Journal of Hospital Infection (2005) **59**, 180–187

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Bed, bath and beyond: pitfalls in prompt eradication of methicillin-resistant *Staphylococcus aureus* carrier status in healthcare workers

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Received 19 March 2003; accepted 2 June 2004

Available online 1 October 2004

KEYWORDS
Methicillin-resistant *Staphylococcus aureus* (MRSA); Staff; Eradication treatment; Household contamination

Summary Healthcare workers (HCWs) in close contact with patients colonized with methicillin-resistant *Staphylococcus aureus* (MRSA) were screened for MRSA acquisition. From 1995 to 2001, MRSA was identified from the nasopharyngeal swabs of 87 HCWs, collected one to two weeks after contact with 592 known MRSA-positive patients. These HCWs were withdrawn from work and treated with topical antibiotics/antiseptics. They were advised to disinfect their bathrooms and personal hygiene articles, and to wash bed linen and pillows. They were screened for successful eradication for up to three months. Seventy-three (84%) HCWs lost their carrier status. The eradication regimen failed in 14 cases. In 11 of these MRSA was detected only in later nasopharyngeal swabs (suspected recolonization). Screening identified nasal colonization of close household contacts in eight of these 11 cases. Environmental sampling detected contamination in seven out of eight screened home environments. When eradication treatment was applied to household contacts and when household surfaces were cleaned and disinfected, the carriage cleared in most cases within a few weeks. However, when home environments are heavily contaminated, despite adequate medical treatment, eradication took upto two years. Due to withdrawal from work, the 14 carriers without prompt and lasting eradication after the first course of treatment accounted for about 70% of all lost working days. These experiences support the hypothesis that control measures should not be restricted to antibiotic or antiseptic treatment of long-term carriers (HCWs as well as patients), but must also include cleaning and disinfection of the household.

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0195-6701/$ - see front matter
doi:10.1016/j.jhin.2004.06.016

Introduction

Epidemiological investigations of hospital outbreaks have demonstrated that colonized healthcare workers (HCWs) may be involved in the transmission of methicillin-resistant *Staphylococcus aureus* (MRSA), and may be capable of initiating or maintaining outbreaks.[1-10] Therefore, several national guidelines have recommended eradication of MRSA in HCWs by appropriate treatment, sometimes in selected circumstances,[11-13] and withdrawing them from patient contact until eradication treatment has been commenced for at least 48 h[13] or proved to be successful.[11]

Few reports exist on long-term issues of eradication regimens in HCWs, especially from sporadic cases where (by definition) an outbreak had not (yet) occurred. This paper reports our experience of MRSA eradication in HCWs whose carriage was detected within one to two weeks of close contact with (mainly) sporadic carriers of MRSA.

Materials and methods

Clinical setting

The study was performed in two tertiary-care hospitals (1500 and 100 beds) in South-west Germany. In accordance with national guidelines,[11] patients known to carry MRSA are located in private rooms under isolation precautions. Patients are screened for nasopharyngeal MRSA carriage if they have a history of MRSA carriage, on being admitted to the intensive care unit, when being transferred from other hospitals or residential homes, or after contact with other MRSA carriers. While increasing, the rate of recognized MRSA carriers among patients is still under 0.5%.

Screening of HCWs

From 01/01/1995 to 31/12/2001, 592 patients (out of a total of about 350 000 patients) were found to harbour MRSA, either from diagnostic clinical or screening specimens. Within one to two weeks of close contact with these patients, HCWs were screened for carriage/acquisition of MRSA by a single nasal swab, collected themselves.

Eradication regimen and confirmation of MRSA carriage

When nasal carriage was diagnosed, the HCW was withdrawn from work for five days and the following treatment was initiated: mupirocin nasal ointment three times a day, tyrothricin lozenges[14] or chlorhexidine mouth rinse up to five times a day, and antiseptic soap for whole body washing (douche) each day, for five days. In a leaflet, the HCW was advised to change and wash their bed linen and pillow at least every other day, to discard possibly contaminated personal hygiene articles, and to clean and disinfect household surfaces, especially in the bathroom, using a household disinfectant.

