CRITICAL CARE

COMMENTARY

Colonization pressure: a critical parameter in the epidemiology of antibiotic-resistant bacteria

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See related research by Arvaniti *et al.*, http://ccforum.com/content/16/3/R102

Abstract

The recognition of colonization pressure as an important risk factor for acquisition of antibiotic-resistant bacteria in the ICU, including Acinetobacter species, has major consequences for our understanding of risk factor analyses. Moreover, the importance of colonization pressure underpins the role of cross-transmission in the dynamics of antibiotic-resistant bacteria in the ICU, which has major consequences for the evaluation of the effectiveness of infection control measures.

Infections caused by bacteria resistant to commonly used antibiotics are rapidly increasing in many ICUs worldwide. Whereas multiresistant Gram-positive bacteria such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci were considered major healthcare threats at the turn of the century, attention has now shifted towards multiresistant Gram-negative bacteria. Many bacteria have become resistant to most β-lactam antibiotics through production of extended-spectrum β-lactamases, rendering carbapenem antibiotics the treatment of choice. More recently, however, outbreaks and increasing infection rates have been reported with Gram-negative bacteria, mainly *Klebsiella pneumoniae*, producing both extended-spectrum β-lactamases and carbapenemases. Only few antibiotics remain active – at least *in vitro* – against these bacteria. Among multiresistant Gram-negative bacteria, Acinetobacter species hold a special position because these bacteria are intrinsically resistant to many antibiotics and are capable of rapidly acquiring new resistance mechanisms for the few antibiotics still considered active [1].

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Patient-to-patient transmission is a prominent mechanism for the emergence of antibiotic-resistant bacteria in hospital settings, especially in ICUs, and prevention of nosocomial spread of these bacteria is becoming more and more important. From a theoretical perspective, with ICU patients confined to their beds, antibiotic-resistant bacteria spread predominantly as a vector-borne disease, with the temporarily contaminated hands of healthcare workers acting as vectors. For this transfer to occur healthcare workers must contact a colonized patient (or their immediate surroundings) to pick up the bug, and then touch another noncolonized patient, while still being contaminated, to pass the bug. Each of these actions happens with a certain rate, and the product of all these rates is the risk of transmission per unit of time. The classical infection control measures all interact somewhere in this sequence of events. Hand hygiene after and before patient contacts and barrier precautions reduce the likelihood that hands remain contaminated, cohorting of healthcare workers reduces the likelihood that one person goes from a colonized patient to an uncolonized patient, and reducing antibiotic use probably reduces the likelihood that a contact will lead to contamination or colonization.

Yet there is also one other important parameter in the equation: the likelihood that a first contact will be with a colonized patient. This has been called colonization pressure, first described for vancomycin-resistant enterococci [2] and later for other bacteria as well [3-5]. In the previous issue of *Critical Care* Arvaniti and coworkers describe the relevance of colonization pressure as a risk factor to acquire carriage with Acinetobacter in a Greek ICU [1]. In their unit 5.6% of all admitted patients were already colonized on admission and 15.7% acquired Acinetobacter carriage during their ICU stay. Colonization pressure was strongly associated with an increased risk of acquisition, and genotyping demonstrated that all Acinetobacter isolates were clonally related.

Identification of colonization pressure as an important risk factor for acquisition strongly suggests frequent occurrence of cross-transmission (which is another description of insufficient hygiene), especially when this

is supported by a clonal relationship of isolates. In the case of Acinetobacter, however, as with vancomycin-resistant enterococci, persistently contaminated environmental surfaces may also contribute to acquisition risks, and it is uncertain how this interacts with colonization pressure estimates [6,7].

The recognition of the importance of colonization pressure also impacts on the methodology of investigating risk factors for acquiring carriage (and infection) with antibiotic-resistant bacteria and the evaluation of the effects of infection control interventions. First, in settings where cross-transmission is potentially relevant (which basically means in virtually all settings with perceived antibiotic resistance problems) the determination of risk factors for acquisition is suboptimal if colonization pressure (or a reliable proxy) has not been included. This invalidates many risk factor analyses performed in the past.

Second, colonization pressure may rapidly change, even without infection-prevention measures. The pressure increases when a newly admitted patient is already colonized and replaces a noncolonized patient that is discharged or when a noncolonized patient acquires carriage (and becomes a colonized patient). *Vice versa*, pressure reduces if a colonized patient is discharged (or succumbs) and is replaced by a noncolonized patient. As ICUs are typically small (with 10 to 20 beds) with rapid patient turnover, the colonization pressure will fluctuate enormously. However, the risk of transmission is not constant and depends on the colonization pressure: the risk is high with high pressure, and the risk is zero if no other colonized patients are present in the ICU. This creates dependency in the data and a patient's status cannot be considered independent from the status of other patients [8]. In fact, this dependency is not surprising because it reflects the *raison d'être* of infectious diseases. The consequence, however, is that evaluation of an intervention aimed to reduce cross-transmission (such as hand hygiene improvement, patient isolation, or modulation of antibiotic use) should not use statistical tests that assume independent observations, such as chi-square tests and Student *t* tests. This, again, invalidates many intervention studies performed in the past [9].

The recognition of the importance of colonization pressure therefore has major consequences for the clinical epidemiology in ICU settings. Colonization pressure provides a simple and reliable indication of failing hygiene, but also complicates our approaches to investigate control measures. Only well-designed trials combined with appropriate statistical analyses can help us in quantifying the effects of interventions to prevent the spread of multiple resistant bacteria. There are some good samples of such studies that, unfortunately, failed to demonstrate effectiveness of such interventions [10,11]. Nevertheless, we are far better off with such studies than with oversimplified analyses reporting positive findings but neglecting the effects of colonization pressure.

Competing interests
The author declares that he has no competing interests.

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