding tube with 10 cc of sterile normal saline. Note irrigated samples on the data collection sheet. Obtain a 10 cc sample and insert into a red top tube.
8. Aseptically connect stopcock between infusion set and feeding tube.
9. Start the formula infusion at the prescribed rate and notify the staff nurse.
10. Place proper identification labels on tubes. Date, Time, Hospital and Unit, Pt number, Sample Site
11. Collect demographic and laboratory data from chart.

APPENDIX C

Nursing Procedure for Aseptic Group

1. Call investigator when tubefeeding ordered for a patient.

   Lynda Davidson (work) [redacted] (home) [redacted]

2. Physician will insert feeding tube. Please remind them to use sterile technique.

3. Please try to prevent the patient from pulling the feeding tube out. If they do pull it out please have the physician re-insert using sterile technique & indicate on the flow sheet.

4. **ASEPTIC GROUP.** Enteral solution will be provided by the investigator. The first bag will be hung by the investigator. The bags are one liter and will be changed by the investigator in 24 hours. If the solution runs out before then, hang a new bag using aseptic technique. Wash hands before hanging a new bag. **Be sure to use sterile bags of formula.** Use the following guidelines for maintaining the enteral feeding.

   Wash hands before beginning procedure.

   Check position of tube using air insufflation and auscultation every 4 hours.

   Use a sterile syringe whenever entering the system.

   Maintain sterility of stopcock cover; if contaminated, replace.

   Use stopcock whenever entering the system: give meds, check residual, irrigation, etc.

   Spike and hang new feeding bag using aseptic technique.

      Did not touch a sterile surface in contact with formula.

   If feeding stopped and tubing disconnected, plug the end of the tubing with a sterile cover.

   If feeding stopped and tubing disconnected, flush feeding tube with 50 cc sterile water and repeat when starting tube feeding again.

Flush feeding tube with sterile water before and after giving medications through the tube.

Use only sterile water or sterile normal saline whenever entering the system, i.e. giving medications, flushing system.

5. Complete the flow sheet for each patient for 4 days from the time the tube is inserted.

6. **MEDICATIONS.** Try to obtain liquid form (without sorbitol) or IV. When giving meds use the stopcock, being careful to keep the caps sterile when removed. If caps become contaminated please replace. Wash hands before opening the system to give meds. Please use a **NEW STERILE** syringe each time the system is entered.

   Flush with 50 cc sterile water, give med, flush with 50 cc **sterile water**, remember to turn tubefeeding back on. If crushing a pill which is not in its own sterile wrapper, use a sterile wrapper from a 4 by 4. Put crushed pill in a 5cc syringe & mix with sterile water.

7. **RATE.** Start the feeding at 25 cc/hour. Check for residual every two hours. If less than two times the hourly rate, continue feeding until 8 hours. Then increase the feeding by 25 cc/hour up to 50 cc/hour. Continue to increase every 8 hours until the desired rate is reached (determined by the physician or dietitian). If the residual is greater than two times the hourly rate, stop the feeding and check the residual hourly. When the residual is less than two times the hourly rate, resume the feeding using the previous protocol. Any time the feeding is stopped, record the time, the reason, and the time resumed on the bedside flow sheet. Once the desired rate is reached, resume checking residuals every 4 hours.

APPENDIX D

Nursing Procedure for the Usual Routine Group

1. Call investigator when tubefeeding ordered for a patient.

   Lynda Davidson (work) [redacted] (home) [redacted]

2. Feeding tube can be inserted using usual normal procedure.

3. Use the following guidelines for maintaining the enteral feeding. Be sure to use the **CANNED OSMOLITE.**

   Wash hands before beginning procedure.

   Check position of tube using air insufflation and auscultation every 4 hours.

   Use 50 or 60 cc syringe to check residual.

   Rinse feeding bag with water prior to adding formula.

   Change equipment down to the feeding tube every 24 hours.

   If feeding stopped and tubing disconnected, clamp or plug the end of the tubing.

   If feeding stopped and tubing disconnected, flush feeding tube with 50 cc water and repeat when starting tube feeding again.

   Flush feeding tube with water before and after giving medications through the tube.