When possible, in order to confirm MRSA carriage, another set of nasal and pharyngeal swabs was collected by the infection control team before eradication treatment was commenced, i.e. two to four days after the initial positive specimen was taken.

Follow-up

Nasal and pharyngeal swabs were repeated three days, 10 days, one month and three months after treatment; swabs from other body regions were collected if clinically indicated. The HCWs were readmitted to work but if the follow-up swabs resulted in MRSA-positive findings, they were withdrawn from work again and the eradication treatment was repeated. Modifications of treatment, e.g. administration of systemic antibiotics, were made where appropriate, e.g. when genital and/or rectal colonization was found.

Screening of household contacts and environmental sampling

When eradication failed, screening of household contacts (including pets) was offered and performed as described above. Carriage among household contacts was confirmed and eradication was initiated as described above.

When eradication failed, a household inspection and environmental sampling by the infection control team was offered to the HCW. Environmental samples (contact plates, swabs) were collected from potentially contaminated surfaces: bed, bath, room textiles (carpets, sofa), hand-contact surfaces (phone, mobile phone, light switch, television remote set, television and tuner switches) and from special items identified as potential contact surfaces by discussion between the HCW and the infection control team. In addition, household dust samples were collected using a standard vacuum cleaner and a standard paper bag, where appropriate.

Microbiological procedures

MRSA from human samples was detected using standard microbiological methods, including broth enrichment. Surfaces were investigated by contact plates filled with a non-selective agar medium; from 2001, oxacillin resistance screen agar contact plates (ORSAB agar; Oxoid, Wesel, Germany) were used. Environmental swabs as well as several aliquots of dust were enriched in casein soy broth and cultured on Columbia agar; from 2001, they were cultured on ORSAB agar. Species was confirmed using API 20 Staph or ATB ID 32 Staph (bioMérieux, Marcy l'Etoile, France), and oxacillin resistance was confirmed by the National Committee for Clinical Laboratory Standard's swab method[15] using Mueller-Hinton agar supplemented with 4 mg/mL NaCl and 6 μg/mL oxacillin.

Typing of MRSA isolates

MIRSA isolates were typed by antibiotyping. When epidemiologically indicated, strains were typed by in-house pulsed-field gel electrophoresis (PFGE) using standard protocols, or were sent to the National Reference Centre (Prof. Dr. Witte, Robert-Koch-Institute, Wernigerode, Germany) for PFGE and phage typing. When PFGE types of isolates were compared, 16 different patterns were observed and the most predominant pattern accounted for 42% of isolates.

Results

From 01/01/1995 to 31/12/2001, 87 HCWs were found with nasal MRSA: 70 nurses; five physicians; four members of room and patient transportation services; two laboratory technicians; and one physiotherapist. Five nurses had been colonized by obviously epidemiologically unrelated MRSA twice at different times; these events were counted as separate colonizations. Pre-treatment confirmatory swabs were collected from 58 HCWs; in 47 of these cases (81%), MRSA carriage was confirmed.

In all 87 cases, eradication treatment was initiated and follow-up was performed as described. The full follow-up time of at least three months was completed in 72 cases; in total, 78 individuals were followed-up for at least one month.

Seventy-three of 87 (84%) HCWs responded with prompt and definite eradication of their carrier status (negative results in all follow-up swabs). Pitfalls in eradication were observed in 14 HCWs (Table I); all further data refer to these cases.

An immediate failure of eradication (i.e. positive swab three days after treatment) was observed in three cases. Two failures were obviously due to non-compliance with the eradication regimen (No. 13) or complicating psoriasis (No. 14). When eradication treatment was repeated and intensified, prompt and definite eradication was achieved in both cases. In the third case (No. 2), massive environmental home contamination was found. In the remaining 11 HCWs, MRSA carriage recurred after initial nasopharyngeal swabs had been negative (see Table I for the MRSA-negative interval after the end of the treatment, as determined by negative swab results).

Screening of close household contacts revealed colonization of eight of 11 carriers (Table I). Among the HCWs with recurrent carriage, four were found to be related with regard to households (No. 1/No. 2, No. 11/No. 12: see Case Reports).

