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Reply to "Selective Digestive Tract Decontamination and Spread of Colistin Resistance: Antibiotic Prophylaxis Is Not a Substitute for Hygiene"

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We thank Krueger and colleagues for their critical comments (1). We fully agree that selective digestive tract decontamination (SDD) is not a substitute for good infection control, especially hand hygiene. With respect to their argument that our findings are in sharp contrast to what is known so far about the effect of SDD on the risk of acquisition of colistin-resistant bacteria, we feel differently.

Although the emergence of antimicrobial resistance has always been a major concern of SDD use (2, 3), the risk of its occurrence has received insufficient attention in most studies, which have focused on morbidity and mortality as the main outcome measures (4, 5). A recent meta-analysis concluded that there is no clear evidence for the association of SDD or selective oral decontamination (SOD) use and the development of antimicrobial resistance (6). This meta-analysis, however, was almost entirely based on studies in which SDD was classically used as a prophylactic measure in settings with a low baseline prevalence of resistant microorganisms. The reason for this might be that the majority of these studies have been performed in The Netherlands, a country with a low prevalence of multidrug resistance (6), while SDD has not been widely accepted and adopted in countries with high prevalences of resistance, particularly because of fear of encouraging resistance to the antimicrobials used (7, 8). In contrast, data on antibiotic resistance, particularly to polymyxins, under SDD used in settings of outbreaks of resistant microorganisms or in settings with high baseline multidrug resistance, such as in our study, are scarce. In some outbreak settings, polymyxin resistance as a consequence of SDD use was not observed (9–11), while in other settings, this did occur (12–14). Unfortunately, information regarding the occurrence of polymyxin resistance among *Enterobacteriaceae* or polymyxin susceptibility testing is not provided in numerous studies assessing antimicrobial resistance (including that to polymyxin E) over time under the use of SDD (15–19).

Although concentrations of topical nonabsorbable antibiotics are usually high in the gut (high enough to exceed minimal bactericidal concentrations [15]), colistin might be biologically inactivated by intestinal contents (20) or sucralfate (21), which is often used in ICU patients; therefore, topical antibiotics lack effectiveness, necessitating high oral doses to achieve suitable fecal concentrations (22). In our ICU, sucralfate was avoided, but concentrations of the SDD components in the gut were not measured. Therefore, we cannot exclude the possibility that in some patients, the concentrations of colistin were below the MICs for ESBL-producing *Klebsiella pneumoniae* strains. This might have contributed to the failure of SDD to eliminate the strain from the carriers and to prevent acquisition of the strain by noncarriers; it may also have contributed to the emergence of resistance among these strains. So, our results are not in sharp contrast to what is known so far about the effect of SDD on the risk of acquisition of colistin-resistant bacteria; rather, our findings are in accordance with some of the limited available data.

When an increase in the number of ESBL-producing *K. pneumoniae*-colonized patients was seen in August 2001, intensive control measures were implemented. An outbreak management team was formed, and infection control practices were reinforced, including hand hygiene, use of contact precautions, labeling and isolation of ESBL-producing *K. pneumoniae*-positive patients, and enhanced disinfection of patient equipment and frequently touched surfaces. On discharge from the ICU to the ward, patients were placed in contact isolation. No spread of the strain outside the ICU was observed. The number of newly colonized patients in the ICU declined toward the end of 2002 but did not reach zero. Since the outbreak could not be controlled despite these measures, an intensified infection control program was started. This included a reduction of the number of ICU beds, the administration, from October 2002 onwards, of SDD to all patients admitted to the ICU, and temporary closure of the ICU from January through May 2003 for thorough cleaning and disinfection. During this period, patients were admitted to a temporary ICU with a 2-bed room for cohort nursing of ESBL-producing *K. pneumoniae*-colonized patients. No patients were transferred from the ICU to the temporary ICU. No new patients with ESBL-producing *K. pneumoniae* were detected in this period until, unfortunately, 1 week before the ICU was moved back to the main location, and this was followed by an increase in the incidence of ESBL-producing *K. pneumoniae*-positive patients after the move back to the main location. The reasons for this are not clear. A common environmental source could not be identified. Cultures obtained from the hands of nursing and medical staff were performed on one occasion and were found to be negative. Nevertheless, patient-to-patient transmission via the hands of hospital staff was probably the most important vehicle (23), enhanced by the continuous presence of colonized patients, an excessive workload, and a crowded ICU.

SDD was, thus, not started as a substitute for hygiene, as suggested by the authors, but rather as an adjunct to an infection control program attempting the interruption of transmission of

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the outbreak strain. This approach has been used in other settings (9–12, 24, 25). The number of patients colonized gradually declined, and after July 2007, no clonally related strains were detected. The exact reason for this decline remains unclear.

As to the carrier state of patients on admission, it is unlikely that the influx of resistant strains significantly contributed to colistin resistance, given the low prevalence of ESBL-producing *K. pneumoniae* strains in the region (26). Furthermore, there was no indication in the laboratory for the increased prevalence of ESBL-producing *K. pneumoniae* strains within the same hospital, where a second ICU for cardiopulmonary surgery is located, or in other ICUs in the region. As we have mentioned in our paper, of the 74 resistant isolates, 71 were clonally related and 3 had different patterns, indicating that most patients acquired the resistant strains, or heteroresistant variants thereof, during admission to our ICU.

Parenteral colistin was not used before the outbreak and was used only sporadically during the outbreak. When indicated, the empirical therapy before and during the outbreak (for noncolonized patients) consisted mainly of parenteral amoxicillin-clavulanate combined with gentamicin. Carbapenems were sporadically used before the outbreak and used during the outbreak in ESBL-producing *K. pneumoniae*-positive patients when clinically indicated.

Regarding Krueger et al.'s final comment, we attempted to analyze ESBL-producing *K. pneumoniae* strains from the same patients obtained before and after the start of colistin. Unfortunately, the primarily susceptible strains belonging to the major clone and those from the 3 nonclonally related resistant strains, isolated in June 2006, October 2005, and March 2007, were not available from the same patients. Although colistin resistance had not been detected before the start of SDD, heteroresistant variants of the outbreak strain were possibly present. Selection and further spread of these strains may have been facilitated by the start and the prolonged use of SDD. If colistin resistance had been identified in a timely manner and SDD consequently been withdrawn, further occurrence of resistance could have regressed (27, 28).

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