4. Complete the flow sheet for each patient for 4 days from the time the tube is inserted.

5. **RATE.** Start the feeding at 25 cc/hour. Check for residual every two hours. If less than two times the hourly rate, continue feeding until 8 hours. Then increase the feeding by 25 cc/hour up to 50 cc/hour. Continue to increase every 8 hours until the desired rate is reached (determined by the physician or dietitian). If the residual is greater than two times the hourly rate, stop the feeding and check the residual hourly. When the residual is less than two times the hourly rate, resume the

feeding using the previous protocol. Any time the feeding is stopped, record the time, the reason, and the time resumed on the bedside flow sheet. Once the desired rate is reached, resume checking residuals every 4 hours.

APPENDIX E

Group: _____ Pt Name:_____

Start Date: _____

ENTERAL FEEDING FLOW SHEET

	Day 1			Day 2			Day 3			Day 4		
	N	D	E	N	D	E	N	D	E	N	D	E
Rate												
Bag Change (Time)												
Tubing Change												
Formula Intake/ 8 hour shift												
Formula Culture												
Gastric Sample												
Stool Frequency Normal												
Diarrhea												
Nurse Initials												

Nurse Signature:

Comments:

APPENDIX F

V.A. Administration Medical Center

Tubefeeding Procedure

Section III

TUBE FEEDING

I. PURPOSE. To provide nutritional support to a patient with functioning GI tract who is unable to meet nutritional requirements orally.

Feeding Techniques:

NASOGASTRIC: May be used safely in alert, unrestrained patients with intact gag reflex. Gravity or pump feeding may be utilized for intermittent or continuous feedings. Check for residual before each feeding or every 8 hours, and withhold feeding if greater than 100 cc.

NASODUODENAL: Used to reduce the risk of aspiration in patients with decreased level of consciousness and/or decreased gag reflex. Position of tube must be confirmed by x-ray. Requires use of continuous pump feeding.

NEEDLE JEJUNOSTOMY: Tube is inserted directly into the jejunum as part of a surgical procedure. Continuous pump feeding of an elemental diet is required. No check for residual is done, but patient must be observed for abdominal distention and ileus.

GASTROSTOMY TUBE: Tube is inserted directly into the stomach as part of surgical procedure. Technique is same as for nasogastric tube. Do not use clamp on tube as it will cause damage to tube. Plug tube with catheter plug and drainage tube protector.

II. EQUIPMENT.

Disposable gavage bag	Syringe - 50 cc.
Appropriate connecting tubing	Stethoscope
IV standard	Feeding pump if required
Formula to be infused	

III. ESSENTIAL STEPS IN PROCEDURE.	KEY POINTS
A. Preparation of Patient.	
1. Explain procedure to patient.	To allay anxiety.
2. Elevate head of bed 30-45°. Head will remain elevated at all times while patient is on continuous feeding and at least 30 minutes after intermittent feeding.	Reduces danger of aspiration.
B. Preparation of Equipment.	
1. Check doctor's orders for solution and strength.	
2. Wash hands.	
3. Dilute formula if necessary.	

4. For gravity feeding or pump feeding, pour required amount of formula into infusion bag using no more than one can of formula at a time.

Formula should be given at room temperature. Formula should not be allowed to stand at room temperature after opening for more than 12 hours as this permits growth of bacteria.

5. Hang bag on IV standard.

6. Clear tubing of air.

Air in tubing can cause gas bubbles.

C. Procedure.

1. Check gastric residual before each feeding or every 8 hours with continuous feeding per nasogastric or gastrostomy tube by very gently aspirating stomach contents. If excessive residual is observed (more than 100 cc), slow infusion rate or skip feeding and notify physician.

Small bore tubes tend to collapse when negative pressure is applied. If unable to aspirate gastric residual, examine the patient for abdominal distention.

3. Verify tube position following each residual check, <u>especially</u> if no residual can be aspirated.

Small bore tubes can become displaced, curled, or kinked with little or no change in patient symptoms.

a. Introduce 5-10 cc of air into tube while listening over epigastrium with stethoscope. Air should produce a rumbling or gurgling sound. If in the oesophagus, patient will belch.

