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CORRESPONDENCE

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Reply to comment on "Prevention of severe *Candida* infections in non-neutropenic, high-risk, critically ill patients"

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Sir: We read with interest the comments of van Saene et al. Their central argument concerns selective digestive decontamination (SDD)-once again. It seems important to recall the difference between the concept of this potentially effective prevention strategy and the so-called "SDD tetralogy," referred to by van Saene et al. The potential benefit of each of the distinct components of the selective decontamination approach remains a matter of debate both in the literature and among experts [1, 2, 3]. After almost 20 years of extensive research, no consensus exists on either the choice of antibiotics, the route of administration, or the necessity to combine intravenous and oral antimicrobials. The reason why SDD is currently not universally accepted is not due to its lack of efficacy to prevent ventilator-associated pneumonia (VAP) among some patient categories or even reduce mortality in some conditions, but because of its parenteral component and consequent concerns regarding shortand long-term emergence of antibiotic resistance, even following the "princeps" study [4, 5]. We are completely aware of the effect of selective decontamination given that our group was among the first to investigate its potential benefit [6], but we have always used it only in highly selected patients and without the parenteral component [6, 7]. We and others [1, 2, 3, 6, 7, 8, 9, 10] continue to challenge the overall appropriateness of the systematic use of intravenous antibiotics in ICU patients, used for as long as 3-5 days in most trials [11 Such a duration is close to that of VAP treatment [12]. Let us recall that the "SDD tetralogy" is based on a nonrandomized trial with an historical control group [4], and that the impact of the strategy has been shown to be inversely related to the quality of the trial [13]. Using a focused hypothesis that colonization of the oropharynx only,

and not of the stomach and gut, is responsible for subsequent VAP, Bergmans et al. [10] confirmed that a reduction in the orotracheal colonization without impact on the endogenic flora of the stomach and gut reduces the incidence of late-onset VAP. In their study no yeast overgrowth or increase in fungal infection was observed despite the absence of an antifungal. VAP prevention by modulating oropharyngal colonization and preserving the endogenous gut flora or minimizing the overgrowth of resistant organisms may impose as a primary measure in the future [3]. However, this could be achieved only with a strictly controlled and limited use of parenteral antibiotics which has been our strategy over two decades.

The incidence of late-onset pneumonia in our study [7] is among the lowest reported in the literature [14], without the use of any parenteral component. We agree with van Saene et al. that the addition of intravenous antibiotics could have further reduced the already low incidence of earlyonset pneumonia, but at the cost of treating a large number of patients for a marginal benefit, and the likely risk of resistance acquisition. Assuming that prophylactic intravenous antibiotic would halve the incidence of early-onset pneumonia, 34 patients would need to be treated to prevent one case.

We agree that, unsurprisingly, the incidence of bacteremia in our study population was high due to the choice that we made to recruit patients at extremely high risk [7, 15], who represented only 4.2% of patients admitted in our ICUs over the study period [7]. Moreover, there was no expectation that the selective decontamination regimen used would impact on bacteremia rates [7]. Such a high infection rate cannot be compared with the rates reported in other SDD studies in which less stringent selection criteria were applied. Regarding prevention of bloodstream infection, we stress again that by far the leading source of primary infection, including candidemia, is vascular devices [16, 17]. Consequently, approaches to prevent gut translocation should only be considered in institutions where effective evidence-based strategies have been implemented [16].

We were surprised by the superficial understanding of the process of *Candida* infection. *Candida* infection arises from endogenous colonization [15]. In all studies appropriately designed to assess this process [7, 15, 18, 19, 20], *Candida* colonization has always preceded infection, with intensity of colonization being the prerequisite and the key predisposing factor for infection [7, 15]. Preventing colonization surely did contribute to the 90% reduction in candidemia incidence [7]. The high proportion of patients colonized with *Candida* certainly does not reflect cross-transmission but is an expected characteristic of highly selected patients at risk for endogenous colonization, as reported in other studies that have focused on high-risk patients only [19, 21, 22, 23, 24].

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