Methicillin-resistant *Staphylococcus aureus* transmission: The possible importance of unrecognized health care worker carriage

Debby Ben-David, MD,[a] Leonard A. Mermel, DO, ScM,[a,b] and Steve Parenteau, MS[b]
Providence, Rhode Island

Background: This study was conducted to evaluate the ongoing transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) in a 10-bed trauma intensive care unit (TICU) in a large teaching hospital.
Methods: Surveillance cultures for MRSA were obtained on admission to the TICU. Colonized or infected patients were placed on contact precautions. On February 21, 2003, 19 burn patients were admitted to the TICU after a local mass casualty event. Universal barrier precautions were implemented for all patients, and point-prevalence surveys (nares cultures) were used to detect MRSA acquisition.
Results: During March 2003, 58% of the burn patients developed MRSA infection or colonization. Six of 133 health care workers (HCWs) had positive MRSA screening cultures. Seven patients and 4 HCWs harbored the pulsed-field gel electrophoresis clone A. Two patients and 1 HCW harbored clone B. Once the colonized HCWs were successfully decolonized, a sustained reduction in MRSA infections occurred.
Conclusion: Transmission of MRSA in an ICU was observed despite various infection control precautions. Identifying and treating colonized HCWs was followed by a significant reduction in the incidence of MRSA. Unrecognized MRSA-colonized HCWs may be an important reservoir in endemic institutions that could impair other control measures. (Am J Infect Control 2008;36:93-7.)

MRSA is a major hospital-acquired pathogen that has become endemic in many health care facilities worldwide.[1,2] Several European countries adhere to vigorous infection control policies, including active surveillance cultures for patients and personnel to identify unrecognized colonization, contact precautions, and isolation of patients transferred from other countries [3,4]In contrast, US hospitals had generally adopted previously published Centers for Disease Control and Prevention (CDC) guidelines,[5] with contact precautions for patients colonized or infected with MRSA and no attempt to actively identify unknown, colonized patients.

Several studies have shown that active surveillance leads to a significant and sustained reduction in MRSA acquisition and is cost-effective.[6-10] Consequently, the Society for Health care Epidemiology of America (SHEA) guidelines recommend active surveillance at the time of hospital admission for all patients with high risk of MRSA carriage, as well as periodic screening of patients during hospitalization in high-risk areas, such as intensive care units (ICUs).[11] Nevertheless, cost-benefit analyses and some mathematical models[12,13] have not considered the potential significance of unrecognized, colonized health care workers (HCWs) in endemic institutions unknowingly spreading MRSA despite active surveillance and contact precautions. More recent modeling has included HCW MRSA colonization.[14] During 2003, we identified ongoing MRSA transmission in the unit despite high compliance with obtaining screening cultures on admission. Intensified control measures that were implemented during admission of several burn patients did not prevent new cases. We identified carriage among HCWs and a reduction in the incidence of nosocomial MRSA acquisition after eradicating carriage among colonized staff members.

From the Division of Infectious Diseases,[a] and Department of Epidemiology and Infection Control,[b] Rhode Island Hospital and Department of Medicine, Warren Alpert Medical School of Brown University, Providence, Rhode Island.

Address correspondence to Debby Ben-David, MD, Sheba Medical Center, Tel Hashomer, Israel. E-mail: debby_bendavid@yahoo.com.

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METHODS

Infection control strategies

Rhode Island Hospital is a tertiary-care teaching hospital and level I trauma center licensed for 719 beds. The trauma ICU (TICU) and the surgical step-down unit (SSDU) each have 10 beds. Since 2001, all patients admitted to the TICU are screened on admission for nasal

MRSA colonization. Cultures are obtained within 48 hours of admission. MRSA-colonized or -infected patients are placed in private rooms or cohorted. HCWs don gowns and gloves before entering these rooms. Patients with nares colonization are treated with topical mupirocin applied to the anterior nares twice daily and bathed with an antiseptic agent containing 5% chlorhexidine, both for 5 days. Weekly surveillance screening cultures and discharge screening were not obtained during 2002. All MRSA-positive cultures are routinely characterized as an infection or colonization. Infections are defined using CDC surveillance guidelines.[15]

On the evening of February 21, 2003, a fire broke out in a Rhode Island nightclub. A total of 180 people were transferred to nearby hospitals. Nineteen burn patients were admitted to the TICU and the SSDU, creating a large, ad hoc burn unit. All previously admitted patients were transferred to other units before the first burn patient was admitted to the unit. During the hospitalization of these burn patients, additional infection control measures were put into practice; after 72 hours of admission, gowns and gloves were required to enter all patient rooms, and nares cultures for MRSA were obtained every 3 to 5 days until April 1, 2003, by which time most of the burn patients had been discharged.