Note that air injected into the right bronchus may be heard in the epigastrium.

b. Ask conscious patient to say E-E-E-E-E-E. If he can't, the tube is probably in the larynx even though he may not have any respiratory distress.

Small inert tubes can pass into bronchus without severe patient discomfort.

c. If there is still any doubt about position, discontinue feedings and notify physician.

Position will need be confirmed by x-ray.

4. For intermittent gravity feeding.

a. Connect infusion bag tubing to feeding tube.

b. Regulate flow of feeding at a rate to run over 20-30 minutes.	Infusing the feeding too rapidly can cause nausea and/or vomiting.
c. Pour water (50-100 cc or amount ordered) into bag following feeding at a rate to run over 20-30 minutes to flush tubing.	Allowing formula to advance down tubing before adding water will cause gas bubbles.
d. When water has infused, clamp off feeding tubing.	
5. For continuous feedings.	
a. Connect infusion bag tubing securely to feeding tube.	
b. Begin infusion slowly, 50 cc/hr maximum, and increase 25-30 cc every 8-12 hours until proper rate is reached.	Maximum should not exceed 150 to 200 cc/hr.
c. Regulate gravity drip or feeding pump rate and check periodically to insure consistent flow.	Tube may become clogged or kinked.
d. Check gastric residual if indicated before each feeding or every 8 hours with continuous feedings by very gently aspirating stomach contents. If excessive residual is observed (more than 100 cc), slow infusion rate or skip feeding and notify physician.	Small bore tubes tend to collapse when negative pressure is applied. Always reinsert residual into stomach.
e. Verify tube position as described previously following each residual, check, especially if no residual can be aspirated.	Small bore tubes can become displaced, curled, or kinked with little or no change in patient symptoms.
f. If tubes are disconnected for a short period of time (shower, x-ray, etc.), flush with 50 cc's of water when disconnected and again when reconnected. Clamp or plug end of tubing.	
6. Change feeding set every 24 hours	To prevent bacterial contamination.

7. Patient should take additional water in a 24 hour period. 400 cc is recommended either orally or by tube if not contraindicated by physician's orders.

8. Monitor progress and response to feedings.

   a. Weigh daily if ordered.

   b. I and O every 8 hours. — Keep accurate records of intake.

   c. Observe for complications.

9. Possible complications.

PROBLEMS	PROBABLE CAUSES
Diarrhea.	Volume too large; rate too rapid; antibiotic treatment; hyperosmolar feeding; contamination of feeding tube or equipment; incorrect feeding temperature.
Aspiration.	Gastric feeding in patient with no gag reflex; improper tube position; patient lying flat during or after feeding; vomiting; irritation/incompetence of esophagogastric valve caused by large bore tubes; slow gastric emptying; tube rupture above stomach.
Fluid and electrolyte disturbance.	Dehydration, hypernatremia, hyperchloremia, and azotemia secondary to high protein intake combined with inadequate free water intake; diarrhea; osmotic diuresis.
Constipation.	Long term feeding with low residue products.
GI: Nausea, abdominal distention, cramping.	Large volume, rapid rate, bolus feeding, inactivity.
Vomiting (discontinue and hold feedings until problem is resolved).	Gastric atony secondary to hyperglycemia, peptic ulcer, or ileus; too large volume; too fast rate; temperature too cold.

Tube clogged.	Coagulation of stomach contents; failure to irrigate tube, especially with more viscous formula; infusion of crushed pills through tube without proper irrigation following.
Tube rupture.	Use of high pressure (IVAC) pump on clogged or partially clogged tube; irrigation of clogged tube with less than 35 cc syringe.

D. Documentation.

1. Record amount infused on I & O sheet.
2. Record feedings on treatment sheet. — Patient's tolerance to initial feeding should be recorded in progress notes.
3. Any adverse reactions are recorded on progress notes.
4. Record daily weight and I & O if ordered.

E. Cleaning of Equipment.

1. At end of each feeding, clean gavage bag with water, allowing solution to run through connecting tubing. Rinse thoroughly. Tuck end of tubing into bag for intermittent feeding. Reconnect tubing to feeding tube if providing continuous feeding.
2. When removing plug from gastrostomy tube, rinse with warm water and place on clean 4 x 4. — To prevent bacterial contamination, replace as indicated.

