Staff Carriage of Epidemic Methicillin-Resistant
Staphylococcus aureus

BARRY COOKSON, MARGARET WEBSTER, IAN PHILLIPS, MARY RAHMAN, AND WILLIAM NOBLE
Division of Microbiology and Institute of Dermatology, UMDS, St. Thomas' Hospital, London SE1 7EH, England

Twenty-six nurses were repeatedly screened for carriage of epidemic methicillin-resistant Staphylococcus aureus (EMRSA) immediately before and after duty periods in which they solely attended six patients widely colonized with two EMRSA strains distinguishable by plasmid analysis. EMRSA carriage was detected in 13 nurses. Three EMRSA carriage patterns emerged: transient carriage in 12 nurses, when the EMRSA was isolated from noses or fingers of nurses after duty but was gone before their next day's duty; short-term nasal carriage, seen on occasion in 4 of these 12 nurses, when EMRSA carriage was detected on two consecutive screens; and persistent nasal carriage, seen in 1 nurse only, when the EMRSA was seen on more than two consecutive occasions. All but one of these incidents of carriage could be explained by close patient, rather than environmental, exposure and occurred despite an intensive control programme. Transient or short-term carriage in nurses probably resulted in transfer of the EMRSA between patients. Staff decontamination should be considered following a period of cohort nursing of EMRSA patients, especially if staff members are shortly to nurse unaffected patients. Our findings may explain some of the difficulties in controlling EMRSA.

In recent years nosocomial outbreaks of methicillin- and multiple-antibiotic-resistant Staphylococcus aureus (MRSA) have become a major infection control problem. Although MRSA strains have not been shown to be more virulent than other strains of S. aureus, very high mortality rates for patients with MRSA infections have been reported from several centers. Our inability to treat these infections at an early stage with first-choice antibiotics and the limited choice and delay in appropriate systemic chemotherapy pose serious therapeutic problems. Many hospitals in the United Kingdom, including those in our own Health Authority, have experienced a number of outbreaks of patient colonization and infection with epidemic MRSA (EMRSA) which resemble Australian strains. EMRSA strains may spread readily, and some hospitals have found them particularly difficult to contain. Others have commented on the paucity of information on MRSA carriage or on the relative importance of the environment and staff in MRSA spread. We reported the phenomenon of transient MRSA carriage during our first EMRSA outbreak. The establishment of an isolation ward for EMRSA patients with cohort nursing provided an opportunity to study the dynamics of the first stages in the spread of EMRSA.

(Material and methods section follows.)

Study population. Six patients (see Table 1) carrying the EMRSA were transferred to a ward designated for them at the South Western Hospital, a hospital with predominately elderly-care patients situated about 3 mi (ca. 4.8 km) from St. Thomas' Hospital. The ward had a central corridor with eight single-bed rooms, a nurses' office, clean and dirty utility rooms, and a patients' day room. There was no controlled ventilation. Although each room had its own wash basin, communal toilet and bathroom facilities were used for ambulant patients and individual commodes were used for those confined to their rooms (patients D and V). Twenty-six nurses and two domestic staff members worked solely on this ward during the 7-week study period. There were also two physiotherapists, who had administrative duties but no patient contact elsewhere, and two doctors allocated, although not solely designated, to patients in the isolation ward.

Three of the patients (D, R, and V) were involved in one outbreak with a chloramphenicol-susceptible EMRSA, and three (C, H, and M) were involved in an outbreak with a chloramphenicol-resistant EMRSA (see Table 1). All were elderly-care patients, except for patient C, who was transferred from an acute-care ward.

Decontamination regimen. All patients were decontaminated each day with a total-body wash with triclosan (Aquasept; Hough Houseman) and two triclosan applications to the face, nose, axilla, and groin, and chlorhexidine dressings (Bactigras; Smith and Nephew) were applied to all infected lesions. Staff members were decontaminated with four nasal applications of neomycin and chlorhexidine (Naseptin; IC1) and a total-body wash with chlorhexidine gluconate (Hibiscrub; IC1) only when they left the ward for the final time. Screening. Patients were screened for MRSA at least weekly with peptone water-moistened swabs from nose, throat, perineum, catheter sites, and any abnormal skin or wounds. Nurses took their own peptone water-moistened nasal swabs before and after each of 12 physiotherapy sessions involving all patients. The domestic and medical staff members were screened at the beginning and end of the
study, and the latter were also screened after examining patients on two occasions. At least once weekly, nose, throat, and perineal swabs were taken from each nurse and examined for methicillin-susceptible *S. aureus* (MSSA).