Laboratory methods

A specimen from the anterior nares was obtained using a dry culturettte swab (BD Microbiology Systems, Cockeysville, MD). Hands were cultured using a modified glove juice method.[16] Cultures were inoculated on CNA agar plates and incubated at 35°C for 48 hours. Isolates were identified as *Staphylococcus aureus* on the basis of colony morphology and a Staphaurex test (Med-Ox Diagnostics, Ogdensburg, NY). Isolates were determined to be oxacillin-resistant if they grew on Mueller-Hinton agar containing 6 μg/mL of oxacillin.

Genotypic analysis

Molecular typing was conducted using pulsed-field gel electrophoresis (PFGE) as described previously.[17] Restriction digestion was performed with *SmaI*, and restriction fragments were separated in a CHEF-DRII system (Bio-Rad, Hercules, CA). Analysis of DNA fragments was conducted using both visual inspection and Bio-Rad software. Strain relatedness was interpreted according to published guidelines.[18]

RESULTS

MRSA transmission in burn patients, February to March 2003

The average age of the 19 burn patients admitted to the Rhode Island Hospital's ad hoc burn unit was 33.7 years (range, 21 to 43 years). None of the patients had been previously hospitalized for other illnesses. Sixteen of 19 patients were mechanically ventilated due to lung injury. Burn injuries involved up to 30% of the total body surface area. The average length stay of the burn patients in the TICU and SSDU was 21 days (range, 3 to 70 days). During their stay in these units, the cost for gloves and gowns was $8990, compared with the previous average monthly cost of $4150. Compliance with obtaining surveillance cultures during this time was 100%. Surveillance cultures on admission were negative for MRSA. The first patient with an MRSA infection was detected on the sixth hospital day. During the second week, 5 patients developed MRSA colonization and 3 developed MRSA infections. During the third and fourth weeks, 1 additional patient developed MRSA infection and another developed MRSA colonization (Fig 1). After 30 days, 11 of the 19 burn patients (58%) had acquired MRSA, including 3 ventilator-associated pneumonias and 2 bloodstream infections.

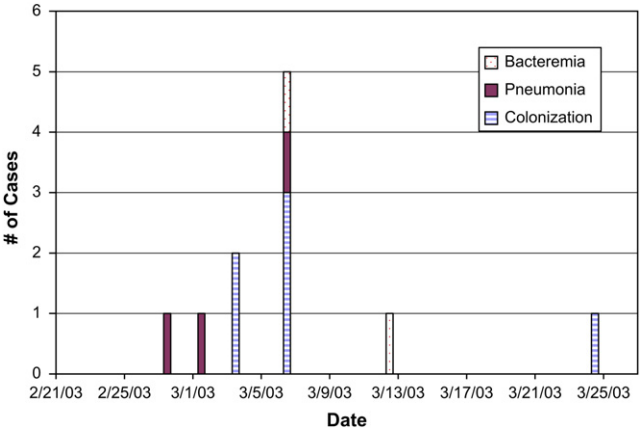

Fig 1. MRSA acquisition in burn patients, February to March 2003.

During the third week, surveillance cultures of the anterior nares and hands were obtained from 133 HCWs, including nurses, physicians, respiratory therapists, and occupational therapists who had worked in the TICU or SSDU over the previous 3 weeks. Six HCWs (4%; 5 nurses and 1 respiratory therapist) were colonized with MRSA. The hands of 2 of the 5 HCWs with nares colonization also grew MRSA. One HCW had a negative nares culture and a positive culture of the hands for MRSA. Colonized HCWs were treated with nasal mupirocin and chlorhexidine showers for 5 days. Follow-up nares cultures performed both 4 weeks and 3 months after the final dose of nasal mupirocin were negative.

MRSA transmission in the TICU

After the discharge of all burn patients, point-prevalence surveys of patients for MRSA were discontinued.

