Editorial

Enteral Nutrition: An Increasingly Recognized Cause of Nosocomial Bloodstream Infection

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Malnutrition is a common occurrence among severely ill hospitalized patients and adequate nutritional support has proved effective in reducing their morbidity and mortality.[1,2] Intravenous administration of nutriment through catheters placed in the central venous circulation, the first approach effective in repleting undernourished patients, is widely accepted. However, requirements for specially trained personnel, equipment and expensive solutions are limitations to its use. Moreover, infectious complications, the most severe being sepsis, are well described and can be prevented only through adhesion to strict infection control procedures during the preparation of the infusate and handling of the intravenous cannula.[3]

The availability of nutrient products allowing individually tailored diets, as well as of small-bore, well-tolerated, flexible nasogastric tubes has, in the last two decades, led to a considerable increase in the use of enteral feeding as an alternative to parenteral nutrition in patients with a functional digestive tract.[1,2] Among the advantages ascribed to this method of hyperalimentation are its closeness to physiologic nutrition, its low cost and the lack of requirement for specialized personnel or equipment. Complications occurring during enteral nutrition have been considered to be rare and essentially non infectious.[1] As a consequence, infection control procedures during preparation and administration of enteral feeds have been less assiduous than for parenteral nutrition.

Considerable evidence now indicates that enteral feedings contaminated by bacteria can be the cause of severe nosocomial infections and that infection control practices for their preparation and administration should be reconsidered. Studies establishing the mechanism of intestinal colonization by the hospital bacterial flora and its possible role in nosocomial infections have been published between 1970 and 1975. Work by Van der Waaij and colleagues[4] led to the recognition that the resistance of the digestive tract to an oral challenge of bacteria is reduced considerably by a variety of factors present in hospitalized patients, such as stress, severe illness, antibiotic treatment or, as established more recently," antacids or histamine type 2 blockers. At about the same time, the role of digestive tract colonization as an initial step leading to gram-negative nosocomial infection was demonstrated, but the source of these organisms remained speculative.[6,7]

In 1978, Casewell and Phillips[8] reported that food prepared in the hospital kitchen was a source of *Klebsiella* that colonized and infected patients in an intensive care unit. Cold meat, salad, ice cream and nasogastric foods, but not hot meals were contaminated with *Klebsiella* of the same serotype as those colonizing and infecting the patients. The kitchen itself rather than the raw materials was the source of the contamination, as suggested by the finding that

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salad, before being washed and processed in the kitchen, did not contain *Klebsiella* from the serotypes found in patients. Also kitchen equipment and utensils were contaminated. This, coupled with other studies indicating that uncooked vegetables used in hospital kitchens carried gram-negative bacteria such as *Pseudomonas aeruginosa, Klebsiella* or *Enterobacter* species, led to the speculation that food with high microbial contents might be a source of gram-negative infection in high risk patients such as those with cancer and granulocytopenia, and that diets with low microbial content should be prepared for these patients."

Confirming the data of Casewell and Phillips, a number of studies have documented the potential for bacterial contamination of enteral feeds under ward conditions. Schreiner et al. found 354 (36%) of 976 cultures taken from formula drip chambers hanging for 12 to 24 hours at the bedside to be contaminated."' Schroeder et al. reported bacterial contamination in eight of nine feeding solutions, also cultured at the patient's bedside.[11] Anderson et al. surveyed 35 solutions and found only 17 (48%) of these to contain fewer than 10 cfu/ml; 5 samples (1.5%) contained over 100,000 cfu/ml.[12] Among 309 randomly selected samples of enteral feeding and infant formula tested in our institution within 24 hours of preparation and kept refrigerated in the ward, 83 (27%) contained bacteria.'" In these and other studies, the contamination rate depended on such variables as the composition of the feeding solution,[14] the presence of preservatives,[14] the number of manipulations involved in the preparation process,[11,12] the mode and duration of administration[11,15] and the timing of sampling.[11]

Bacterial contamination of enteral nutrition solution can occur during the preparation process. A number of studies have documented that feeding solutions contained bacteria before leaving the preparation unit.[8,13,14] Preparation utensils have been found to harbor the same bacteria as contaminated diets,[8,16] but the origin of the contaminations in the dietetic kitchen is seldom found.