Swabs were usually transported and processed on the same day. All media were made with Columbia agar base (CM33; Oxoid Ltd.). Swabs for MRSA screening were first inoculated directly on mannitol salt agar (CM58; Oxoid) containing 5 mg of methicillin per liter (SM) and then placed in salt broth (no. 2 CM67, with 7.5% added sodium chloride; Oxoid), which was subcultured on MSM after 24 h. These subcultures were incubated at 37°C, the plates were examined after 24 and 48 h, and mannitol-fermenting colonies were tested for coagulase. Swabs for the screening of MSSA were inoculated directly on blood agar with a 10-μg methicillin disk (BAM) and then placed in salt broth, which was subcultured after 24 h on BAM; all BAM plates were incubated for 48 h at 30°C, and any staphylococcal colonies were tested for coagulase.

Antibiotic susceptibilities of all *S. aureus* isolates were determined on lysed blood agar by the comparative disk diffusion method.

Each nurse recorded the procedures she performed each day on predesigned forms, so that acquisition of the EMRSA could be correlated with activity. The degree of staff EMRSA exposure was divided into three grades, and the overall grade for each day was defined by the highest grade of procedure performed on that day.

(i) Grade 1 was superficial contact—brief exposure to a contaminated environment but no direct contact with a colonized or infected patient, e.g., delivering meals or speaking to a patient.

(ii) Grade 2 was casual contact—patient contact but no manipulation of colonized or infected sites, e.g., helping patients to wash and dress themselves.

(iii) Grade 3 was close contact—physical contact with infected or colonized sites, e.g., changing wound dressings, bathing widely colonized patients, or urethral catheterization. Our infection control policy included the use of aprons and gloves for all contact procedures, but apart from chest physiotherapy, masks were not used by staff for any close-contact procedures with these patients. The infection control team repeatedly emphasized the importance of appropriate hand decontamination with chlorhexidine preparations (Hibiscrub and Hibisol; ICI) after patient contact but did not inform staff members of their carriage unless it was persistent (see Results).

**Environmental screening.** The environment was screened once each week before ward cleaning, which was performed once daily during the first 2 weeks and twice daily thereafter. Air from each patient’s room, the nurses’ station, corridors, and the day room was sampled with a portable air sampler (Surface Air System; Cherwell Laboratories); 180 liters of air was sampled in 1 min on MSM and BAM plates. In the last 3 weeks of the study 900 liters of air was sampled in 5 min; phenolphthalein phosphate (SR31; Oxoid) agar plates were substituted for BAM plates. Peptone water-moistened swabs were used to sample floor dust, windowsills, bedsteads, and points of frequent hand contact, such as the drug trolley, nurses’ patient card index system, telephone, taps, door handles and light switches. These swabs were plated on MSM and then placed in salt broth. BA and MSM settle plates (4.5-in. [ca. 11.4-cm] diameter) were left at floor level for 2 h, 2 and 8 ft (ca. 61 and 244 cm, respectively) from each patient’s bed, and others were left in the corridor, nurses’ office, utility rooms, and day room. Weekly MSM sweep or impression plates were taken at patients’ bedclothes and on 30 occasions in the last 3 weeks from nurses’ disposable aprons and clothes.

**Strain identification.** The identity of EMRSA isolates was confirmed by a characteristic antibiotic susceptibility and phage typing pattern (6). Plasmid analysis was performed as previously described (7) on all EMRSA isolates from staff members on EMRSA isolates from patients at the start of the study and whenever the chloramphenicol susceptibility pattern changed. Phage typing was also performed on MSSA isolates by the Staphylococcus Reference Laboratory of the Central Public Health Laboratory, Colindale, London, England.

**Statistical analysis.** An unpaired *t* test was used to compare the mean of the number of days of each activity grade and the mean of the number of each grade of procedure performed on each day for nurses who carried the EMRSA with the corresponding means for nurses who never carried it. Days of carriage were assumed to follow a Poisson distribution, with the mean being dependent on the number of each grade of procedure performed. The interaction of the number of procedures (grade 2 or 3) performed by each nurse on each patient was then investigated with the computer program GLIM3.77 (GLIM system release 3.77, 1985; C. D. Payne, ed., Numerical Algorithms Group, Oxford).

