Letters to the Editor

Bacteriological Side Effects of Gut Decontamination With Polymyxin E, Gentamicin, and Amphotericin B

To the Editor:

Selective decontamination of the digestive tract has been advocated by several European authors since 1984 in order to reduce the incidence of nosocomial infections in intensive care unit patients.[1-3] In most studies, selective decontamination of the digestive tract was achieved by application of wide-spectrum nonabsorbable antibiotics to the oropharynx and to the gastrointestinal tract in association with intravenous cefotaxime during at least four days. The incidence of nosocomial pneumonias was decreased by selective decontamination of the digestive tract in all of these studies, whereas mortality remained unchanged in most of them. Because of numerous possible methodological biases, the results and conclusions of these reports remain controversial.

Recently, the occurrence of secondary infections with multiresistant gram-positive bacteria have been attributed to selective decontamination of the digestive tract in first a descriptive[4] and then in a double-blind study.[3] The first European Consensus Conference in Intensive Care Medicine on "Selective Decontamination of the Digestive Tract in Intensive Care Unit Patients," which was held in Paris in December 1992, concluded that the effects of selective decontamination of the digestive tract on antimicrobial resistance had to be more extensively evaluated.[15] We report here the impact of a gastric decontamination with polymyxin E, gentamicin, and amphotericin B on the fecal flora in the mechanically ventilated patients of our general intensive care unit.

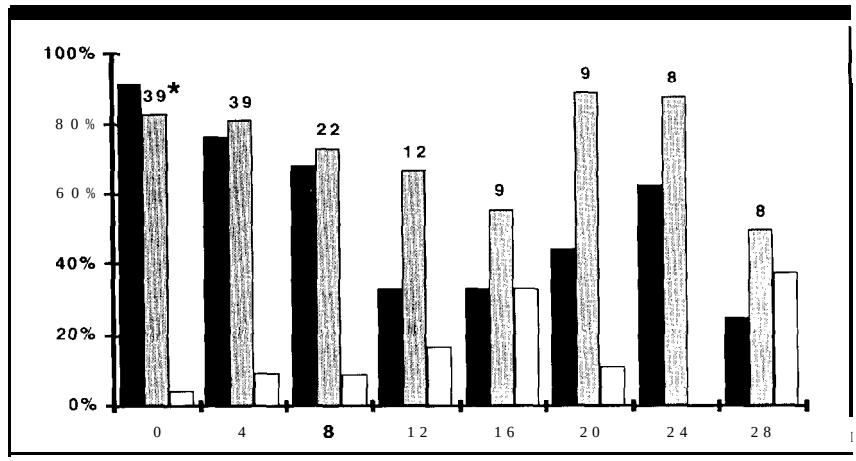


FIGURE. Colonization with aerobic gram-negative bacteria (black bars) and gram-positive cocci (gray bars) during decontamination. White bars indicate sterile stools. (*Number of stools sampled in 39 patients mechanically ventilated for at least 4 days.)

The study was performed over a four-month period in 64 consecutive patients, 39 being mechanically ventilated for more than four days. They received polymyxin E (100 mg), gentamicin (80 mg), and amphotericin B (500 mg) every six hours via a nasogastric tube from the onset of mechanical ventilation until the tube was removed. No oropharyngeal decontamination nor prophylactic systemic antibiotics were used. Cultures of stools (or rectal swabs) and gastric juices were made prospectively every four days for all patients. Colonization was assessed using a semiquantitative method in stool samples and a qualitative method in rectal swabs and gastric samples. In stool samples, colonization was indicated by the presence of $> 10{,}000$ bacteria/g of stool. The duration of the evaluation was limited to 28 days for each patient.

The mean age of the patients was 61 ± 18 and their simplified acute physiologic score[6] was 14 ± 4. Fecal colonization was assessed in 173 samples. One hundred fifty-three samples (89%) remained colonized with either aerobic gram-negative bacilli or gram-positive cocci during the entire

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course of the study. Of the 308 colonizing bacteria, 145 (47%) were gram-positive cocci, 72 (24%) were *Esherichia coli*, and 89 (29%) were other aerobic gram-negative bacilli. The Figure indicates that overall colonization with aerobic gram-negative bacilli and gram-positive cocci was poorly affected by selective decontamination of the digestive tract. Initial colonization with *E coli* (65%) disappeared after 20 days of treatment whereas colonization with the other aerobic gram-negative bacilli remained stable at about 40%. After day eight, 45% of these aerobic gram-negative bacilli were *Klebsiella pneumoniae, Enterobacter aerogenes,* or *Serratia marcescens*; 31% were *Pseudomonas aeruginosa* or *Acinetobacter calcoaceticus; 6%* were *Proteus morganii;* and 11% were *Citrobacter freundii.* Colonization fluctuated between 33% and 75% for streptococci and between 25% and 61% for staphylococci. Results remained unchanged when stools and rectal swabs were analyzed separately (data not shown).

Of the 43 gastric samples obtained on and after the fourth day of study, only four were colonized with aerobic gram-negative bacilli (9%). The proportion of fecal aerobic gram-negative bacilli resistant to the antibiotics used for decontamination was initially 15% for polymyxin E and 26% for gentamicin. This increased progressively to more than 50% at the end of the treatment. Nineteen of 38 (50%) of the staphylococci were sensitive to gentamicin on the first day; all strains (36/36) were resistant during treatment.