In seven of eight screened environments, MRSA was detected. In most cases, contamination was restricted to some transmission-relevant items (Table I); however, heavy contamination was found in the home environment of the four household-related individuals (No. 1/No. 2 and No. 11/No. 12).

When eradication treatment had also been applied to household contacts, and when household surfaces had been cleaned and disinfected, eradication was achieved in most recolonized carriers within a few weeks. However, in the case of heavily contaminated homes, eradication may take a long time to achieve (more than two years) and may require additional measures (see Case Reports).

From 1995 to 2001, the indirect cost of workload, as expressed by loss of work because of withdrawal, was about 1050 days, resulting in about 1.8 lost working days per MRSA patient. Whereas HCWs with prompt and definite eradication each caused a loss of about four days of work, resulting in about 300 days of lost work in total (0.5 lost working days per MRSA patient), failed eradication caused about 750 lost working days (1.3 lost working days per MRSA patient), i.e. these 16% of cases were responsible for about 70% of lost work.

However, at least for three HCWs, recurrent carriage was documented as the source of MRSA transmission to patients and other HCWs (Table I).

Case reports

Cases are summarized in Table I.

Table I MRSA-free swabs and MRSA-free interval; conditions, results of screening of household contacts and household environment, eradication treatment, decontamination process and evidence of transmission to other patients and/or HCWs in 14 cases of initially refractory or recurrent MRSA nasopharyngeal carriage among HCWs

Case no.	MRSA-free swabs[a]	MRSA-free interval[b]	Occupation	Conditions other than household contamination possibly contributing to initial eradication failure	Nasal carriage of household contacts identified	Contaminated sites identified by environmental investigation	Eradication treatment (in addition to repeated standard regimen)	Decontamination process (in addition to repeated standard regimen)	Clinical history and colonization status after simultaneous treatment of cases and contacts as well as household decontamination	Evidence of transmission to patients and/or other HCWs[c] (after first eradication; despite control measures)
1	2	7d–1m	Nurse	Vaginal carriage	Mother (No. 2), father, friends	Virtually all items and surfaces in living and bed room, incl. house dust	+Oral rifampicin + povidone-iodine vaginal suppositories	Disinfectant (quaternary ammonium base); steam cleaning; later: formaldehyde vapour, renewal of wallpaper and floors	Eight recurrent episodes during 2.5 y; eventual successful clearance with 1.5 y follow-up	At least two incidents: to one patient; to two HCWs
2	0	3d	Technician	-	Daughter (No. 1), spouse	Surfaces in household working room; clothes basket	+Oral rifampicin		Initially refractory carriage and relapse during 3 m; eventual successful clearance	-
3	2	7d–14d	Nurse	-	No contacts screened	Not investigated	-	-	One recurrent episode during 1 m; eventual successful clearance	-
4	2	2m–3m	Nurse	-	Spouse	Not investigated	-	-	One recurrent episode during 3 m; eventual successful clearance	-
5	2	1m–2m	Nurse	-	Spouse, daughter	Not identified	-	-	One recurrent episode during 2 m; eventual successful clearance	-
6	3	16d–1m	Nurse	-	Not identified	Not investigated	-	-	One recurrent episode during 1 m; eventual successful clearance	-
7	1	3d–2y[d]	Nurse	-	Spouse	Not investigated	-	-	One recurrent episode during 2 y; eventual successful clearance	-
8	3	20d–2m	Room server (laundry supply)	-	Not identified	Sportswear: helmet and gumshield	-	Disinfectant (quaternary ammonium base)	One recurrent episode during 2 m; eventual successful clearance	-
9	2	1m–5m	ICU nurse	-	Spouse	Electrical switches; pillows; hand-held computer	-	Disinfectant (quaternary ammonium base)	One recurrent episode during 6 m; eventual successful clearance	-
10	4	2m–4m	Surgeon	-	Not identified	Seat; inside summer shoes, unworn for 4 months; razor	-	Disinfectant (quaternary ammonium base)	Two recurrent episodes during 6 m; eventual successful clearance	At least to one patient
11	12	4m–5m	Nurse	Axillary hidradenitis suppurativa, infected by MRSA; genital carriage	Partner (No. 12), son	Biker's leather clothes	+Oral fusidic acid + oral rifampicin + topical tetracycline	Disinfectant (quaternary ammonium base, formaldehyde); later on: formaldehyde vapour, renewal of wallpaper and floors	Up to now six recurrent episodes during 2.5 y; no lasting clearance until end of 2003	At least to three patients
12	1	3d–10d	Nurse	Intermittent vaginal and rectal carriage	Partner (No. 11), son	Bed; carpets; couch; electric switches; toilet tank; breastfeeding pillow; baby changing table; inside shoes; kitchen surfaces	+Povidone-iodine vaginal suppositories		Up to now at least four recurrent episodes during 2.5 y; no lasting clearance until end of 2003	(Suspended her work)
13	0	3d	Nurse	Weak compliance to treatment regimen	No contacts screened	Not investigated	-	-	Initially refractory carriage; successful clearance	-
14	0	3d	Physician	Psoriasis	No contacts screened	Not investigated	-	-	Initially refractory carriage; successful clearance	-