**RESULTS**

**Strain identification.** All MRSA phage typed weakly with phage 85 at RTD100 (routine test dilution ×100) and with the experimental phages 88A and 932. Plasmid analysis, unlike chloramphenicol susceptibility testing, reliably distinguished between the two outbreak strains (Fig. 1). Chloramphenicol-susceptible isolates from patients D, V, and R always contained a ca. 1-megadalton (MDa) cryptic plasmid and were designated CY. Plasmid analysis of isolates from patients C, M, and H, with the chloramphenicol-resistant EMRSA, always revealed a ca. 3-MDa plasmid, and these isolates were designated CR. However, a minority population of chloramphenicol-susceptible isolates was occasionally detected from some sites on patients C and M, and these had merely lost the 3-MDa chloramphenicol resistance plasmid (designated CR−).

**Patient EMRSA carriage.** Table 1 gives details of patient colonization and infection with the EMRSA and the approximate time taken to perform wound dressings. The most heavily colonized patient, D, died on day 23 of the study. Table 1 also lists the residual sites colonized after the first 2 weeks of decontamination. The decontamination regimen produced a diminution in the extent of EMRSA colonization by week 3 in all patients except V, in whom the triclosan caused folliculitis and had to be discontinued.

**Environmental screening.** Environmental EMRSA isolates were obtained only in the first four weekly screens and were never isolated from the room of patient M or in any of the slit samples of ward air. Settle plates in the first 3 weeks indicated a low contamination rate of between 1 and 2 CFU of EMRSA per h in the rooms of patients D and R, in one instance immediately after a change of patient D’s dressings. Only one surface swab was positive on a direct culture; two colonies of EMRSA were isolated from the taps and door handle of the room of patient C, the most mobile of all the patients. All other positive results were from broth enrichment cultures of swabs. These isolates were widespread but low-level EMRSA contamination in the dust in the rooms of patients R and D and horizontal surfaces up to 8 ft (ca. 244
FIG. 1. Ethidium bromide-stained plasmid agarose gel. Lane 1 contains the molecular size standards; all plasmids were of the sizes previously reported (7). The ca. 20-MDa plasmid carries genes for resistance to ethidium bromide, propamidine isethionate, several aminglycoside antibiotics, and often trimethoprim and penicillin (6). CY isolates have aca. 20- and 1-MDa cryptic plasmids. CR iso isolates have ca. 20- and 3-MDa chloramphenicol resistance plasmids; an open circular form of such a plasmid is also present. CR− isolates have only the ca. 20-MDa plasmid. CRCY isolates have the ca. 20-, 3-, and 1-MDa plasmids.

From the bed of patient D. Less contamination was found in the rooms of patients V and H, where only horizontal surfaces less than 2 ft (ca. 61 cm) from the bed were positive, and that of patient C, where, in addition, a windowsill 8 ft away was positive. EMRSA was not detected on the nurses’ clothes or aprons. The environmental EMRSA isolates were of a plasmid type consistent with that found for the patient in that room.

Staff carriage. Neither physiotherapist acquired the EMRSA despite close patient contact. However, the procedures they performed, such as mobilization or chest physiotherapy, were rarely classifiable as grade 3. The medical staff members were also clear of carriage, but their environmental and patient contact was minimal. The domestic staff mem-

bers were also clear of carriage despite their environmental contact.

A total of 870 screens were performed on the 26 nurses, and EMRSA carriage was detected on 50 occasions in 13 of them. Three carriage patterns were observed in the 13 nurses (Table 2).

(i) Transient carriage. Nasal or finger EMRSA carriage was detected immediately after a duty period but was lost by the next day. This type of carriage was seen on 32 occasions in nurses 1 to 12 and was mostly nasal; EMRSA was cultured on only 5 occasions from two nurses’ fingers.

(ii) Short-term nasal carriage. EMRSA was detected on two consecutive occasions. In three of the four nurses in whom this type of carriage was observed, the EMRSA was detected before and after the same duty period.

