

## Analysis of Transmission of Methicillin-resistant *Staphylococcus Aureus* in an Intensive Care Unit by Pulsed-field Gel Electrophoresis

Taku TAKEDA<sup>1)</sup>, Kakuko YASUNAKA<sup>2)</sup>, Keiichi TANAKA<sup>1)</sup>,  
Tohru TAKATA<sup>3)</sup> and Yoshiro SAWAE<sup>4)</sup>

<sup>1)</sup>*Departments of Emergency & Critical Care Medicine,* <sup>2)</sup>*Microbiology,* <sup>3)</sup>*First Department of Internal Medicine, Fukuoka University School of Medicine and* <sup>4)</sup>*Shinkokura Hospital, Fukuoka, Japan*

**Abstract:** The relationship between the carriage of nasal methicillin-resistant *Staphylococcus aureus* (MRSA) by medical staff and the detection of MRSA in intensive care unit (ICU) patients was studied by a prospective comparison of the pulse-field gel electrophoresis (PFGE) patterns of MRSA bacterial isolates. Nasal cultures were obtained from medical staff both at the beginning and the end of the study. One hundred and twenty-nine consecutive patients were screened by a nasal swab at the time of ICU entry and weekly thereafter until either discharge or death. Extra-nasal samples were taken when infection was suspected. Isolated MRSA were classified into 12 PFGE types. More than half of the nasal MRSA carriers (16 of 27) and more than three-quarters of the patients with extra-nasal MRSA isolates (15 of 19) had identical PFGE types. Furthermore, the PFGE types of all 14 isolates from extra-nasal sites of the carriers were identical to the nasal isolates. The most prevalent strains did not appear to be transmitted to the ICU patients by staff nasal carriers. However, other strains were readily transmitted from staff carrier to patients. The strain difference in transmissibility may explain why there continue to be conflicting reports regarding the involvement of nasal carriage of MRSA by medical staff and outbreaks in patients.

**Key words:** Methicillin Resistant *Staphylococcus Aureus*, Intensive Care Unit, Transmission, Pulsed-Field Gel Electrophoresis, Mupirocin

### Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most common causes of endemic and epidemic infection acquired in hospitals, and it also results in substantial morbidity and mortality. Nasal carriage serves as a major reservoir of *S. aureus*.<sup>1)-14)</sup> Several studies using molecular typing methods that have been conducted at a single point of outbreak reveal a clonal relationship between MRSA that are carried in the nares of medical staff and the epidemic strains from patients.

Such clonal relationships among strains have led to the suggestion that the nasal carriage of MRSA by medical staff may be responsible for patient outbreaks.<sup>9), 15)-18)</sup> However other studies have failed to document such clonal relationships.<sup>19)-21)</sup> In an attempt to resolve the differing results in studies on the clonal relationships of MRSA detected during nasal carriage by medical staff and MRSA transmitted to patients, we eradicated nasal MRSA in the medical staff by mupirocin nasal ointment before entry into our study. We subsequently obtained the MRSA isolates from the nares and the extra-nasal sites in intensive care

unit (ICU) patients in a 6-month long prospective study. Pulsed-field gel electrophoresis was used to compare DNA types of the patient isolates with isolates from the nares of the medical staff that were obtained at the end of the study.

## Subjects and Methods

### Patient study

This study was conducted at the 32-bed Department of Emergency and Critical Care Medicine of Fukuoka University Hospital. The Fukuoka University Hospital has several ICUs and the ICU used for this study was the one in our department. The ICU has 10 beds with 2 private rooms and provides medical and surgical treatment, including pediatric and burn care. All patients enter the ICU through admission bays designed for initial assessment and treatment.

Swabs were prospectively obtained from the anterior nares of patients at the time of ICU entry after admission to our department and then weekly thereafter, until they were either discharged from the ICU or death. Sample collection was carried out between 1 July and 31 December 1997. Clinical specimens from extra-nasal sites were cultured whenever any infection was suspected. When MRSA was isolated from extra-nasal sites, additional nasal cultures were also obtained immediately thereafter.

The patient data was collected for age, gender, underlying disease, body sites from which MRSA had been recovered, and the length of stay in the ICU. The physical location of the patient prior to admission to ICU; for example, a non-hospital site, another hospital, or another ward within our hospital was also recorded. The severity of illness at the time of ICU entry was assessed using the acute physiology and chronic health evaluation (APACHE) III score.<sup>22)</sup> MRSA infections were defined according to the Centers for Disease Control (CDC) standard definitions.<sup>23)</sup>

### Identification of medical staff carriers and eradication of MRSA

Nasal cultures were obtained from the medical staff nurses and physicians who came in close contact with patients with MRSA. The initial nasal

screening (first surveillance) was done before entry into the study. During the month of June, nasal swabs were collected 3 times over a 2 week period. Nasal cultures were obtained 3 times over a 2 week period because of irregular schedules. Any medical staff members that were relocated to our ICU during this study were also screened at the beginning of their employment. The individuals with an MRSA isolate from 1 or more cultures were considered to be staff carriers and treated with mupirocin nasal ointment (Bactroban®, SmithKline Beecham Seiyaku K.K., Tokyo) 3 times a day for 3 days before study entry. Nasal cultures were performed 4 weeks after mupirocin treatment to assess whether or not MRSA had been eradicated. Nasal carriers among the medical staff who had relocated during the study period were also eradicated by mupirocin nasal. Patient screening was initiated in July, following the first period of staff surveillance and it continued through December. The final period of obtaining cultures from the medical staff (second surveillance) occurred during a 2 week period in December and proceeded through the last period of patient screening.