d, day; m, month; y, year; HCWs, healthcare workers; MRSA, methicillin-resistant *Staphylococcus aureus*.

[a] Number of swab collections after initial eradication treatment completed.

[b] Last negative—first positive swab after initial eradication treatment completed.

[c] Not systematically investigated in this study.

[d] Regular follow-up not completed as the nurse was not engaged any more; found positive for an indistinguishable strain when re-engaged about two years later.

Cases No. 1 and No. 2

In February 1997, No. 1 was found to carry an MRSA strain that was indistinguishable from that of a patient she had cared for. After eradication treatment, she proved to be recolonized by the same strain one month later. Cross-contamination by other staff or patients was excluded. Eradication treatment was repeated and further control swabs were negative. In September 1997, however, a patient acquired a strain indistinguishable from that of No. 1, and No. 1 tested positive again.

In October 1997, No. 1's mother (No. 2), who worked in another department, was screened because of contact with another patient. No. 2's strain proved to be different from that of the contact patient, but indistinguishable from No. 1's strain. No. 1 and No. 2 lived in the same house and shared some rooms. MRSA was identified from dust specimens and virtually all surfaces of No. 1's room, as well as in adjacent rooms, including No. 2's utility room.

In November 1997, after the house had been cleaned intensively with a standard disinfectant, nasopharyngeal control swabs repeatedly tested negative. However, in December 1997, No. 1 and No. 2 were found to be positive again with the same mupirocin- and rifampicin-sensitive strain, indicating recolonization from the environment rather than unsuccessful eradication, as both received oral rifampin prophylactically during cleaning. Specimens from No. 1's rooms were heavily contaminated. All surfaces and movable items were disinfected by the hospital disinfection team, and both received standard eradication treatment plus oral rifampicin.

No. 2 remained negative from this point onwards, but in January 1998, No. 1 was retested as MRSA positive (rifampicin- and mupirocin-sensitive) by nasopharyngeal as well as vaginal swabs. In addition, vaginal povidone-iodine suppositories were administered.

In March 1998, after two months of negative weekly swabs, No. 1 tested positive again. Screening of co-workers, all of whom had tested negative previously, revealed transmission to two colleagues and to the hospital environment (nursing office, nursing items, No. 1's locker). No. 1's private rooms were contaminated again. The rooms were sanitized by formaldehyde vapour, and carpets and wallpaper were replaced. Meanwhile, No. 1 stayed outside her private environment and all nasal and pharyngeal swabs, taken twice a week, tested negative for more than two months.

At the end of October 1998, when No. 1 had returned home, nasal swabs were found to be positive again. During the following year, periods of about one to two months when nasopharyngeal swabs were negative were interrupted by positive findings from either nose or throat. In vitro sensitivity of the strain was unchanged and other regimens were attempted without lasting success. In September 1999, the last positive finding was obtained and swabs have stayed negative since.

Cases No. 11 and No. 12

These two HCWs were working in different wards of the hospital until the delivery of their son in April 2002 when the woman (No. 12) decided to suspend her work. In June 2001, No. 12 and No. 11 were screened independently after caring for MRSA-positive patients and were found to be colonized in their nares by the same strain. Both had been found to be negative during previous screenings.