Only 4 of the 40 instances of transient or short-term carriage were detected by direct culturing, and in each less than 17 colonies of EMRSA were grown. Table 2 includes details of the number of clear screens before each culture and after the last culture of EMRSA.

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<th>TABLE 2. EMRSA carriage and duty days of nurses 1 to 13</th>
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* All nasal and transient carriage except as follows: NF, nasal and finger carriage; F, finger carriage alone; +, short-term EMRSA carriage.

 Also carried an S. aureus isolate resistant only to penicillin.

—, Persistent carrier.

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<th>TABLE 1. Patient sites colonized or infected with the EMRSA and EMRSA transmission to staff performing grade 3 procedures</th>
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* A. Abdominal wound; H, heel sore; N. nose; P. perineum; R. rectum; S. sacral sore; T. toe sores; Th, throat; U. urethra. +, Infected site. —, The patient died.
(iii) Persistent nasal carriage. EMRSA was isolated on three or more consecutive occasions. This type of carriage was seen in only one nurse (nurse 13): EMRSA was isolated on four and then six consecutive occasions, although in only two of these occasions was EMRSA detected by direct culturing. This nurse was subsequently found to be carrying the chloramphenicol-resistant EMRSA in her throat and perineum and to be taking a course of trimethoprim and sulfamethoxazole for a urinary tract infection. Her carriage was subsequently cleared with mupirocin (Bactroban; Beecham Pharmaceuticals). One chloramphenicol-susceptible strain was isolated from this nurse (Fig. 1, CR) but, as with the isolates from patients C and M, this was a CR isolate which had lost the chloramphenicol resistance plasmid. No other nurses carried the EMRSA at other sites in their weekly screens. We were unable to determine when nurse 13 became a persistent carrier, so she was excluded from the data on EMRSA acquisition. EMRSA carriage was detected in 6% of the screens of the 25 nurses thus analyzed and 11% of the screens of nurses 1 to 12.

No EMRSA acquisition was detected after any of 14 grade 1 activity days and after only 1 of 196 grade 2 activity days. In marked contrast, grade 3 activity days were associated with all other incidents of transient or short-term EMRSA carriage. There was no significant difference in the number of grade 2 (P = >0.2) or three (P = >0.2) activity days for nurses 1 to 12, who carried the EMRSA, and nurses 14 to 26, who did not. However, nurses 1 to 12 did perform far more wound dressings (P < 0.02) and grade 3 activities (P < 0.001) on grade 3 days than did nurses 14 to 26 (Table 1). The number of grade 3 procedures performed significantly (P < 0.001) increased the mean number of days of EMRSA carriage by nurses, but the differences between patients were not significant (P > 0.05).

Table 2 shows the plasmid patterns of the EMRSA acquired by nurses 1 to 12. Plasmid analysis confirmed that all the chloramphenicol-susceptible strains had the CY pattern. Thus, we were able to show that the two EMRSA outbreak strains had been acquired at different times in seven of the nurses rather than that there was continued carriage of the CR strain with plasmid loss. Nurse 5 is particularly worthy of comment in that six of her eight CY strains were detected solely at the end of duty periods in which she treated only patients with the CY EMRSA plasmid profile. It was impossible to ascertain in two of the four incidents of short-term carriage whether the EMRSA strains had been reacquired or persisted during the duty period, as they had the same plasmid pattern (CR). In a third incident (nurse 8) the strains differed in plasmid pattern in that one was CR and the other was CRCY (containing both cryptic and chloramphenicol resistance plasmids and acquired from patient V; see below). It appears that this pattern was derived from in vivo plasmid transfer between the strains with patterns CR and CY rather than that the two strains were detected at the same site, although these strains have not appeared to be very stable on serial subcultures, even on media containing 50 mg of chloramphenicol per liter.

In 33 of the instances of staff EMRSA acquisition, plasmid analysis enabled us to implicate procedures on specific patients. Every patient except M was involved (Table 1), and patient D was responsible for most of the transmission (Fig. 2), but more grade 3 procedures were performed on her. No obvious relationship could be observed between EMRSA transmission to staff and the length of the wound dressing procedure or the extent of EMRSA colonization of patients. For instance, the greatest percentage of dressing procedures followed by EMRSA transmission to staff occurred with patient H, a minimally colonized patient, who required only brief wound dressing of infected toe sores. MSSA was detected in nurse 13 and six other nurses in whom the EMRSA was also detected (Table 2). Phage typing distinguished among all the isolates, except those of nurses 5 and 8.

