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SDD: don't be selective in considering pros and cons

Accepted: 2 May 2010
Published online: 7 July 2010
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Dear Editor,
We thank Dr. Zandstra and
colleagues [1] for their interest in
our work [2]. Although in their sci-
entific careers they have amassed
impressive data on selective digestive
microbial decontamination (SDD),
they have not fully appreciated what
our paper adds to this large body of
knowledge.

The intestinal microbiota contains
many more cells than the human body
itself. Furthermore the intestinal
microbial gene set is approximately
150 times larger than the human
genome [3]. Last year marked the
150th anniversary of Darwin's *On the
Origin of Species*. How can we
explain any genetic advantage for
humans to carry so many microbes
along? What benefit does our mi-
crobiome provide us during health?
And what happens during critical ill-
ness? How does the intensive care
unit (ICU) environment impact on our
microbiota? What impact does SDD
have on our microbiota? And what is
the impact of SDD on the emergence
of resistant bacteria in the ICU?

Zandstra et al. rightly allude to the
fact that *Enterobacteriaceae* increase
during critical illness—we also found
a more than tenfold relative increase
(as a percentage of total bacteria)

compared to data from healthy
volunteers [4, 5]. To fight overgrowth
of *Enterobacteriaceae* seems like a
good idea—but is there a trade-off?
Why did SDD—though providing a
small but significant survival advan-
tage compared to a control group—
fail to further reduce mortality
compared with patients receiving
only oral topical antimicrobial
products, even though these study
participants had similarly increased
percentages of *Enterobacteriaceae*?

A potential advantage of having
such massive numbers of anaerobic
bacteria in the colon is that colono-
cytes feed on bacterial products.
Indeed colonocytes feed on butyrate,
produced by a limited number of
colonic bacterial species. The *Fae-
calibacterium prausnitzii* group is
predominant amongst these butyrate-
producing groups. This group is
already reduced during tube feeding,
resulting in a significantly reduced
concentration of butyrate [4]. We
describe a significant reduction in two
groups of microbiota that help in
maintaining the integrity of the large
intestinal mucosa. Quoting Vollaard's
and Donskey's work, Zandstra et al.
agree that SDD is a contradiction in
terms. We apparently disagree in our
concern that SDD might have a “dark
side”, i.e. that some important bene-
ficial microbiota are harmed by SDD.
Besides, there is additional collateral
damage: in the analysis of point-
prevalence cultures from the de Smet
study [6], an increase of intestinal
colonisation by resistant organisms
was observed after cessation of
SDD [7].

None of the articles cited by
Zandstra et al. describe the use of
molecular methods for detection and/
or enumeration of the intestinal mi-
crobiota. Bacteria from the
F. prausnitzii group are highly sensi-
tive to oxygen and require very
specific growth media. Culture-based
quantification yields a high degree of
culture bias. These limitations of

culture-based microbiological
techniques have precluded reliable
testing of the effects of antibiotics
(i.e. SDD) on the intestinal microbi-
ota. We are obviously not the first to
claim that SDD is not selective. We
are, however, the first to back up
these claims using absolute numbers
of faecal bacteria derived from a
quantitatively reliable, molecular
method.

Referring to Wensinck as an
argument that not *F. prausnitzii* but
clostridia contribute to colonisation
resistance (CR), Zandstra et al. dis-
play a misunderstanding of the
composition of the intestinal micro-
biota. Although phenotypically
Gram-negative, *F. prausnitzii* are
genetically closely related to the
Gram-positive clostridia Zandstra
et al. refer to. In fact, they belong to
clostridial cluster IV [8]. These phy-
logenetic relations have only been
discovered since the dawn of the
molecular era.

We agree that the clinical impact
of *F. prausnitzii* reduction in the
critically ill is unclear—at least, that
this should be further studied; we do
not know whether there is a critical
threshold of butyrate substrate for
colonocytes to survive, or to maintain
the integrity of the large intestinal
mucosa. Recent studies have shown
an anti-inflammatory effect of
F. prausnitzii in Crohn's disease that
could also be beneficial for the criti-
cally ill [9]. We have, however,
provided novel information that may
explain the discrepancy of effective
reduction of *Enterobacteriaceae* by
SDD, which fails to translate into
further survival benefit in comparison
with selective oropharyngeal decon-
tamination (SOD).

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