

CORRESPONDENCE

The innovative microbiology of selective digestive decontamination requires a new mindset – Letter to the editor

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Dear Editor,

After 30 years of selective digestive decontamination (SDD) research, the lack of generally accepted definitions and concepts on infection and infection control still hinders a constructive discussion. The recent review by Muskiet et al.¹ and the related editorial² suggest a disturbing lack of understanding of the essentials of the classical SDD strategy. More specifically, both authors fail to discuss the classification of infections, crucial for any infection surveillance program and the classification of microorganisms according to their pathogenicity. Furthermore, important concepts such as carrier state, overgrowth and the distinction between carriership, colonisation and infection are lacking. Finally, neither Muskiet nor Van Essen gave an indication of knowledge of the four components of the SDD strategy, thereby reducing this life-saving strategy to administration of antibiotics in throat and gut. As with all ICU interventions, a thorough knowledge and appreciation of at least the basics behind an intervention is required. Armed with the insights a sound judgment on the available literature on resistance during SDD is possible.

Important concepts³ in the SDD strategy include ‘normal’ versus ‘abnormal’ potentially pathogenic microorganisms (PPM) and the carrier state classification of infection. ‘Normal’ PPM include *S. pneumoniae*, *H. influenzae*, *M. catarrhalis* in the throat, *E. coli* in the gut, and *S. aureus* and *C. albicans* in throat and gut. They are carried by healthy individuals. In contrast, only diseased individuals carry abnormal PPM consisting of eight aerobic Gram-negative bacilli (*Klebsiella*, *Enterobacter*, *Citrobacter*, *Proteus*, *Morganella*, *Serratia*, *Acinetobacter*, and *Pseudomonas* spp) and methicillin-resistant *S. aureus* (MRSA). The carrier state concept allows the distinction between three types of infection (table 1):

Primary endogenous infection is defined as an infection caused by potential pathogens present in overgrowth concentrations in the admission flora. It is the most common intensive care unit (ICU) infection (55%) and develops within one week of admission.

Secondary endogenous infection is an infection due to ‘abnormal’ PPM not present in the admission flora but acquired later during ICU treatment. ‘Abnormal’ PPM are first acquired and carried in the throat, subsequently in the gut in overgrowth concentrations. One-third of ICU infections are secondary endogenous infections and occur after one week of ICU treatment.

Exogenous infection is an infection not preceded by throat and/or gut carriage in overgrowth. The causative potential pathogens are invariably ‘abnormal’ PPM directly introduced into the internal organs. The frequency is 15% and this type of infection can occur at any time during ICU treatment.

The acknowledgement of these different definitions is crucial to the understanding of the pathogenesis and control of ICU infections.

What is SDD?

SDD is a four component strategy aiming to control infections of the lower airways and blood, and to reduce mortality in critically ill patients requiring treatment in the ICU.

The first component is four days of high doses of parenteral cefotaxim to prevent primary endogenous infections and to eradicate oropharyngeal carriage in overgrowth concentrations of ‘normal’ bacteria.

Second, enteral administration, i.e. in throat and gut, of non-absorbable antimicrobials, to control oropharyngeal and gut carriage in overgrowth of abnormal bacteria.

Third, a high level of hygiene throughout ICU treatment to prevent transmission, via the hands of carers, to control secondary endogenous and exogenous infections.

Finally, surveillance cultures of throat and gut taken on admission and afterwards twice weekly are essential to classify the three different types of infection, to assess the efficacy of the first three components, as well as the possible side effects such as the emergence of resistance.

It is obvious that SDD is completely different from the traditional approach to infection control in the ICU. Applying

Table 1. Classification of infections in the ICU.

Infection	PPMs	Timing	Frequency (%)	Preventing manoeuvre
Primary endogenous	6 normal 9 abnormal	< 1 week	55	Parenteral antibiotics
Secondary endogenous	9 abnormal	> 1 week	30	Enteral antibiotics in throat and gut; hygiene
Exogenous	9 abnormal	Any time	15	Topical antibiotics and hygiene

PPMs = potentially pathogenic microorganisms.

the SDD strategy involves more than just administering antibiotics in throat and gut, but requires a new and proactive mindset instead of adhering to the classical reactive approach where the carrier state of PPM is ignored. It is common sense that ICU interventions such as glucose control or vasopressor therapy require continuous and close monitoring and if necessary adjustment of the drug dosage. In the same way, the effect of SDD has to be evaluated daily and, if necessary, the antimicrobials adjusted. For example, if a patient is not decontaminated due to a tobramycin-resistant *Morganella* (a microorganism that is intrinsically resistant to colistin) tobramycin should be replaced by amikacin. Another example: as the SDD antimicrobials of polymyxin, tobramycin, and amphotericin B (PTA) do not cover MRSA, vancomycin has to be added to the classical combination to eradicate the MRSA carrier state.