IV. REFERENCES.

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APPENDIX G

OKLAHOMA MEMORIAL HOSPITAL
NURSING DIVISION
PROCEDURE

PROCEDURE TITLE: Tube Feeding (Bolus and Continuous) Enteral Feeding

APPROVED: Policy and Procedure Committee

Review Date:

Revised Date: 4/27/86, 10/28/86, 8/3/87, 10/24/89, 4/4/90

DATE ISSUED: 6/77 DATE EFFECTIVE: 6/77

PURPOSE:

To provide guidelines for feeding a patient via a feeding tube.

EQUIPMENT NEEDED:

1. Feeding Tube in place (see procedure for insertion)
2. Type and amount of feeding ordered
3. 60cc syringe
4. Tape
5. Tube Feeding Bag (Gavage and Continuous Feedings)
6. Tube Feeding Infusion Pump (optional)
7. Measuring Container

PROCEDURE:

Responsible Party:	Action:
RN, LPN or NA	1. Obtain physician's order. 2. Assemble equipment and take to bedside. 3. Explain procedure to patient. 4. Wash hands. 5. Check proper placement of tube: a. Aspirate contents of stomach with 60cc syringe. Return aspirate to stomach.

Disc. P&P #3 "Tube Feeding(Bol&Con)"

h. Place stethoscope over epigastrium and inject 20-30ml. of air in feeding tube- blurb or swoosh sound indicates tube is in stomach.

6. Elevate HOB 45° - of not contraindicated by patient condition. If contraindicated, turn patient to side.
7. Attach 60cc syringe to end of feeding tube.
8. Check for residual at least every four hours or before each bolus feeding. If more than 100cc or 1/3 of previous bolus feeding remains or more than one hour volume of continuous feeding is aspirated stop feeding and recheck residual in one hour before continuing with feeding. Return aspirate to stomach. If problem persists contact physician.
9. Syringe/Bolus Method:
   a. Remove plunger from syringe after checking for placement of tube as above and for residual as above.
   b. Attach end of syringe to end of feeding tube.
   c. Pour formula into the syringe.
   d. Allow the formula to run in slowly by gravity. Add more formula before syringe empties to prevent air from entering stomach and possibly causing bloating.
   e. Adjust the height of syringe to control speed of feeding.
   f. Use plunger with syringe if necessary. Do not force feeding. Hold barrel of the syringe while pushing down slowly on plunger.
   g. Disconnect syringe with plunger and refill with formula. Clamp tubing when disconnecting syringe to prevent air from entering stomach.
   h. Repeat process until prescribed amount of formula is given.
   i. Give total feeding over 10-15 minutes.
   j. Follow feeding with at least 60cc of warm water to rinse feeding tube.
   k. Close off end of feeding tube to prevent air from entering the tube.
10. Gavage/Bolus Method:
   a. Fill tube feeding bag with ordered amount of formula and clear tubing of air.
   b. Flush feeding tube with water.
   c. Attach end of feeding bag to end of feeding tube and tape to secure.
   d. Attach bag to IV pole.

e. Adjust drip rate. Allow to run slowly over 15-20 minutes.
f. Check patient frequently to assess flow rate and patient status.
g. Follow end of feeding with at least 60cc of warm tape water.
h. Clamp tube and disconnect feeding bag.
i. Close off end of feeding tube.

11. Continuous Method:
    a. Fill tube feeding bag with no more than 4 hours of formula.
    b. Clear tubing of air.
    c. Time label feeding bag in hour increments in order to monitor infusion of feeding.
    d. Flush feeding tube with water.
    e. Attach end of feeding bag to end of feeding tube.
    f. Adjust drip rate and or attach to feeding pump.
12. Rinse all equipment.
13. Document:
    a. Time
    b. Type and amount of feeding
    c. Route of administration
    d. Patient's tolerance
14. Record as P.O. intake on Nursing Action Record.
15. Nursing Guidelines:
    a. Check for position of tube every 4 hours.
    b. Check for residual at least every 4 hours.
    c. Keep Head of bed elevated 30-45^{0} at all times, even during sleep if continous tube feeding. (Placing patient in reverse trendelenburg is optimal.)
    d. Tube feeding formula should not stand at room temperature for more than four hours.
    e. Flush feeding tube with at least 60cc of warm tap water once every four hours.
    f. Tube feeding bag must be rinsed thoroughly after each feeding (even if continuous).
    g. Bag must be changed every 24 hours. Date each new bag hung.
    h. Never use a syringe smaller than 60cc to irrigate with; anything smaller creates too much pressure and may rupture the tube.
    i. If at all possible obtain liquid form of medications. Do not crush pills or instill any foods through the tube. If pills are crushed, dissolve and test in formula to check reaction and possible precipitation.

