Correspondence

Effect of Colonization with Methicillin-Resistant *Staphylococcus aureus* on Subsequent Infection

Sir—We are indebted to Davis et al. [1] for their valuable study, which strengthens the role of active surveillance. The follow-up period of 12 months is laudable, because infections detected after a patient's discharge from the hospital could also be observed.

One important and very alarming finding in the study [1] is that 2.7%–4.4% of patients in the studied population were infected with methicillin-resistant *Staphylococcus aureus* (MRSA) during their hospitalization, regardless of their colonization status. Also alarming is the higher risk of MRSA infection for noncolonized patients, compared with colonized patients, in the intensive care units of surgical and trauma departments. Only one-third of MRSA infections occurred in patients who were previously colonized with MRSA. Two-thirds of MRSA infections are apparently acquired via transmission. This is a strong argument for the roles of active surveillance, contact isolation precautions, and hand hygiene (the utility of the latter has recently and repeatedly been questioned). A systematic review has shown moderate evidence for a preventive effect of isolation precautions [2], but we postulate that concerted use of these precautions could have prevented, at least partially, the morbidity and mortality associated with 19 MRSA infections reported in Davis et al. [1]. We would like to obtain more information on the use of barrier precautions and hand hygiene in the institution discussed in Davis et al. [1].

There are 4 additional comments that we wish to make. First, the rate of MRSA prevalence is generally defined in the literature as the proportion of all *S. aureus* isolates that are methicillin resistant. Thus, the actual rate of MRSA in the study population would be 15.9% of isolates (26 MRSA isolates out of 163 *S. aureus* isolates), rather than the 3.4% of isolates reported by Davis et al. [1].

Second, the question of whether MRSA is more virulent than methicillin-susceptible *S. aureus* (MSSA) cannot be answered by comparing the incidence rates of MRSA infection in patients who are colonized with either MSSA or MRSA. Ideally, the rate of MSSA infection in patients who are colonized with MSSA would have been compared with the rate of MRSA infection in those who are colonized with MRSA. The latter figure is reported as 19%, but how many patients with MSSA colonization acquire MSSA infection? Wertheim et al. [3] have recently reported a relative risk of 3.0 for MSSA bacteremia in MSSA carriers. A case-case-control study design, as shown by Kaye et al. [4], would answer this question, because risk factors for infection might be different in the 3 groups (MSSA, MRSA, or no colonization).

Third, the use of susceptibility patterns to determine whether MRSA strains are nosocomial or community-acquired strains seems somewhat outdated. Modern molecular techniques for making this determination are available, including PFGE for strain typing and epidemiological analysis [5] and PCR for determination of the *mecA* genetic element and virulence factors associated with community-acquired strains [6]. It is not clear whether the infections in noncolonized patients originate from patients with MRSA colonization or from another source.

Finally, Davis et al. [1] used only swabs of the nares to determine colonization status. Adding cultures of the throat, as is common in epidemiological studies, would have increased the sensitivity of testing [7] and thus changed the statistical significance of the findings.

In conclusion, the findings of Davis et al. [1] are plausible and valuable from a pathogenetic and epidemiologic point of view. Colonization with MRSA clearly leads to infection, but not only in patients who are colonized. Reduction of transmission is the key, and intervention studies are needed. As stated by Cooper et al. [2] in their systematic review evaluating the evidence for barrier precautions: "lack of evidence … should not be mistaken for evidence of lack of effect" [2, p. 538].

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Andreas Tietz, Andrej Trampuz, and Andreas F. Widmer

Division of Infection Control and Hospital Epidemiology, University Hospital Basel, Switzerland

References

1. Davis KA, Stewart JJ, Crouch HK, Florez CE, Hospenthal DR. Methicillin-resistant *Staphylococcus aureus* (MRSA) nares colonization at hospital admission and its effect on subsequent MRSA infection. Clin Infect Dis **2004**; 39: 776–82.
2. Cooper BS, Stone SP, Kibbler CC, et al. Isolation measures in the hospital management of methicillin-resistant *Staphylococcus aureus* (MRSA): systematic review of the literature. BMJ **2004**; 329:533–40.
3. Wertheim HFL, Vos MC, Ott A, et al. Risk and outcome of nosocomial *Staphylococcus aureus* bacteraemia in nasal carriers versus noncarriers. Lancet **2004**; 364:703–5.
4. Kaye KS, Engemann JJ, Mozaffari E, Carmeli Y. Reference group choice and antibiotic resistance outcomes. Emerg Infect Dis **2004**; 10: 1125–8.
5. Tenover FC, Arbeit RD, Goering RV. How to select and interpret molecular strain typing methods for epidemiological studies of bacterial infections: a review for healthcare epidemiologists. Molecular Typing Working Group of the Society for Healthcare Epidemiology of Amer-

ica. Infect Control Hosp Epidemiol **1997**; 18: 426–39.
6. Francois P, Renzi G, Pittet D, et al. A novel multiplex real-time PCR assay for rapid typing of major staphylococcal cassette chromosome *mec* elements. J Clin Microbiol **2004**; 42: 3309–12.
7. Uemura E, Kakinohana S, Higa N, Toma C, Nakasone N. Comparative chracterization of *Staphylococcus aureus* isolates from throats and noses of healthy volunteers. Jpn J Infect Dis **2004**; 57:21–4.

