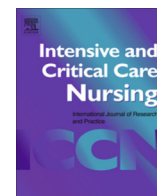




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## Editorial

## Dilemmas in infection control in the intensive care unit

## Introduction

Intensive care unit (ICU) patients are at a particular risk for infection with multidrug resistant micro-organisms because they experience high severity of acute illness, present with predisposing underlying conditions, are exposed to a plethora of invasive procedures and are at the extremes of age, either neonatal or very old (Depuydt et al., 2006; Blot, 2008; Blot et al., 2014b; Verstraete et al., 2015; Afonso and Blot, 2017). Healthcare-associated infection and multidrug resistance are a major concern in ICUs as it is associated with considerable morbidity and possibly mortality (Blot et al., 2002, 2003; Verstraete et al., 2016). As a consequence substantial efforts in infection prevention and control are required to reduce the burden of infectious complications (Rello et al., 2013; Blot et al., 2014a; Sousa et al., 2018). While infection prevention targets the avoidance of specific infections at an individual patient level, infection control is more focused on containing the problem and preventing further spread of epidemiologically important pathogens throughout the unit or the hospital.

Infection control is a key element in the management of multidrug resistant organism (MDRO) carriers/infected patients in ICU. The infection control measures are based on two different, but complementary approaches. The first is based on a search and isolate policy and could be considered as the targeted approach, whereas the second is considered as the universal approach and is based on improving hand hygiene and compliance to standard precautions. Targeted policy based on screening and isolation (the search and isolate policy) seems until now the most accepted and recommended in clinical practice. Indeed, until recently contact precautions have been recommended for MDRO carriers or infected patients, admitted in ICU. Also, specific situations as infected patients with airborne pathogens (tuberculosis, measles, varicella virus) and neutropenic patients require additional measures and single room. Several studies suggested the effectiveness of the target policy, to control the spread of MDRO in ICUs and general wards (Jarlier et al., 2010). These programs focused on a bundle of measures aimed at decreasing cross-transmission including active surveillance, single room placement, contact precautions, promotion of hand hygiene, quick notification of cases, active decolonisation and feedback.

Despite several clinical studies that assessed the ability of various infection control measures in reducing the spread of MDRO in ICU, it remains impossible to determine the exact and relative importance of the different infection control measures. Several methodological limitations could explain why we cannot identify the most effective measures (Landelle et al., 2013). We performed

a narrative review to concisely summarise recent literature in the field of infection control in the intensive care setting and to highlight remaining dilemmas.

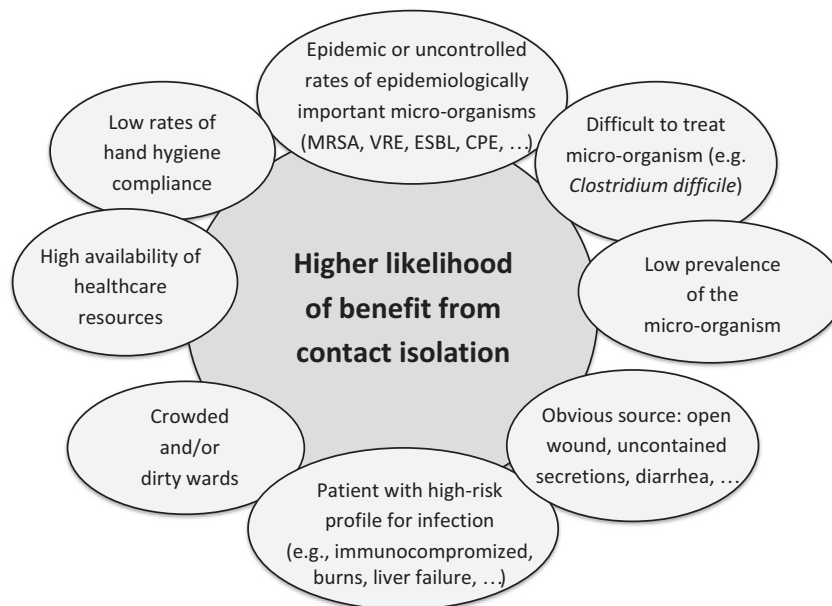
## The epidemiological problem

The most and urgent threats for ICU include carbapenemase-producing *Enterobacteriaceae* (CPE) and extended-spectrum beta-lactamase (ESBLs). One of the most striking epidemiological changes of the last ten years is the increasing spread of resistance enzymes in *Enterobacteriaceae* species, as MDRO is evolving to an endemic situation in many countries. These worrisome phenomena, result in an increase of the reservoir into the community and the hospital as transmission of these resistant isolates is further complicated by genes being encoded on self-transmissible plasmids which can be exchanged among the different species of *Enterobacteriaceae*. Also this epidemiological phenomenon makes it more difficult to implement the targeted policy since several MDRO carriers may not have the classical risk factors at ICU admission (Vogelaers et al., 2010). Thus, the targeted policy should be based on a broad screening indication. One of the main limitations in this strategy is the sensitivity of the different screening techniques (Dyakova et al., 2017).