EMRSA transmission between patients. Acquisition of the CR EMRSA in patient R’s sacral sore and perineum and patient V’s sacral sore (both patients were carriers of the CY strain) occurred in week 1 of the study. A chloramphenicol-resistant strain with the CRCY pattern was also isolated at this time from patient V’s perineum. The acquired strains did not establish themselves on these patients in that they were not isolated from screens repeated 48 h later or from subsequent screens in the next 6 weeks. Nurse 13, colonized with the EMRSA with the CR plasmid profile, did not perform any procedures on either of these patients, and the EMRSA was thought to have been transmitted to these patients by nurses with transient or short-term carriage.

DISCUSSION

It has often been suggested that certain epidemic strains of S. aureus have a special ability to colonize patients and staff (20) and that certain MRSA strains (EMRSA) are among these (6). There is little information on the carriage and transmission of MRSA, and in a recent review of the subject Caswell and Hill (4) had to extrapolate from the conclusions of studies of the carriage of MSSA, but even in these there has been no comparable attempt to correlate staff carriage with duties performed. In this study we were presented with an opportunity to examine staff EMRSA acquisition and thus the early stages of its spread.

A number of factors contributed towards the success of this study. Firstly, nurse cooperation was achieved by intensive education and the use of personal activity sheets. Secondly, many wound dressing procedures were of such a long duration that the nurses involved would often perform grade 3 procedures on only one patient on any given day. Thirdly, the twice-daily screening of each nurse yielded
much more detailed information than that obtained in most other studies, in which intermittent screening has been the norm. Fourthly, we used broth enrichment culturing to increase the sensitivity of detection of EMRSA carriage: in fact, without it carriage would have been entirely missed in eight of our nurses. Finally, plasmid analysis enabled us to distinguish among the outbreak strains and clarify the source of carriage. We were fortunate that the strains did not extensively cross-colonize the patients and that the cryptic plasmid was such a stable marker. The emergence of a third EMRSA plasmid type (CRCY) during the study is interesting, especially as it is very rare in the United Kingdom (J. Naidoo, personal communication). However, this pattern predominated in MRSA from one of the Australian hospitals, where similar if not identical strains have been described (6, 23).

Our study, although detailed, was not designed to avoid the possibility of it causing an alteration in the nurses' behavior (the Hawthorne effect) in that we educated highly motivated nurses in the importance of correct procedures and hand hygiene and they screened themselves. Despite this, the incidence of transient and short-term carriage was unexpectedly high. EMRSA acquisition was almost totally related to close patient contact, especially wound dressing, rather than walking into a contaminated environment or having minor contact with a patient (grade 1 or 2 activities). Seven of twelve nurses carried each epidemic strain at different times, supporting the hypothesis of continued acquisition rather than intermittent detection of EMRSA carriage. This hypothesis was also supported by the large number of clear screens between each EMRSA carriage episode in many of our nurses and by the fact that the EMRSA was predominantly detected after, rather than before, a duty period.

We did not perform regular finger sampling or screening immediately before and after procedures in this study and so cannot comment on the exact method of EMRSA acquisition. The observation that EMRSA transmission was not simply related to the extent of patient colonization but could follow simple dressing procedures on minimally colonized patients made it difficult to predict which patient was likely to transmit the organism. S. aureus carriage on fingers has been correlated with perineal carriage (11), which was not evident in either of our two nurses with finger carriage, and with nasal carriage (17), as was observed in one nurse. Nor did they have any colonization of minor lesions or overt infection with the EMRSA. The persistence of MRSAs on the hands of nursing staff and its subsequent clearance by simple handwashing or disinfection have been demonstrated previously (21). The EMRSA may have been acquired from direct contact with contaminated wounds or dressings and bed-clothes, as Hare (10) hypothesized. We feel that this is unlikely in that gloves were usually worn for contact with patients, judging by the large numbers that were used during the study. We could not demonstrate contamination of nurses' clothes. It is more likely that the EMRSA was acquired from inhaled airborne EMRSA particles such as we have observed during physiotherapy on a patient with exfoliative dermatosis (5) and after wound dressing and bed-making (B. D. Cookson, unpublished observations). EMRSA transmission would then presumably follow transfer from the nose to the hands.