Reprints or correspondence: Dr. Andreas Tietz, Div. of Infection Control and Hospital Epidemiology, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland (atietz@uhbs.ch).

Clinical Infectious Diseases 2005; 40:767–8
 1058-4838/2005/4005-0023$15.00

Reply to Tietz et al.

Sir—We appreciate the comments on our recent article [1] by Tietz et al. [2] and would like to address some of the issues they raise. In accordance with the most recently published guidelines by the Society for Healthcare Epidemiology of America (SHEA) for the prevention of nosocomial transmission of multidrug-resistant *Staphylococcus aureus* [3], patients admitted to our facility who are colonized or infected with methicillin-resistant *S. aureus* (MRSA) are placed in contact isolation, and strict hand hygiene is encouraged of all health care personnel who have contact with patients. Tietz et al. [2] questioned the utility of including samples of the pharynx to increase the sensitivity of testing for MRSA colonization. The findings of previous studies by our group [4, 5] and others [6, 7], in addition to the previously mentioned SHEA guidelines, support the sampling of only the nares to assess for MRSA colonization. On this basis, we are confident that very few subjects who were colonized with MRSA were not identified during our investigation, and we doubt that obtaining samples from multiple sites would have yielded significantly different results.

Tietz et al. [2] point out that two-thirds of the absolute number of MRSA infections occurred in patients who were not colonized with MRSA. Although this is correct, the appropriate evaluation of the data, as we reported [1], is the discordance in the rates of MRSA infection among the different patient populations studied. The incidence of MRSA infection was significantly higher among patients who were colonized with MRSA (19% of colonized patients) than among patients who were not colonized with MRSA (1.9% of non-colonized patients). Furthermore, patients who were found to be colonized with MRSA at admission were more likely to develop infection during the hospitalization in which MRSA colonization was identified than during a future hospitalization. The patients who developed MRSA infection but who were not colonized with MRSA at admission were more likely to develop infection during a future hospitalization. Although our study [1] did not specifically address the question of increased virulence of MRSA compared with that of methicillin-susceptible *S. aureus* (MSSA), there is increasing evidence that community-acquired MRSA may be more virulent. Another recent report by our group [8] demonstrated a higher rate of soft-tissue infection in subjects colonized with community-acquired MRSA, compared with subjects colonized with MSSA or not colonized with *S. aureus.* The findings of that study [8] and others [9] add to the growing evidence that most community-acquired MRSA isolates now express a specific exotoxin, encoded by the Panton-Valentine leukocidin gene, that is likely to be responsible for increased virulence.

The role of MRSA eradication in reducing the rates of subsequent MRSA infection of MRSA-colonized patients and in decreasing the transmission of MRSA in health care facilities needs to be adequately addressed. We are currently pursuing these questions with a randomized, double-blind, placebo-controlled study to determine the effect of topical mupirocin when used to eradicate MRSA colonization of nares identified at admission to the intensive care unit. Our hypothesis is that MRSA eradication will decrease the rate of subsequent MRSA infection in these patients. If true, this would significantly decrease the negative impact that MRSA infection has on hospitalized patients.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Kepler A. Davis and Duane R. Hospenthal

Infectious Disease Service,
Brooke Army Medical Center,
Fort Sam Houston, Texas

References

1. Davis KA, Stewart JJ, Crouch HK, Florez CE, Hospenthal DR. Methicillin-resistant *Staphylococcus aureus* (MRSA) nares colonization at hospital admission and its effect on subsequent MRSA infection. Clin Infect Dis **2004**; 39: 776–82.
2. Tietz A, Trampuz A, Widmer AF. Effect of colonization with methicillin–resistant *Staphylococus aureus* on subsequent infection. Clin Infect Dis **2005**; 40:767–8 (in this issue).
3. Muto CA, Jernigan JA, Ostroswsky BE, et al. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and enterococcus. Infect Control Hosp Epidemiol **2003**; 24:362–86.
4. Kenner J, O'Connor T, Piantanida N, et al. Rates of carriage of methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* in an outpatient population. Infect Control Hosp Epidemiol **2003**; 24:439–44.
5. Fishbain JT, Lee JC, Nguyen HD, et al. Nosocomial transmission of methicillin-resistant *Staphylococcus aureus:* a blinded study to establish baseline acquisition rates. Infect Control Hosp Epidemiol **2003**; 24:415–21.
6. Sanford MD, Widmer AF, Bale MJ, Jones RN, Wenzel RP. Efficient detection and long-term persistence of the carriage of methicillin-resistant *Staphylococcus aureus.* Clin Infect Dis **1994**; 19:1123–8.
7. Papia G, Louie M, Tralla A, Johnson C, Collins V, Simor AE. Screening high-risk patients for methicillin-resistant *Staphylococcus aureus* on admission to the hospital: is it cost effective? Infect Control Hosp Epidemiol **1999**; 20:473–7.
8. Ellis MW, Hospenthal DR, Dooley DP, Gray PJ, Murray CK. Natural history of community-acquired methicillin-resistant *Staphylococcus aureus* colonization and infection in soldiers. Clin Infect Dis **2004**; 39:971–9.
9. Boubaker K, Diebold P, Blanc DS, et al. Panton-Valentine leukocidin and staphylococcal skin infections in schoolchildren. Emerg Infect Dis **2004**; 10:121–4.

The views expressed herein are those of the authors and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the US Government.