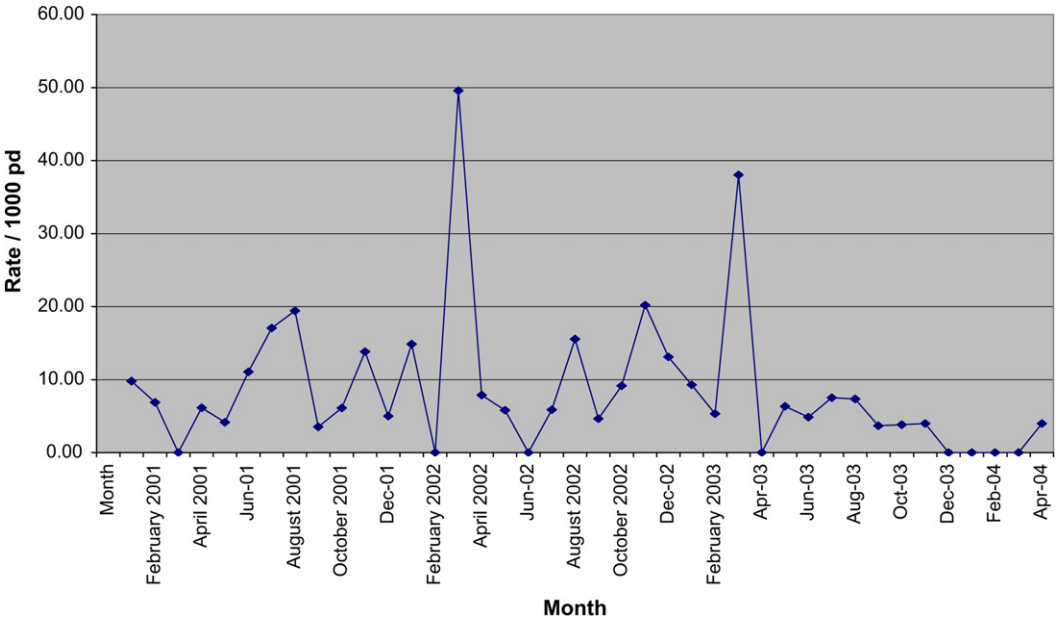

Fig 2. MRSA infection or colonization per 1000 patient-days in the TICU between April 2001 and April 2004. HCWs were screened during 2 periods of increased incidence (March 2002 and March 2003).

Nosocomial MRSA colonization and infection decreased from 10.2 per 1000 patient-days (April 2002 to February 2003) to 3.2 per 1000 patient-days (exact binomial test, $P < .001$) during the subsequent year (April 2003 to March 2004), as shown in Figure 2.

Molecular typing

PFGE identified 5 banding patterns among the isolates from the patients and HCWs (Fig 3). Seven patients and 4 HCWs had clone A, 2 patients and 1 HCW had clone B, and 2 patients and 1 HCW harbored 3 unrelated clones. Comparison with isolates obtained from patients in the TICU and SSDU during 2001–2002 showed that clones A and B were predominant; of the 31 isolates, 20 were clone B and 4 were clone A. A colonized HCW from the TICU identified during March 2002 was clone B.

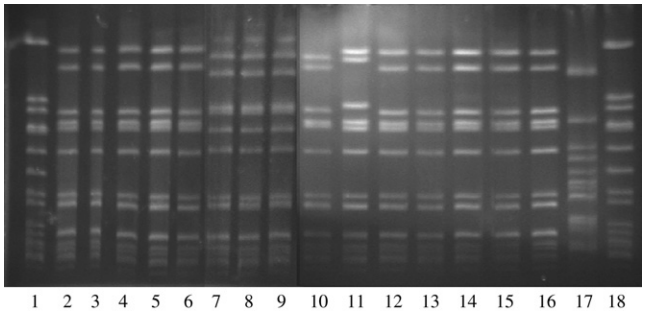

Fig 3. PFGE of MRSA strains from the outbreak in the burn patients admitted to the TICU during February 2003. Lanes 1 and 18: molecular-size ladder. Lanes 2 to 4: isolates obtained from HCWs 1 to 3, clone A. Lanes 5, 6, and 12 to 16: isolates obtained from patients 1 to 7, clone A. Lane 7: HCW 4, clone B. Lanes 8 and 9: patients 8 and 9, clone B. Lane 10: HCW 5, clone C. Lane 11: patient 10, clone D. Lane 17, patient 11: clone E.