Selective decontamination of the digestive tract has been proposed because nosocomial infections are usually due to microorganisms found in the digestive flora of patients. In the present study, we used a selective regimen for the lower digestive tract without either oropharyngeal paste or parenteral systematic antibiotics in order to assess the bacterial impact of the topical antibiotics on the digestive flora. Our choice of polymyxin E, gentamicin, and amphotericin B was based on the results obtained in previous studies.[1,2] Most of our study patients had a prolonged intensive care unit stay with a high risk for developing nosocomial infections, particularly with resistant strains and should be privileged subjects for such preventive treatment. Therefore we could assess the persistence of the bacteriological (either beneficial or adverse) effect of selective decontamination of the digestive tract over a long period of time. Although we did not study a control group, it is well known[1,2] that without topical treatment, the digestive flora remains predominantly colonized with *E coli* and that other aerobic gram-negative bacilli appear progressively during the intensive care unit stay. We found that this topical regimen was accompanied by a decrease in *E coli* but not in other aerobic gram-negative bacilli. This decrease in *E coli* is in accordance with other studies on selective decontamination of the digestive tract, but the persistence of aerobic gram-negative bacilli had not yet been reported.

The first explanation could be that the oropharyngeal paste as well as the systemic antibiotics used by most authors may contribute to the fecal decontamination, but we found a colonization in only 9% of the gastric samples, attesting the antibacterial efficacy of either the local acidity or the antibiotics administered directly in the stomach. Secondly, parenteral prophylactic antibiotics were not systematically used in our patients, but most of them received a curative betalactamine during the first week of intensive care unit stay. Moreover, biliary concentrations of cefotaxime are usually <2μg/ml 214 g/ml after intravenous injections of 1 g every 6 hours,[7] and the increase of fecal levels obtained with intravenous tobramycin should be negligible with regard to those obtained with enteral tobramycin.

The high incidence in this population of patients already colonized with resistant bacteria before starting selective decontamination of the digestive tract might have diminished the efficacy of selective decontamination of the digestive tract. In this regard, it is noteworthy that we have included a high proportion of patients already present in a hospital ward before their intensive care unit stay. However, the initial bacterial distributions were similar for these patients and for patients directly admitted from home and comparable to the colonization published by other authors.

Another concern is the acquired resistance of the colonizing bacteria to the antibiotics used. The presence of streptococci and enterococci, even if they can produce nosocomial infections, should not be considered as a failure of the treatment because these strains are not in the spectrum of this regimen. This result as well as the progressive increase in resistance of aerobic gram-negative bacilli to polymyxin E and gentamicin was probably due to a selection of resistant strains by the antibiotics as many cultured bacteria are naturally (e.g., *S marcescens* and *P morganii*, gram-positive cocci) or frequently (e.g., *P aeruginosa* and *A calcoaceticus)* resistant to at least one of the antibiotics used. The possibility of "exogenous" colonization of the gut during selective decontamination of the digestive tract is highly unlikely in this study since the gastric samples were almost always sterile.

Based on these results, we believe that selective decontami-

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nation of the digestive tract may be ecologically unsafe, and we recommend careful monitoring of the fecal colonization of patients undergoing selective decontamination of the digestive tract in order to detect the fecal carriage of gram-positive and multiresistant gram-negative bacteria.

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Chemical Disinfection of Medical Waste—A Totally Wrong Approach

To the Editor:

I have read with great interest the excellent study and careful evaluation of a mechanical/chemical infectious waste disposal system published in *Infection Control and Hospital Epidemiology* (1992;13:387-393).

The Canadian researchers concluded that under the study conditions, the mechanical/chemical infectious waste disposal system, model Z-5000 HC (Medical SafeTEC Inc., Indianapolis, Indiana), reduced the microbial populations tested by a factor of 5 $\log^{10}$ except for certain tests with bacteriphage f2. The machine produced a bacterial aerosol, a problem that remains to be solved, and highly toxic chemical by-products that will require further investigation.

I consider chemical disinfection of medical waste a totally wrong approach to solve the medical waste problem, which all of us have internationally:

1. Chemical disinfection will never be safe. Chemicals, unless used in extremely high concentrations, will never kill spores and many resistant viruses. This has already been demonstrated with the bacteriophage f2, which is much less resistant to chemicals than to many other bacteria and viruses.

2. A 95 $\log^{10}$ reduction will never be sufficient for safe disinfection of medical waste, which often contains much higher concentrations of microorganisms. Many organisms, whose concentrations have been reduced by the machine from 10^7 to 10^2/g, will be able to continue to grow in medical waste (e.g., on the transport in a warm climate). Waste very often contains organic material that provides optimal conditions for bacterial growth.

3. Chemicals can never kill microorganisms in difficult to clean objects, such as connections between needles and syringes, or microorganisms inside small tubes. No chemical disinfection machine will ever be able to get rid of small air bubbles in tubings, which constitute a large part of any medical waste.

4. It is quite clear that chemicals, when used in great amounts as is necessary for the disinfection of medical waste, largely increase the pollution of the environment. This is especially true for sodium hypochlorite, which was the chemical used by the model Z-5000 HC. Sodium hypochlorite is also highly inactivated by organic material, which is part of any medical waste. Furthermore, sodium hypochlorite is one of the most toxic disinfectants for the environment. Hyperchlorination of the sewage system should certainly be avoided.

5. It is irresponsible to use a chemical disinfectant that produces toxic and cancerogenic by-products, such as Trihalomethanes.

In Germany, chemical disinfection of waste is forbidden by law.

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