The history of eradication attempts and failures in No. 11 and No. 12 and the contribution of environmental contamination resembles No. 1 and No. 2, but was complicated by some factors: intensive interactions between two, and subsequently, three colonized individuals; restrictions of aggressive eradication treatment due to pregnancy and MRSA carriage of the baby; a history of axillary hidradenitis suppurativa infected by MRSA in the man (No. 11); and subsequent contamination of four households.

Despite multiple eradication and decontamination efforts, the recurrent carriage in all three individuals did not clear until mid 2003, i.e. two years after the first report of MRSA carriage. Further architectural sanitation was performed in late 2003.

Discussion

Unlike in MRSA-colonized patients, where failures of eradication are frequent, eradication treatment of MRSA-colonized HCWs seems to be effective and failures in eradication are less common. In our series of 87 colonized HCWs, prompt and definite eradication was achieved by standard eradication treatment in 84% of cases. Since confirmatory swabs, taken a few days after the initial positive swab and before eradication treatment began, had been negative in 19% of cases and follow-up swabs were not positive in any of them, one might speculate whether the presumably short carriage might have been 'transient' or 'short term'[16] and would have been lost even without any treatment in

some cases.[17] However, in about 16% of all cases, we observed failure of prompt eradication. From the viewpoint of cost due to loss of work, these were responsible for about 70% of lost working days.

Failures eradication are often discussed with regard to suspected inappropriate or ineffective use or choice of antiseptics/antibiotics, as effectiveness of eradication treatment has mainly been judged two to seven days after treatment.[18] Regardless of the chosen antiseptics/antibiotics, this might be particularly true when eradication treatment focuses solely on the application of nasal ointment, therefore neglecting intercurrent pharyngeal and/or skin colonization.[19–21] However, our standard regimen is based on a holistic strategy in treating nose, pharynx and skin, regardless of swab-positive body sites, and in vitro ineffectiveness of the chosen antiseptics/antibiotics was not obvious in any of the observed recurrent colonizations. Reboli *et al*.[10] highlighted the role of rectal carriage for eradication failure in HCWs; we did not perform rectal or vaginal swabs in each case requiring more than one course of treatment, but found rectal colonization in only one out of four tested cases requiring more than two courses of treatment.

Horizontal and vertical spread of MRSA between household contacts and families has been reported in patients as well as in HCWs.[10] It is well known from hospital outbreaks that contamination of contact surfaces in the environment may support transmissions between patients. However, reports of refractory carriage of MRSA by HCWs and the role of household contacts and/or the home environment are rare.

Recurrent, refractory colonization of HCWs has been reported to have led to or maintained hospital outbreaks in some cases;[9,22–24] recolonization was attributed to non-effective topical treatment, and investigations of the home environment or household contacts were not reported by these authors.

In 1980, Gawler *et al*. described the case of an intractable carrier state in a nurse that disappeared after removal of the staff member from the hospital environment.[25]

In 1997, Allen *et al*. reported the case of a nurse, which was very similar to our cases. Contaminated home environment and carriage in household contacts were found to be responsible for recolonization of the nurse, which resulted in a hospital outbreak involving three patients. The problem was finally solved after cleaning the house, disinfecting all linen, and replacing the soft furnishings.[26]

Our data, obtained by systematic post-exposure screening of HCWs for MRSA carriage, eradication treatment and follow-up over a period of seven years, allow us to highlight the outstanding significance of co-colonized household contacts and contaminated home environment in eradication failure. As shown in our cases, household contacts and contaminated home environment may play a major role in maintaining the HCW's carrier status.

To achieve permanent eradication, household contacts, especially those with oropharyngeal contact, should be screened and concomitantly treated as refractory carriers. As for other oropharyngeal bacteria (e.g. *Streptococcus pyogenes* or *Haemophilus influenzae*), oropharyngeal carriage in sexually active people may lead to genital colonization and vice versa. Therefore, vaginal and/or praeputial colonization (No. 1, No. 11, No. 12) should be looked for and treated in refractory nasopharyngeal carriers.