DISCUSSION

A major impediment to MRSA control is the potential reservoir of patients who have unrecognized MRSA colonization. Active surveillance of high-risk patients is an integral component in successful infection control programs, as recently emphasized in the SHEA recommendations.[11] Many hospitals have recently implemented active surveillance to identify MRSA-colonized patients; however, ongoing MRSA transmission may persist in endemic institutions despite an active surveillance program. There are several possible explanations for ongoing nosocomial MRSA transmission, including poor compliance with obtaining surveillance cultures, unscreened patients who are not included in the local definitions of high-risk patients, low adherence with contact precautions, poor hand hygiene compliance, transmission of MRSA during the 72 hours before colonized patients are identified and isolated, a lack of point-prevalence surveys to detect MRSA carriage after admission, and insufficient measures to clean the contaminated environment. Thus, when evaluating ongoing MRSA transmission in a unit or institution, several

hypotheses must be considered and reviewed. Our experience demonstrates that despite active surveillance cultures on admission, frequent point-prevalence surveillance cultures, and use of reverse-isolation, MRSA transmission still may occur from unrecognized, colonized HCWs to high-risk patients.

Several reports have described prolonged MRSA transmission associated with colonized HCWs, and successful control was demonstrated only after these colonized HCWs were identified.[19-21] In a neonatal ICU, ongoing MRSA transmission has been observed despite contact precautions, weekly surveillance cultures, cohorting patients and staff, universal glove use, universal bathing with hexachlorephene, and topical mupirocin use.[21] A total of 235 HCWs were screened for MRSA, and 3 were found to be colonized with an MRSA strain identical to that of the patients. The outbreak was contained after the colonized HCWs were identified and MRSA carriage was eradicated.

During March 2003, reverse-isolation was used for all of the burn patients admitted to the unit. Reverse-isolation is used in many burn units to prevent transmission of multidrug-resistant pathogens,[22] and has led to decreased MRSA acquisition for a prolonged period in a burn unit.[23] However, reverse-isolation may fail to prevent MRSA transmission in the presence of colonized HCWs[20,21] or from contaminated environmental reservoirs.[24]

Routine screening of HCWs is associated with high cost, possible stigmatization of the colonized HCWs, and uncertain benefit. There is no consensus regarding the best time to screen HCWs. Some institutions screen HCWs periodically or after each exposure to colonized or infected patients[25,26]; in contrast, other reports suggest that screening HCWs has a low yield and a limited role in the control of outbreaks.[27,28] Some authors have recommended screening HCWs only as a last resort after all other interventions have failed to prevent MRSA transmission.[6] The CDC has recommended culturing personnel who are implicated as the source of MRSA transmission based on epidemiologic data.[29] Other guidelines recommend screening HCWs if there is ongoing MRSA transmission despite active surveillance,[30,31] much as we have done in our outbreak investigation. Colonized HCWs are most often transiently colonized, but they may become persistent carriers if they have skin lesions, leading to prolonged MRSA transmission. Finding an MRSA-colonized HCW associated with colonized or infected patients does not establish the directionality of transmission. Nevertheless, none of the burn patients was colonized on admission, suggesting that the HCWs did not initially acquire MRSA from these patients.

In endemic settings, it is difficult to determine whether ongoing MRSA transmission is secondary to multiple introductions of different clones or to the spread of 1 or 2 endemic clones. Molecular subtyping of MRSA isolates is helpful in elucidating potential routes of transmission; however, the optimum time to carry out such an analysis in endemic settings is not well defined. We perform molecular typing only when there is a cluster of several cases in the same unit.

The interpretation of molecular subtyping results is multifaceted. The presence of a single clone may suggest indirect spread from a single patient to other patients by hands of transiently colonized HCWs, direct spread from persistently colonized HCWs, or spread from contaminated environmental reservoirs. Indeed, several outbreak investigations suggesting clonal spread have failed to identify colonized HCWs.[27,28] Our findings demonstrate that the presence of multiple clones in a single unit where MRSA is endemic may reflect ongoing transmission involving HCWs colonized with different strains.

We investigated a cluster of nosocomial MRSA in our TICU during March 2002. We only screened HCWs working in the TICU, not those working in the SSDU. One colonized HCW was identified and treated. Yet ongoing MRSA transmission continued. Many patients are transferred between the TICU and SSDU, and they may have been exposed to a colonized HCW in the SSDU. A significant decrease in MRSA transmission was found once we screened large numbers of HCWs in the 2 units during our 2003 investigation, when we eradicated carriage among colonized HCWs. This may have contributed to prolonged reduction in the incidence of nosocomial MRSA in these units.