If precipitation does occur, do not give medication and contact physician. Do not use any time released medications. Flush before and after all medications.

j. If tube feeding is turned off, flush with 60cc of water and clamp end of tube free from air.

k. When giving bolus tube feedings, patients with a trach must have the cuff inflated during tube feeding and remain inflated 30 minutes after feeding is finished.

l. If patient is scheduled for a procedure that requires a supine or head down position (i.e. postural drainage or x-ray) turn feeding off 30 minutes prior to procedure and flush feeding tube with water and clamp off end.

m. Record all tube feeding intake and water administration on the P.O. intake section of the appropriate nursing form.

n. Record continuous tube feeding indicating time started, amount and type of solution. Carry over balance remaining for next shift.

o. Indicate whether formula was taken per tube or orally.

p. Assess patient's tolerance every shift (i.e. stomach distention, nausea, complaints of fullness, hunger, or diarrhea).

16. Discontinue immediately and notify physician if:
    a. Vomiting occurs
    b. Respiratory distress

17. If the feeding tube becomes difficult to flush, the following are methods that may be used to clear the tube. (If any question arises as to whether or not this should be done on a specific patient, contact the physician.)
    a. Flush tube with 20-60cc warm water.
    b. If tube is still occluded flush with 20-60cc undiluted cola or cranberry juice if patient is on salt restricted diet and allow solution to remain in tube for 30minutes before flushing with water.

NOTE: Meat tenderizer is contraindicated in clearing an obstructed feeding tube because of the high solium content. If aspiration is suspected there are two methods to check above.

a. Dextrostix may be used to test for presence of glucose in tracheal secretions specimen. (Normal trach secretion do not contain glucose.)
b. Food coloring may be added. Use only enough to lightly tint tube feeding solution. (Food coloring may be absorbed in patients skin if too much used!)

APPENDIX H

ENTERAL FEEDING STUDY

ELIGIBILITY TO ENTER STUDY

DOES THE PATIENT FIT THE FOLLOWING CRITERIA?	YES	NO
1. Admitted to a general medical/surgical floor or ICU	_____	_____
2. Is 18 years or older	_____	_____
3. Has an order for a feeding tube & enteral feeding	_____	_____
4. Has not received any feeding for last 48 hr	_____	_____

Answers to these questions should all be 'yes'

DOES THE PATIENT HAVE ANY OF THE FOLLOWING CONDITIONS/ TREATMENTS ORDERED?		
1. Has a needle jejunostomy tube	_____	_____
2. Has pre-existing bowel disease (Crohn's, ulcerative colitis), gastric disease (active bleeding ulcers), diverticulitis, ileus	_____	_____
3. Has diarrhea currently or has had diarrhea in the previous 48 hours	_____	_____
4. Is receiving laxatives or lactulose	_____	_____
5. Has received enteral feeding within the last two days	_____	_____

Answers to these questions should all be 'no'