The finding of MRSA on surfaces with oropharyngeal contact, i.e. pillows, bed linen, razor, brushes and cosmetics, and on hand-contact surfaces, i.e. switches and room textiles, as well as in household dust (including carpets), is not surprising. Contaminated surfaces may maintain carriage via contact transmission and even via airborne transmission. The finding of transient nasal carriage in visitors of a room containing MRSA-contaminated dust (No. 1) supports the latter hypothesis; airborne transmission has also been observed in the hospital environment.[27,28] Therefore, HCWs found to be colonized by MRSA should be advised to thoroughly clean and disinfect such surfaces and to discard cosmetic items.

Our data suggest that investigating dust specimens is an easy and effective way to recognize massive contamination of the home environment. We propose that HCWs should take these specimens themselves and bring them for investigation, at least in refractory cases. Cases No. 1, No. 11 and No. 12, as well as the case described by Allen *et al*.,[26] show that sanitation of massive contamination might be crucial. We propose thorough cleaning and steaming as a potential first step.

The finding of MRSA inside shoes (No. 10 and No. 12) was unexpected, but may be explained by moisture and hand contact. Leather clothing with direct skin contact was obviously implicated in No. 11. We advise close inspection of such items in refractory cases.

The finding of MRSA in personal or leisure items (No. 8: gumshield, helmet; No. 9: hand-held computer; No. 11: biker's clothing), especially those with oropharyngeal or direct skin contact, is not surprising, but may be overlooked. Such items may only be identified in a confidential interview about personal habits with the affected HCW, after explaining how, where from and where to MRSA may be transmitted.

Soft tissue infections of HCWs are rare but do occur. Among 87 carriers, we observed one case of infection (No. 11). Muder *et al.* described five cases of cellulitis, impetigo, folliculitis, paronychia and conjunctivitis in HCWs after contact with MRSA-positive patients.[29] In addition to the negative aspect for the HCW, infection complicates eradication. It might therefore be wise to ask confirmed HCW carriers for signs of infection and for complicating skin diseases (as observed in No. 14: psoriasis).

In 84 of 87 colonized HCWs (97%), initial post-eradication swabs were negative. Immediate eradication failure, indicated by positive swabs taken three days after the eradication treatment had finished, occurred in only three of 84 cases (4%). However, recurrent colonization was observed in another 11 cases (13%); the recolonization was detected after an MRSA-free interval of about seven days to five months (median: one month). At least in our experience, recolonization rather than true eradication treatment failure has been the main problem leading to ineffective eradication. These findings support the hypothesis that definite eradication needs to be documented by long-term follow-up; they therefore support the recommendation of the German national guideline to perform control swabs after one and three months.[11]

On the other hand, in only 4% of cases, immediate eradication failure, as a result of non-compliance, inadequate treatment or massive environmental contamination, was detected by specimens taken during the first days after eradication treatment had ended. The German national guideline recommends waiting for negative results before returning to work,[11] which may result in an additional five to 10 lost working days after eradication treatment of five days. When compliance with topical eradication treatment is achieved, we doubt that this recommendation is appropriate as it seems to cause additional cost (in terms of loss of work) without adequate benefit, at least in non-outbreak situations.

Our data clearly demonstrate that failure to eradicate MRSA carriage in compliant HCWs mainly results from recolonization rather than from ineffective treatment. Recolonization is due to the spread of MRSA in the animate and inanimate household environment. As the reported cases show, eradication of carriage of household contacts and sanitation of the contaminated home environment are essential but can be difficult to achieve. This may be true for both colonized HCWs and colonized patients (where our knowledge about contaminated home environment is limited to a few cases). On the other hand, it seems obvious that the longer the carriage lasts, the more the possibility of environmental contamination exists. Therefore, when trying to avoid carriage at limited cost (in terms of loss of work), early detection of carriers seems to be essential; however, the problem regarding whether to exclude transient carriage remains unsolved. In our series, less than 19% of affected HCWs were transient carriers, resulting in less than 7% of total work loss due to withdrawal from work. Refractory carriers were responsible for about 70% of work loss.

This study supports the hypothesis that attempts to eradicate MRSA in long-term carriers (HCWs as well as patients) should not be restricted to antibiotic or antiseptic treatment, but must also include cleaning and disinfection of the household.

Acknowledgements

We thank Silva Crawford for her careful review of the manuscript and her helpful suggestions.

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