Staphylococcus aureus transmission in the intensive care unit: the potential role of the healthcare worker carriage

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Introduction

Healthcare-associated infection is associated with high morbidity and mortality.

Staphylococcus aureus (S. aureus) is a major agent of healthcare-associated infections and causes a wide range of diseases from mild to life-threatening conditions. Carriage of S. aureus usually precedes infection. The transmission from carrier to non-carrier is therefore at great concern in intensive care units (ICUs). Furthermore, patients in ICUs are exposed to an increased antibiotic selective pressure favoring cross-transmission of resistant bacteria such as methicillin-resistant S. aureus (MRSA) (1,2).

S. aureus colonization

Patients are identified as carriers or non-carriers, and the former are generally classified as “persistent” or “intermittent”. Approximately one fifth of the individuals are persistent carriers in the community (3) and also at ICU admission (4). The main habitat for S. aureus is the anterior nares. Most individuals will be exposed to the organism transiently throughout their lifetime. It was shown that intermittent and non-carriers shared similar nasal elimination kinetics; thus, two types of nasal carriers might be recognized: persistent carriers and “others” (5).

Persistent carriers usually have a higher load and are frequently colonized by a single strain of S. aureus, whereas intermittent carriers may carry different strains over time (6,7).

Furthermore, S. aureus colonization depends on several factors such as genetic or environmental factors, host immunity and bacterial interference (3). Surprisingly, persistent carriers who are artificially colonized with a mixed culture will specifically re-acquire their autologous strain (5). Finally, 80% of strains causing septicemia were endogenous. While the risk of infection in nasal carriers is estimated to be 2- to 12-times higher than in those who are not colonized with S aureus, authors highlighted a lower rate of mortality in persistent carriers compared to others, all possibly explained by a higher rate of anti-staphylococcal antibodies.

Routes of transmission (Figure 1)

Carriers can be broadly divided into two categories: those already carrying S. aureus at ICU admission, and those with ICU-acquired S. aureus. The first category determines a great part of the colonization pressure. The colonization pressure is the ratio of carriers (colonized or infected) over the number of patients treated in the unit; it remains a major risk factor of S. aureus and MRSA acquisition (8,9).

S. aureus acquisition is rarely related to patient-to-patient transmission. It is usually due to transmission through and
from healthcare workers (HCWs) or the environment (10). Thus, vectors of transmission largely remain temporarily contaminated hands of the HCWs, either via direct contact with a colonized/infected patient or through simple contact of contaminated surfaces (11). This transmission could come from the contaminated environment around the carrier or through the hands of the health-care workers. The hand-associated transmission explains why the extensive use of alcohol-based hand-rub solutions for hand disinfection in the 90's resulted in a sustained reduction of MRSA burden (12).

Studies considering *S. aureus* acquisition by patients in a room previously occupied by an infected or colonized patient reported contrasting results, suggesting a low risk of direct transmission from the environment, despite the high rate of contaminated surfaces at hospital (10,13).

The risk is maximized if HCW have a sustained carriage (14). For MRSA, carriage among HCWs is favored by chronic skin diseases, poor hygiene practices, and having worked in countries with endemic MRSA (15).

Overall, the proven risk factors associated with a higher risk of MRSA cross-colonization are the colonization pressure, health care workload and absence of single room (16).

**Strategies to prevent the transmission by HCWs**

Therefore, strategies to limit transmission that consider both patient's colonization status and risk of transmission from health care worker and the environment were developed.

First, targeted policies are based on active surveillance and contact isolation (the screen-and-isolate strategy). Second, universal policies include universal decolonization and improving hand hygiene. Prior to them, targeted policies were considered as the gold standard. However, recent studies highlighted the effectiveness of universal decolonization including chlorhexidine bathes and nasal mupirocin to prevent MRSA infection outbreak in the ICU (17,18) and may limit the spread of MRSA. Furthermore,
it seems to be as effective as contact precaution without the adverse events associated with patient isolation (19,20). It should be noticed that the respective role of improvement of hand hygiene and universal decolonization remains unknown.