DATA SHEET

Pt diagnosis _____

_____

Age _____ Weight _____kg

Sex _____ Height _____cm Pt Class 1 2 3

Hosp Admit date _____ Left Arm Circumference _____

ICU Admit date _____ Triceps Skin Fold #1_____#2_____#3_____

Study date _____ % Body Fat (Futrex) #1_____#2_____#3_____

Albumin _____ Pitting edema: yes no

Transferrin _____ Type of tube _____

Total Lymphs _____ Days since last meal _____

Urine Nitrogen _____ Obtained from _____

Pre-albumin _____ Septicemia: yes no

Organism _____

Usual Weight _____kg

	Day 1	Day 2	Day 3	Day 4
TF Osmotic Load				
Gastric pH				
Sample Quality				

MEDICATIONS

Dose, Route, Frequency, Time of last dose, Sorbitol Content

	Day 1	Day 2	Day 3	Day 4
ANTIBIOTICS (Start date)				
ELECTROLYTES				
ANTACIDS/H2 BLOCKERS				
ANTIDIARRHEAL				
CARDIAC DRUGS (antiarrhythmic, B-Blockers, Ca+ Channel Blockers)				
OTHER (salt poor albumin)				

APPENDIX I

Schedule of Laboratory & Sample Collection

	First ICU Day	Study Days			
		Day 1	Day 2	Day 3	Day 4
Albumin		X			
Transferrin					X
Whole Blood Count	X	X			
Total Lymphocyte Count		X			
Urine Nitrogen					X
Serum sodium	X	X			
Serum potassium	X	X			
Serum creatinine	X	X			
Hematocrit	X	X			
pH, pCO_2, HCO_3	X	X			
Serum CO_2 Content (if no ABGs)	X	X			
Samples					
Tubefeeding		X	X	X	X
Gastric pH		X	X	X	X

APPENDIX J

Nutrition Index

Degree of Malnutrition

	None (0)	Mild (1)	Moderate (2)	Severe (3)
Albumin (gms/deciliter)	> 3.4	2.8 - 3.4	2.1 - 2.7	< 2.1
Transferrin (mgms/deciliter)	> 200	150 - 200	100 - 149	< 100
Absolute Lymphocyte Count (thousands of cells per milliliter)	> 2.0	1.2 - 2.0	0.8 - 1.19	< 0.8
Ideal Body Weight	> 90%	80 - 90%	70 - 79%	< 70%

From: Cerra, F.B. (1984). Assessment of nutritional and metabolic status. In: A pocket manual of surgical nutrition, (pp. 24-48), St. Louis: C.V. Mosby.

Ideal body weight was determined using the following formula:

$$\% \text{ Ideal Body Weight} = \frac{\text{Patients Present Weight}}{\text{Ideal Body Weight}} \times 100$$

Ideal body weight was obtained from the NHANES I & II data reported by Frisancho (1984).

For each parameter a number was assigned as follows:

0 = normal value
1 = mild
2 = moderate
3 = severe

Then the score was summed. The degree of malnutrition was assigned accordingly:

0 (0 - 2) = no malnutrition
1 (3 - 5) = mild malnutrition
2 (6 - 9) = moderate malnutrition
3 (10 - 12) = severe malnutrition

APPENDIX K

Routine Checklist

1. ___ **Wash hands before beginning procedure.**
2. ___ Check position of tube using air insufflation and auscultation every 4 hours.
3. ___ Check gastric residual every 4 hours.
4. ___ Use 50 or 60 cc syringe to check residual.
5. ___ Rinse feeding bag with water prior to adding formula.
6. ___ **Change equipment down to the feeding tube every 24 hours.**
7. ___ If feeding stopped, clamp or plug the end of the tubing.
8. ___ If feeding stopped and tubing disconnected, flush feeding tube with 50 cc water and repeat when starting tube feeding again.
9. ___ Flush feeding tube with water before and after giving medications through the tube.
10. ___ To check for aspiration, add small amount of food coloring.

Major behaviors: 1 & 6. If these behaviors are not done, the patient data will be discarded.

COMMENTS:

Aseptic Checklist

1. ___ Wash hands before beginning procedure.

2. ___ Check position of tube using air insufflation and auscultation every 4 hours.

3. ___ Check gastric residual every 4 hours.

4. ___ Use a sterile syringe whenever entering the system.

5. ___ Maintain sterility of stopcock cover; if contaminated, replace.

6. ___ Use stopcock whenever entering the system: give meds, check residual, irrigation, etc.

7. ___ Spike and hang new feeding bag using aseptic technique. Did not touch a sterile surface in contact with formula.

8. ___ If feeding stopped and tubing disconnected, plug the end of the tubing with a sterile cover.

