

# Abnormal flora and infection in critically ill patients

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All critically ill patients go through a period of inflammatory response as they suffer from tissue injury caused by infection, trauma, surgical procedure, pancreatitis, ischaemia or burn. The inflammation can be measured by high levels of pro-inflammatory cytokines (e.g., IL-6, TNF- $\alpha$ ) and the hyper metabolic state. A paradox immunosuppression occurs consecutively with higher levels of anti-inflammatory cytokines (e.g., IL-10) and reduced immune functions [1]. This depressed immune state is an important reason for the fact that critically ill patients are prone to infection. In addition, treatment in the ICU adds to the risk of secondary infection by crossing natural barriers (intubation, central lines and catheters) but also by interference with the carriage of normal bacterial flora. This interference is on one hand caused by the use of antimicrobials and on the other hand by the (initial) decrease in gut motility, both leading to abnormal carriage and overgrowth of pathogenic microorganisms. The immune suppression, the interruption of natural barriers and the abnormal carriage of microorganisms are the three main reasons that patients in the intensive care department develop secondary infections. Secondary infections significantly worsen the outcome of intensive care treatment [2]. Critical care physicians should therefore have a focus on strategies to prevent secondary infection. Sidler et al. [3] discuss potential strategies to prevent secondary infection but limit themselves to three types of microorganisms that have been involved in these infections in intensive care patients: Enterococci, Clostridium difficile and ESBL-producing bacteria [3]. Enterococci and Clostridium are part of the normal gut flora in humans. However, critical illness leads to colonisation of normally sterile organs, to overgrowth and to subsequent infection. This sequence (acquisition, colonisation, overgrowth, infection) underlies every secondary infection in ICU patients independent of the pattern of resistance of the microorganism [4]. However, the resistant strains are more worrisome because of the difficulty in treatment.

Sidler et al. nicely review the literature concerning these (multi) resistant microorganisms and their increased prevalence in the community and the ICU. Their review, however, seems to stress the danger of these multi-resistant strains too much as prevention of infection with these strains is basically the same as for the sensitive strains. Infections caused by sensitive and multi-resistant strains can be prevented by blocking the sequence: acquisition, colon-

isation, overgrowth, and infection. Hygiene is the major intervention to prevent acquisition (outbreaks) and to prevent exogenous infection. Exogenous infections are caused by introducing microorganisms directly into normally sterile sites (lines, catheters, intubated respiratory tract). Unfortunately, high compliance to hygienic measures is hard to achieve. The colonisation pressure on critically ill patients is so great and the immune status is so much impaired that hygiene alone cannot be enough to prevent gut colonisation with pathogenic microorganisms. The only strategy proven to prevent secondary colonisation and infection with pathogenic pathogens is the use of topical antibiotics to achieve selective decontamination of the digestive tract [5]. Decontaminating the digestive tract from aerobic gram-negatives appears to prevent colonisation and infection of normally sterile sites such as respiratory tract, blood and urinary tract with these microorganisms. Intravenous antibiotics alone can treat concurrent infections but are not able to decontaminate the digestive tract. Moreover, intravenous antibiotics result in low concentration in the gut where a large number of microorganisms is present. That situation is probably the cause of the development or selection of multi-resistant strains and vice versa explains the decrease in resistant strains during digestive decontamination [6]. The increasing background prevalence of ESBL producing gram-negative strains is a worldwide concern but can be handled on the local level by focussing on hygiene, preventive strategies (e.g., isolation measures) and careful antibiotic use. For the ICU setting topical decontamination of the digestive tract should be seriously considered for its effect on both patient-level and unit-level outcomes [6]. Sidler et al correctly review the current knowledge on preventive strategies but they overrate the pathogenicity of Enterococci. A high level of hygiene together with the intrinsically low pathogenicity of Enterococci reduces the clinical relevance of Enterococci, including VRE. This was previously described by themselves with a successful reduction of VRE using hygienic measures [7]. Clostridium difficile can be a significant problem in patients with a disturbed normal gut flora. It is therefore important to increase patients own colonisation resistance by respecting the indigenous flora. In the selection of antibiotics one should bear this in mind, which is also one of the pillars of digestive decontamination strategies in the ICU.

Enterococci, *C difficile* and ESBL producing gram-negatives have in common that they may infect critically ill patients but also that an intervention combining hand hygiene, contact isolation measures and a balanced antibiotic strategy including digestive tract decontamination can handle their threat.

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