Our study has a number of limitations. We did not obtain surveillance cultures from burn wounds, and *S. aureus* can colonize extensive body surface areas in burn patients.[32] Thus, patients with colonized wounds may have transmitted MRSA to other patients. MRSA may spread in burn units by the airborne route or on contaminated surfaces and fomites.[33,34] We obtained only a limited number of environmental cultures, so we cannot exclude a possible role of airborne transmission or environmental contamination in ongoing MRSA transmission. We did not obtain cultures from the topical antimicrobial agents used; however, these agents are not multipatient use items and thus are unlikely to play a role in cross-transmission. Some clusters of nosocomial infection in other burn units have been associated with hydrotherapy, but hydrotherapy was not used in our patients. In addition, we did not measure HCWs' compliance with reverse-isolation and hand hygiene. However, infection control professionals were present daily in the unit during the burn patients' stay. Breaches in control measures were discussed with staff. Transmission may have occurred

during the first 72 hours of admission; yet none of the patients were colonized on admission.

In conclusion, we have described prolonged MRSA transmission in a TICU despite active surveillance. A significant and persistent reduction in MRSA transmission occurred only after colonized HCWs were detected and successfully decolonized, while active surveillance was continuing on admission. In many endemic institutions, colonized HCWs may be a substantial, unrecognized reservoir, limiting the success of other control measures. Evidence-based guidelines for MRSA screening of HCWs are needed for hospitals with endemic and epidemic MRSA.