9. ___ If feeding stopped and tubing disconnected, flush feeding tube with 50 cc sterile water and repeat when starting tube feeding again.

10. ___ Flush feeding tube with sterile water before and after giving medications through the tube.

11. ___ Use only sterile water or sterile normal saline whenever entering the system, i.e. giving medications, flushing system.

12. ___ Use the correct formula type and form.

13. ___ Do not change the tubing.

Major behaviors: 1, 4, 5, 6, 7, 8, 11, 12. If these behaviors are not done, the patient data will be discarded.

COMMENTS:

APPENDIX L

THE UNIVERSITY OF OKLAHOMA HEALTH SCIENCE CENTER
OKLAHOMA MEMORIAL HOSPITAL, VETERANS ADMINISTRATION MEDICAL CENTER

INDIVIDUAL'S CONSENT FOR PARTICIPATION
IN CLINICAL RESEARCH PROJECT

I, _____, voluntarily consent to participate in a study the purpose of which is to investigate the occurrence of diarrhea after the initiation of enteral nutrition. This study will be carried out under the supervision of Lynda Davidson, R.N.

I understand:

1. PURPOSE: Patients who receive enteral nutrition (liquid feedings given through a small tube into the stomach or intestine) often develop diarrhea. The purpose of this study is to compare two methods of preparing and giving enteral feedings, to investigate the presence of bacteria that might grow in the feeding solutions, and to investigate whether such bacteria might contribute to diarrhea.

2. STATUS OF THE INVESTIGATIONAL PROCEDURES: There are no investigational drugs or devices used in this study. All procedures are standard protocols for care.

3. DESCRIPTION OF THE STUDY: After my physician has ordered enteral feedings, I will have a feeding tube inserted. I understand that this treatment is necessary for my care and is not being done for research purposes only. I will then be assigned to one of two different nursing procedures for preparing and giving the feeding. One procedure is the usual routine procedure for preparing and giving tube feeding normally used by this hospital. The other procedure involves a more strict method for keeping the tube and the feeding germ free. These procedures will be carried out by the registered nurses caring for me. The nurses will also record the number and consistency of my stools for 4 days. Each day for 4 days a small sample of the feeding solution will be obtained and sent to the laboratory for culture (a test to check for bacteria). Also, each day, about one teaspoon of stomach secretions will be obtained to check the pH of stomach juices. The feeding solution will be drawn from the feeding bag and the stomach secretions will be drawn through the feeding tube by the investigator. No pain or discomfort is expected to occur during the drawing of these samples. If not already ordered during routine tests, an extra blood sample (two teaspoons) will be drawn on day 4. On the first day of the study, the size of my biceps and the thickness of the skin on the p4@0 back of my arm will be measured. If I am under 40 years old and have had a head injury,

I will also have an extra teaspoon of blood drawn on the day 4 and my urine will be collected for 24 hours to measure the nitrogen content.

4. BENEFITS: It is possible that diarrhea might be prevented or decreased in duration. Also, if bacterial contamination is found, the physician will be notified as soon as possible.

5. POSSIBLE RISKS: While the risks in this study are small, there is the potential for bruising and pain associated with the blood drawing site. Also, there may be a risk of anxiety related to specimen collection.

6. ALTERNATE PROCEDURES: If I do not wish to participate in this study, I will receive the standard care given by nurses in my unit.

7. IN THE EVENT OF INJURY, INFORMATION CONCERNING MEDICAL TREATMENT AND COMPENSATION:

FOR OMH PATIENTS:

The investigator will pay for laboratory tests above and beyond those ordered routinely by the primary physician in the course of treatment. I will be responsible for all other costs.

It is clear to me that no compensation will be available to me from the University of Oklahoma Health Sciences Center or its employee unless I otherwise qualify for the University's health insurance or for other employee or student benefits. I understand that if I am injured, emergency medical treatment will be available to me. However, I will be required to pay a reasonable fee for such care. I understand I will not give up any of my legal rights by signing this form. I understand that if I have any questions or desire further information concerning the availability of compensation or medical care, I may contact the OMH Chief of Staff at [redacted]

FOR VA PATIENTS ONLY:

a) Compensation and medical treatment will be provided and may be payable under Title 38, United States Code, Section 310 or 351 or there may be recovery under the provisions of the Federal Tort Claims Act (Title 38 United States Code, Sections 1346 (b), 2671 through 2680) to eligible veterans.

b) Emergency treatment, free of charge, will be provided and compensation may be payable under Title 38, United States Code, Section 351 or there may be provisions of the Federal Tort Claims Act to non-eligible veterans.

c) Emergency treatment, free of charge, will be provided and there may be recovery under the provisions of the Federal Tort Claims Act to non-veterans.