SDD has been consistently shown to provide a survival benefit as long as the sample size of the study is large enough. Intensivists should realise that *lege artis* use of the four component SDD strategy, resulting in eradication of carriage and overgrowth of PPM, is required for maximal survival benefit. If all ICU patients are decontaminated, a 42% mortality reduction is achieved.⁴

SDD and resistance

The mechanism of action of SDD is control of gut overgrowth. Gut overgrowth is a risk factor for endogenous infections and emergence of resistance.³ Applying only parenteral antibiotics, which are excreted in low concentrations in the intestinal tract, carries a high risk of inducing resistance in view of the overgrowth concentrations of PPM present in the gut. In contrast, the enteral component of SDD will result in very high intestinal concentrations of antimicrobials thereby eradicating the PPM carrier state in overgrowth and preventing, even eradicating, the carrier state with resistant microorganisms. Theoretically, eradication of overgrowth should control resistance and outbreaks. Indeed, not only in

the Netherlands, but also in ICUs in countries with a high level of resistance, e.g., Spain, Italy, and UK, the SDD strategy has been shown to reduce resistance.³ This is in contrast with the conclusion of Muskiet and Van Essen that the use of SDD can only be justified in ICUs with low levels of antibiotic resistance. The concerns about colistin resistance and an increase in Gram-positive infections are based on low level observational studies.^{5,6} In addition, a recent review again underlined the absence of resistance induction when applying SDD.⁷ The ongoing multi-continental cluster-randomised Canadian SDD study (SUDDICU) in 25,000 patients will hopefully finalise the discussion regarding the use of SDD in critically ill patients. The proactive mindset required for the SDD strategy may be crucial in preventing a further increase of global multi-resistance and in controlling outbreaks.

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Response E.H.R. van Essen

Dear Editor,

Over the last ten years, three large clinical trials convincingly showed that selective digestive decontamination (SDD) and selective oropharyngeal decontamination (SOD) lower mortality in ICU patients. Rommes and co-authors suggest that a proactive mindset is the key to its success. Specifically, they advocate adjusting antibiotics included in the SDD/SOD regime on a daily basis. Unfortunately, this assumption is not supported by evidence from the literature. As far as we know, daily adjustment of antibiotics of the SDD/SOD regime has never been studied. Over the last years, increasing the dose of SDD has been advocated if potentially pathogenic microorganisms were still cultured from the stools of patients treated with SDD. However, concerns for tobramycin toxicity limit this adjustment of SDD.¹

Rommes and al. also suggest that SDD is equally effective in areas with high levels of antibiotic resistance. This may be true, but I want to emphasise that all large trials showing improved outcome in ICU patients were conducted in ICUs with low levels of antibiotic resistance.²⁻⁴ Consequently, new studies in other countries are needed before the use of SDD or SOD can be advocated in other parts of the world.

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Response E.R.R Muskiet

Dear Editor,

I thank colleagues Rommes et al. for their remarks, and agree with the importance of knowledge of the principles of selective digestive decontamination (SDD) described in their letter and in various publications during the last decades. To describe these extensively in this review on SDD and the relation to emergence of antibiotic resistance would have resulted in an unacceptable lengthening of the paper; the four basic components were mentioned.

The studies which led to the suggestion of Rommes et al. that SDD might be as effective in not inducing antibiotic resistance in surroundings with pre-existing higher levels of antibiotic resistance compared with the Netherlands are certainly hopeful, but still need to be confirmed and validated by larger (ongoing) trials performed in regions with these higher levels

of resistance. Daneman et al. not only stated that there was absence of induction of resistance but they also stated that the effect of SDD on ICU level antimicrobial resistance rates is understudied.¹

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