References

1. Fluit AC, Wielders CL, Verhoef J, Schmitz FJ. Epidemiology and susceptibility of 3051 *Staphylococcus aureus* isolates from 25 university hospitals participating in the European SENTRY study. J Clin Microbiol 2001;39:3727-32.
2. Diekema DJ, Boots Miller BJ, Vaughn TE, et al. Antimicrobial resistance trends and outbreak frequency in United States hospitals. Clin Infect Dis 2004;38:78-85.
3. Vandenbrouck-Grauls CM. Methicillin-resistant *Staphylococcus aureus* control in hospitals: the Dutch experience. Infect Control Hosp Epidemiol 1996;17:512-3.
4. Rosdahl VT, Knudsen AM. The decline of methicillin resistance among Danish *Staphylococcus aureus* strains. Infect Control Hosp Epidemiol 1991;12:83-8.
5. Garner JS, and the Hospital Infection Control Practices Advisory Committee. Guidelines for isolation precautions in hospitals. Infect Control Hosp Epidemiol 1996;17:53-80.
6. Hartstein AI, Denny MA, Morthland VH, LeMonte AM, Pfaller MA. Control of methicillin-resistant *Staphylococcus aureus* in a hospital and an intensive care unit. Infect Control Hosp Epidemiol 1995;16:405-11.
7. Jernigan JA, Clemence MA, Stott GA, Titus GA, Alexander CH, Palumbo CM, et al. Control of methicillin-resistant *Staphylococcus aureus* at a university hospital: one decade later. Infect Control Hosp Epidemiol 1995;16:686-96.
8. Girou E, Pujade G, Legrand P, Cizeau F, Brun-Buisson C. Selective screening of carriers for control of methicillin-resistant *Staphylococcus aureus* (MRSA) in high-risk hospital areas with a high level of endemic MRSA. Clin Infect Dis 1998;27:543-50.
9. Chaix C, Durand-Zaleski I, Alberti C, Brun-Buisson C. Control of endemic methicillin-resistant *Staphylococcus aureus*: a cost-benefit analysis in an intensive care unit. JAMA 1999;282:1745-51.
10. 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.
11. Muto CA, Jernigan JA, Ostrowsky BE, Richet HM, Jarvis WR, Boyce JM, 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.
12. Sebille V, Chevret S, Valleron AJ. Modeling the spread of resistant nosocomial pathogens in an intensive-care unit. Infect Control Hosp Epidemiol 1997;18:84-92.
13. Cooper BS, Medley GF, Scott GM. Preliminary analysis of the transmission dynamics of nosocomial infections: stochastic and management effects. J Hosp Infect 1999;43:131-47.
14. Bootsma MCJ, Diekmann O, Bonten MJ. Controlling methicillin-resistant *Staphylococcus aureus*: quantifying the effects of interventions and rapid diagnostic testing. Proc Natl Acad Sci 2006;103:5620-5.
15. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections. Am J Infect Control 1988;16:128-40.
16. Larson EL, Hughes CA, Pyrek JD, Sparks SM, Cagatay EU, Bartkus JM. Changes in bacterial flora associated with skin damage on hands of health care personnel. Am J Infect Control 1998;26:513-21.
17. McDougal LK, Steward CD, Killgore GE, Chaitram JM, McAllister SK, Tenover FC. Pulsed-field gel electrophoresis typing of oxacillin-resistant *Staphylococcus aureus* isolates from the United States: establishing a national database. J Clin Microbiol 2003;41:5113-20.
18. Tenover FC, Arbeit RD, Goering RV, Mickelsen PA, Murray BE, Persing DH, et al. Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. J Clin Microbiol 1995;33:2233-9.
19. Boyce JM, Opal SM, Potter-Bynoe G, Medeiros AA. Spread of methicillin-resistant *Staphylococcus aureus* in a hospital after exposure to a health care worker with chronic sinusitis. Clin Infect Dis 1993;17:496-504.
20. Meier PA, Carter CD, Wallace SE, Hollis RJ, Pfaller MA, Herwaldt LA. A prolonged outbreak of methicillin-resistant *Staphylococcus aureus* in the burn unit of a tertiary medical center. Infect Control Hosp Epidemiol 1996;17:798-802.
21. Saiman L, Cronquist A, Wu F, Zhou J, Rubenstein D, Eisner W, et al. An outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. Infect Control Hosp Epidemiol 2003;24:317-21.
22. Lee JJ, Marvin JA, Heimbach DM, Grube BJ, Engrav LH. Infection control in a burn center. J Burn Care Rehabil 1990;11:575-80.
23. Safdar N, Marx J, Meyer NA, Maki DG. Effectiveness of preemptive barrier precautions in controlling nosocomial colonization and infection by methicillin-resistant Staphylococcus aureus in a burn unit. Am J Infect Control 2006;34:476-83.
24. Huang SS, Datta R, Platt R. Risk of acquiring antibiotic-resistant bacteria from prior room occupants. Arch Intern Med 2006;166:1945-51.
25. Blok HE, Troelstra A, Kamp-Hopmans TE, Gigengack-Baars AC, Vandenbroucke-Grauls CM, Weersink AJ, et al. Role of healthcare workers in outbreaks of methicillin-resistant *Staphylococcus aureus*: a 10-year evaluation from a Dutch university hospital. Infect Control Hosp Epidemiol 2003;24:679-85.
26. Tomic V, Svetina Soril P, Trinkaus D, Sorli J, Widmer AF, Trampuz A. Comprehensive strategy to prevent nosocomial spread of methicillin-resistant *Staphylococcus aureus* in a highly endemic setting. Arch Intern Med 2004;164:2038-43.
27. Cox RA, Conquest C. Strategies for the management of healthcare staff colonized with epidemic methicillin-resistant *Staphylococcus aureus*. J Hosp Infect 1997;35:117-27.
28. Bowler I. Strategies for the management of healthcare staff colonized with epidemic methicillin-resistant *Staphylococcus aureus*. J Hosp Infect 1997;36:321-2.
29. Siegel JD, Rhinehart E, Jackson M, Chiarello L and the Healthcare Infection Control Practices Advisory Committee. Management of multidrug-resistant organisms in healthcare settings. Available at: http://www.cdc.gov/ncidod/dhqp/pdf/ar/MDROGuideline2006.pdf. Accessed October 27, 2007.
30. Kluytmans-VandenBergh MFQ, Kluytmans JAJW, Voss A. Dutch guideline for preventing nosocomial transmission of highly resistant microorganisms. Infection 2005;33:309-13.
31. Coia JE, Duckworth GJ, Edwards DI, Farrington M, Fry C, Humphreys H, et al. Guidelines for the control and prevention of methicillin-resistant *Staphylococcus aureus* in healthcare facilities. J Hosp Infect 2006;63S:S1-44.
32. Heggers JP, Phillips LG, Boertman JA, Carethers J, Weingarten M, Lentz CW, et al. The epidemiology of methicillin-resistant *Staphylococcus aureus* in a burn center. J Burn Care Rehabil 1988;9:610-2.
33. Farrington M, Ling J, Ling T, French GL. Outbreaks of infection with methicillin-resistant *Staphylococcus aureus* on neonatal and burns units of a new hospital. Epidemiol Infect 1990;105:215-28.
34. Embil JM, McLeod JA, Al-Barrak AM, Thompson GM, Aoki FY, Witwicki EJ, et al. An outbreak of methicillin-resistant *Staphylococcus aureus* on a burn unit: potential role of contaminated hydrotherapy equipment. Burns 2001;27:681-8.