Eligible veterans, non-eligible veterans, and non-veterans who participate in VA Medical Center research protocols in any physical setting other than the Oklahoma City VA Medical Center, or in the VA setting by non VA employees may not be covered under the conditions described in a., b., and c. above.
It is the responsibility of the VA Principal Investigator to explain the conditions above.

_____Subject _____Date

_____Principal Investigator _____Date

Should any grievances develop during my participation in this study, I may take them to the Veterans Administration Medical Center, 921 N.E. 13th, Telephone [redacted].

8. SUBJECT'S ASSURANCE: Whereas no assurance can be made concerning results that may be obtained (because results from investigational studies cannot be predicted), the investigator will take every precaution consistent with the best nursing practice.

By signing this consent form, I acknowledge that my participation in this study is voluntary. I also acknowledge that I have not waived any of my legal rights or released this institution from liability for negligence.

I may revoke my consent and withdraw from this study at any time without penalty or loss of benefits. My treatment by, and relations with the physician(s) and staff at the University of Oklahoma Health Sciences Center, now and in the future, will not be affected in any way if I refuse to participate, or if I enter the program and withdraw later.

Records of this study will be kept confidential with respect to any written or verbal reports making it impossible to identify me individually.

If I have any questions or need to report an adverse effect about the research procedures, I will contact the principal investigator, Ms. Lynda Davidson, by calling ([redacted] during the workday or ([redacted] at night or on weekends.

If I have any questions about my rights as a research subject, I may take them to the Director of Research Administration, University of Oklahoma Health Sciences Center, Room 121, Library Building, Telephone [redacted] or; VA PATIENTS ONLY: If I have any questions about my rights as a research subject, I may take them to the Associate Chief of Staff, Veterans Administration Medical Center, Telephone ([redacted] extension [redacted].

I have read this informed consent document. I understand its contents and I freely consent to participate in this study under the conditions described in this document. I have received a copy of this informed consent agreement.

_____

Patient's Signature Date

_____

Witness' Signature Date

I, the undersigned, have defined and fully explained the studies involved to the above patient.

_____

Signature Date
(Responsible Investigator)

APPENDIX M

APACHE II DATASHEET

Pt admitted from_____
(See Directions)

Primary admit dx_____
(See Directions

Hospital & ICU _____ Age_____Sex_____

ICU Admit Date_____ Study Date_____

PHYSIOLOGY VALUES

	ADMIT	STUDY
Temperature (C^O)		
Systolic BP mmHg		
Diastolic BP mmHg		
Heart Rate		
Respiratory Rate		
Oxygenation		
FiO2		
PaO2		
PaCO2		
pH		
*Serum CO2(no ABGs)		

	ADMIT	STUDY
Serum Sodium		
Serum Potassium		
Serum Creatinine		
*if >1.4, recent increase associated with oliguria? (y/n)		
Hematocrit		
White Blood Count		
Glasgow Coma Score		
Eye opening		
Verbal response		
Motor response		
Total		

Glasgow Coma Scale

Eye Opening:
- 4 - Opens spontaneously
- 3 - To verbal command
- 2 - To pain
- 1 - No response

Motor Response:
- 6 - Obeys verbal command
- 5 - Responds to painful stimuli
- 4 - Flexion, withdrawal
- 3 - Decorticate rigidity
- 2 - Decerebrate rigidity
- 1 - No response

Verbal Response:
- 5 - Oriented & converses
- 4 - Disoriented & converses
- 3 - Inappropriate words
- 2 - Incomprehensible sounds
- 1 - No response

If intubated:
- 5 - Appears able to converse
- 3 - ?? ability to converse
- 1 - Generally unresponsive