Nonetheless, universal decolonization is at risk of alteration of the endogenous human microbiota and may increase the risk of pathogenic infection through a loss of “colonization resistance” (21). Furthermore, this approach presents an inherent risk of emergence of bacterial resistance associated with chlorhexidine and mupirocin use. The potential risk of emergence of resistance to chlorhexidine with the use of universal chlorhexidine baths is debated in the literature (22-25). Failures of universal decolonization have been linked to chlorhexidine resistance in some recent studies (26,27).

Considering the evidence, it is therefore important to better understand the route of transmission to privilege HCW hand disinfection or universal patient decolonization for interrupting S. aureus transmission.

Whole-genome-sequencing (WGS) and new insight

WGS allows comparison of the genetic difference between organisms and can characterize highly related strains with sufficient resolution to inform on routes of transmission (28). In the context of MRSA outbreak investigation, WGS is useful to identify the source of transmission (14). Moreover, the use of this new technology has revealed that resident type heterogeneity is not exceptional in persistent S. aureus carrier. Polyclonal nasal colonization was identified as well as a colonization by different strains in different niches. Senn et al. even identified a “stealthy colonization of the gut”, revealing a particular clone which prefers digestive tract over the nasal cavity as primary colonization niches. Stealthy carriers probably facilitated the spread of this unrecognized strain of MRSA (29,30).

Prices et al.’s study

Using whole genome sequencing, Price et al. studied those different routes of transmission of S. aureus in ICU and high dependency (31). This longitudinal cohort study collected during 14 months, isolates from 1,854 patients, 198 HCWs and 40 environmental locations. Patients were screened at admission and weekly thereafter whereas HCWs were screened at 4-week intervals.

The rate of S. aureus nasal carriage was 37% for HCWs and 21% for the patients, with 5% and 2% of MRSA respectively. Isolates were defined to be the same subtype if they differed by no more than 40 single-nucleotide variants. Transmissions were defined as an acquisition of a subtype culture from a HCW or the environment either at the same time or at any previous timepoint.

During the period, 97 patient’s acquisition of S. aureus were identified and the transmission source was identified in 25 cases: 7 were from HCWs, 2 from the environment and 16 from other patients. Thus, in 72/97 acquisitions, the source was not identified. The authors concluded that the transmission of S. aureus unlikely came from HCWs.

However, several confounding factors may compromise this finding.

First, an unrecognized HCW intermittent carriage may occur during the 4-week interval between screenings. Of note, in the substudy in which nurses underwent swabbing before and after shifts, no transient carriage was identified.

Second, only two cases of transmission from the environment were identified. Yet, on the 88 strains found in the environment, 51 (57%) were also shared with HCW and/or patients. Transmission from the environment may possibly be underestimated considering the presence of shared rooms.

Third, as only nasal swabs were analyzed, non-nasal or “stealthy” carriage may also explain some unrecognized transmission. However, an overall heterogeneity with multiple different strains was identified during the study without few strains spreading over the ICU. This is in agreement with a cryptic personal carriage of S. aureus which can be developed during the ICU stay.

This study provided very helpful information in the field. However, the external generalizability of the result should be questioned. Indeed, infection control included monthly audits of hand hygiene which may have increased the HCWs compliance with hand hygiene. Furthermore, all patients received skin washes with 4% chlorhexidine solution which may have decreased the patient-to-HCW transmission. Without evaluation of hand-hygiene compliance, no information can be found on which intervention provided this low transmission rate.

Conclusions

In ICU, with a low colonization pressure and good compliance with standard precaution measure, a low rate of HCW-based transmission is highly probable. Thus, additional measures that improve compliance and quality of
hand disinfection might be minimally effective to decrease *S. aureus* cross-transmission and infection.

Future exploration may rely on the transition from colonization to infection. Whole genome sequencing is a valuable tool and could provide information on genetically-related virulence factor. Thereby, the risk of *S. aureus* infection may be stratified considering the association of genetics features of the bacteria and the personal risk of a patient, allowing targeted intervention (32).

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**Footnote**

_Conflicts of Interest:_ The authors have no conflicts of interest to declare.

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