The definitions used in other studies have differed from ours because of the lower frequency of subject sampling used. The first allusion that we found to brief S. aureus carriage was in a weekly study of nasal carriage in 500 medical students over a 3- to 12-month period (9); 42% of the students were "occasional" carriers in that the organism was detected in less than 10% of their screens. These isolates were of a phage type different from that previously found, and these workers postulated that these students' noses were not true S. aureus hosts but acted rather like filters of the inspired air.

The further elucidation by this study of the phenomenon of transient or short-term EMRSA carriage has a number of implications. These forms of carriage probably caused the two instances of EMRSA transfer from one patient to another in that the patients had no contact with each other, the persistent carrier (nurse 13) had no contact with these patients, the environmental contamination did not extend outside the rooms of these patients, and no fomites could be implicated. We are also convinced that they have contributed to the failure of standard isolation techniques to control EMRSA spread. These observations justify the use of designated staff when the consequences of EMRSA transmission may be especially serious, such as in an intensive-care therapy unit (5) or a burn unit (16).

Transient MRSA carriage in agency staff members might also result in interhospital spread, as these staff members often work in more than one hospital in a 24-h period. A central agency coordinates the employment of all our agency nurses and ensures that we do not employ staff members who have worked on EMRSA patients elsewhere unless they have been screened and decontaminated. A similar approach is adopted with our own staff nurses who have had close contact with EMRSA patients.

All three types of carriage should be considered in MRSA clearance studies with antibiotics or disinfectants. Such studies rarely state whether screens were performed on staff members immediately after they had performed procedures on patients. Thus, transient carriers may have been mislabeled as persistent carriers, leading to erroneous conclusions as to the efficacy of specific decontamination regimens. We have not previously found chlorhexidine, povidone iodine, or hexachlorophene used alone to be effective in eradicating the EMRSA from wounds. The relationship between staff EMRSA acquisition and wound dressings emphasizes the importance of rapid elimination from wounds. We agree with others (24) that thrice-daily triclosan total-body washes or baths are poorly accepted by patients. Furthermore, triclosan did not eradicate the EMRSA from our patients' wounds, although only minimal wound exposure would have occurred during a bath, since dressings were not removed.

Although it was clear that the performance of close-contact (grade 3) procedures was the most important difference between nurses 1 to 12 and those who did not carry the EMRSA, we could not be certain that other additional factors did not exist. Others have pointed out the possible roles of human leukocyte antigen type (13) and bacterial interference (19) in the carriage of S. aureus. Only weekly screens were performed for carriage of MSSA, so we cannot be certain of the dynamics of bacterial interaction, but it is interesting that all the carriers of MSSA were also carriers of the EMRSA. Bacterial interference might have discouraged the establishment of prolonged EMRSA colonization, but is unlikely to be the sole explanation in that half of nurses 1 to 12 did not carry such S. aureus strains. The association between antibiotic administration and MRSA acquisition in patients has been alluded to previously (8); it might also have been a factor in staff acquisition, as in nurse 13.

There is still much dispute over the significance of environmental contamination in the nosocomial spread of S.
The more outlying areas were clear, despite the use of these areas for mobilization and rehabilitation. People commonly blamed the environment as the source of EMRSA spread, but we demonstrated that walking into a contaminated environment alone did not lead to EMRSA acquisition. In situations similar to ours, we are confidently able to predict that staff members are unlikely to acquire EMRSA unless a close-contact (grade 3) procedure is performed. We have therefore concentrated our efforts on those procedures most likely to cause EMRSA transmission by the designation of nursing staff and have minimized the control measures imposed on the other staff.

It seems probable that many of our observations are common to all outbreaks of staphylococcal infection. However, one must take care when extrapolating the results of this study to different circumstances. Other hospitals may have a more heavily contaminated environment. Conversely, in an open ward, even with minimal environmental contamination, staff members may be at risk via the airborne route when passing close to an area where a close-contact (grade 3) procedure is being performed. Further studies of similar detail and intensity of screening, but with different environmental and staffing conditions, are required. Undoubtedly, the use of plasmid analysis and an activity grading system would facilitate such studies.

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LITERATURE CITED