We have shown that the plasmid profile of gram-negative enteric pathogens recovered from enteral nutrition remained identical for several months, indicating long lasting contamination with a limited number of strains.[13] Despite repeated surveys, we could not detect a source for these organisms. Powder feeds requiring reconstitution have been considered virtually sterile when received from the manufacturers.[12,17] However, two recent studies have challenged this opinion. Anderton, studying 19 complete feeds and feed constituents, found six of them to contain viable bacteria, mainly aerobic spore formers, in counts ranging from 50 to 3.10 cfu/g.[18] No coliforms or *Staphylococcus aureus* were isolated. All contaminated products were dried powders containing milk or whey proteins. In 1988, Muytjens et al. detected enterobacteriacae in 52.5% of 141 different powdered substitutes for breast milk obtained from 28 countries.[19] The species they recovered most frequently were *Enterobacter agglomerans, Enterobacter cloncae, Enterobacter sakazakii* and *Klebsiella pneumoniae.* Concentrations of bacteria were low, around 1 cfu/100 g. If enteral feeds are contaminated minimally during preparation, subsequent growth depends on the transport and storage conditions. At room temperature logarithmic bacterial growth has been observed, whereas there was no increase in the bacterial growth at 4" C.[14,20] Contamination can also occur during assembly of the delivery system on the ward,[21] or by bacteria colonizing the nasogastric tube or ascending from the patient's gut.[22]

If the high frequency of microbial contamination of enteral nutrition is well established, the clinical consequences of the phenomenon have, until recently, remained ill defined. Reports[16,23] in 1981 of an outbreak of *Klebsiella* sepsis in newborns fed human milk contaminated with this organism's and of one case of *E cloacae* sepsis in a patient fed a diet containing the same bacteria have established that contamination of enteral nutrition solutions can lead to bacteremia.[16] Subsequent reports have linked the occurrence of diarrhea," feeding intolerance and suspected sepsis in newborns[24] and adults"" to administration of contaminated feeds. However the potential hazard has remained largely overlooked; infection was not listed among the complications of enteral nutrition in a report by Cataldi-Betcher et al. in 1983.[26] Bengoa and colleagues in 1985 suggested that enteral nutrition was safe, in spite of their finding of high levels of contamination.[15] Recently, we have published data suggesting that contaminated enteral nutrition might represent a significant cause of nosocomial sepsis.'" Blood culture isolates from ten out of 40 patients who had developed nosocomial *E cloacae* bacteremia over a seven-year period had plasmid contents linking them to strains contaminating enteral nutrition. Epidemiological data from a case control study revealed that nine out of these ten patients had indeed been fed with enteral nutrition, compared to ten of the 30 others (odds ratio 18, $p = 0.002$). Importantly, the role of enteral nutrition as a source of infection was suspected on a clinical basis in only two of these patients.

The article by Simmons and colleagues, published in this issue of *Infection Control and Hospital Epidemiology* (pp 398-401), describes an outbreak of *E sakazakii* colonization and infection convincingly related to the use of contaminated formula. This study fills some of the major gaps in our comprehension of the mechanism of contamination of enteral feeds. The authors have succeeded in isolating fi-om a can of powdered formula *E sakazakii* with the same plasmid and enzyme multilocus profile as those from infected patients. Although this can was already opened at the time of study and contamination in the neonatal intensive care unit (NICU) cannot be ruled out, this finding, in the prospective of the high contamination rate of unopened powdered formula cans reported by Muytjens et al.[19] strongly suggests that contamination of the feed ingredients themselves may provide the source of pathogenic microorganisms. Also of

major interest are the observations that the blender used for mixing the formula was contaminated highly with *E sakazakii* and that adequate sterilization of the blender between uses was associated with the end of the outbreak. This underscores the role of utensils and equipment contamination, as well as of other factors such as transport and storage conditions, in upgrading into a clinically relevant problem a contamination that might have remained minimal, had adequate infection control procedures been observed.

Enteral nutrition by liquid diets plays an important role in patient care. We have learned in the last decade that contamination of these solutions is a frequent occurrence and that severe septic complications can result from the administration of contaminated feeds. As the studies by Simmons et al.[27] and by Muytjens et al.[19] suggest, the contaminating bacteria might be present in the powdered ingredients. Stringent infection control measures for the preparation and administration of enteral feeds are mandatory to avoid bacterial growth. Revision by public health authorities of the adequacy of the manufacturing procedures as well as of the regulations on the bacterial content of powdered feeds is needed.

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