Also, compared to other patients, ICU patients are exposed to a higher risk of acquisition and to multiple other MDRO such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and methicillin-resistant *Staphylococcus aureus* (MRSA). Obviously, targeted isolation in ICUs can be justified as these patients have a greater inherent risk for acquiring MDRO because of the intensity of care, the use of invasive procedures, and exposure to antimicrobials. However, contact isolation in the ICU has a dark side as well since it is associated with an increased rate of medical errors and adverse events (including non-infectious events) (Zahar et al., 2013). Therefore, future research should bring insights into how to balance the benefits and the threats.

## Is there another solution?

Contaminated hands of healthcare workers (HCW) are the primary vehicle leading to the acquisition of MDRO in ICU patients (Nseir et al., 2011). The spread of MDRO depends on several factors including the importance of the reservoir (Ruppé et al., 2013; Lerner et al., 2015), the compliance of HCW to hand hygiene (Pelat et al., 2016), and the level of environmental contamination as is particular concern with *Clostridium difficile*, vancomycin-resistant enterococci (VRE), *A. baumannii* and MRSA.



**Fig. 1.** Factors influencing the benefits of contact isolation. MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci; ESBL, extended-spectrum beta-lactamase-producing *Enterobacteriaceae*; CPE, carbapenemase-producing *Enterobacteriaceae*.

Concerning the reservoir, two factors could be associated with the risk of diffusion: a) the relative faecal abundance as suggested by several authors (Ruppé et al., 2013; Lerner et al., 2015), and b) the colonisation pressure. For the first factor (individual risk) there are no known data to identify if there is any threshold of colonisation that is associated with a higher risk of spread. For the second one (collective risk) as far as we know there are no studies, suggesting a breakpoint in the proportion of colonised and infected patients for which the risk of spread substantially increases, as highlighted for MRSA (Merrer et al., 2000).

Consequently, to prevent transmission, it seems necessary to 1) reduce the reservoir, 2) improve hand hygiene and 3) control the environment. In a cluster-randomised study, Derde et al. suggested that for MDRO colonisation and transmission declined with improving hand hygiene and universal chlorhexidine body-washing policy. In this study no additional benefit was found after introduction of screening and isolation (Derde et al., 2014). However, the MDRO decrease was mainly driven by a reduction in MRSA while no effects were noticed concerning vancomycin resistant enterococci (VRE) or highly resistant *Enterobacteriaceae*. This observation was recently confirmed by a meta-analysis demonstrating a significantly reduced risk for Gram-positive bacteraemia but not for Gram-negative bacteraemia, thereby indicating that chlorhexidine body-washes are less effective in containing the reservoir of Gram-negative pathogens (Afonso et al., 2016). Also a recent prospective observational study conducted in a French 12-bed ICU suggested a low incidence of ESBL-*Enterobacteriaceae* transmission in ICUs (Repassé et al., 2017) thereby confirming non-ICU study results (Tschudin-Sutter et al., 2016). Several studies suggested the effectiveness of the universal strategy to control the spread of specific MDRO (McKinnell et al., 2017). Indeed, in a break-point time series analysis conducted in an ICU, from April 2013 to August 2016, Bradley et al. suggested that routine decolonisation for MRSA is an effective strategy to reduce the spread and incidence of MRSA across the whole hospital (Bradley et al., 2017). Finally, in a longitudinal cohort study, Price et al. demonstrated by using whole genome sequencing, that in the presence of standard infection control measures, HCW rarely are the source of *S. aureus* transmission. Notwithstanding, achieving

high rates of hand hygiene compliance in an ICU is not for granted. First, knowledge levels of hand hygiene of ICU personnel appear to be unsatisfactory (Labeau et al., 2016; El-Soussi and Asfour, 2017). Besides practical and organisational conditions, such as sufficient sinks or hand alcohol dispensers and an acceptable workload, behavioural determinants play a vital role (De Wandel et al., 2010; De Wandel, 2017; Sadule-Rios and Aguilera, 2017). Self-efficacy, attitude, perceived barriers, local culture and social influence are much harder to change though absolutely necessary to reach high compliance with hand hygiene recommendation (Bouadma et al., 2010; Battistella et al., 2017; Piras et al., 2017).

However, to be effective, universal policy requires a high level of compliance to standard precautions and hand hygiene observance (Derde et al., 2014). Additionally, some ICU patients such as those with severe burn injury, could be more exposed to risk of acquisition and need specific measures as contact isolation (Raes et al., 2017).

In the future we think that contact isolation based on a screening policy is an inapplicable policy in view of the endemic character of MDROs carriers. The standard of care for infection control however, should be high compliance to hand hygiene and standard precautions. In addition, two complementary measures could be added in case of high individual risk of transmission: 1) chlorhexidine bathing for specific patients and 2) targeted contact isolation. These two measures may be driven by several factors (Fig. 1) according to ward and individual patients characteristics and specific factors related to involved species (Kirkland, 2009).

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