To assess the extent of contact with the patients by medical staff, the names of all staff members who had signed records during a patient's hospital stay were reviewed. Infection control precautions were instituted when MRSA was isolated from a patient. In addition to standard precautions, contact precautions were encouraged by the use of surgical masks, gowns, gloves, and handwashing by the medical staff. In addition, all patients who were found to have MRSA were either cohorted or isolated.<sup>24)</sup>

### Microbiological methods

Anterior nares cultures were obtained by rotating rayon-tipped swabs (Seedswab No. 1, Eiken Kagaku Co., Ltd., Tokyo) in the nostrils. The swabs were sent to the hospital clinical laboratory where they were first inoculated directly on 5% sheep blood agar (Nissui Co., Ltd., Tokyo). After incubation for 48 h at 35°C, suspected colonies of *S. aureus* were subcultured on salt egg yolk agar (Nissui Co., Ltd., Tokyo) for 24 h at 35°C. Identification of *S. aureus* was based on both morphology and a *S.*

*aureus* specific agglutination test Staphaurex (Murex Biotech Ltd., Dartford, United Kingdom). The methicillin susceptibility of *S. aureus* isolates was determined using standardized methods<sup>25)</sup> after 24 h incubation at 35°C on Mueller–Hinton agar containing 4% NaCl and 6 µg of oxacillin per milliliter (Becton Dickinson & Company, Franklin Lakes, NJ). Any growth on these plates was an indication of methicillin resistance. The isolates were stored frozen at –60°C until further use.

Genomic DNA from MRSA isolates was digested with SmaI before analysis by PFGE.<sup>26)</sup> We interpreted the PFGE patterns according to Tenover's criteria.<sup>27)</sup> Specifically, isolates with identical restriction patterns or those with differences in 1–3 bands were considered to be clonally identical, while isolates differing by 4 or more bands were considered to be different.

### Case Definitions

Patients with a positive nasal culture within 48 hrs after ICU entry were defined as nasal carriers at the time of ICU entry. Those with a negative nasal culture at the time of ICU entry but a positive culture 48 hrs later were defined as nasal carriers after ICU entry. In addition, patients were designated as index nasal carriers when their isolates exhibited PFGE patterns encountered for the first time during the study period.

### Statistical Analysis

The values are presented as the mean ± standard deviation. Fisher's exact test was used to compare proportions and Student's *t*-test to compare means. *P* values of less than 0.05 were considered to be significant and all reported *P* values are two-tailed.

## Results

### Patient characteristics

Of the 129 patients (58.5 ± 19.4 yr.; 84 male, 45 female), 86 were medical and 43 were surgical patients, and the mean APACHE III score on admission was 59.5 ± 31.8. There were 46 patients admitted from other facilities, 4 from another ward within this hospital, and 79 had been transferred from an accident site by emergency medical

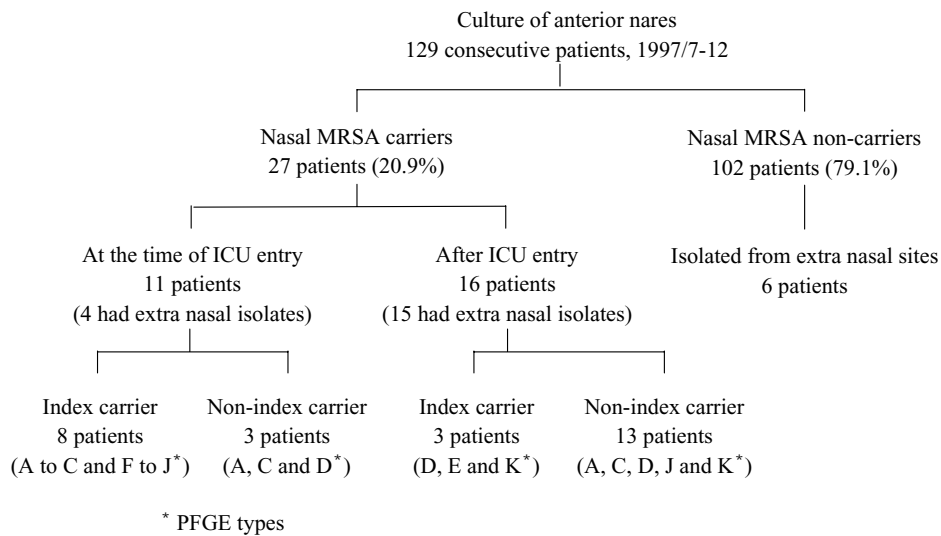
services. The mean duration of ICU hospital stay was 7.0 ± 8.4 days. The diagnoses on admission included either congestive heart failure or cardiovascular disease (n=27), trauma (n=26), gastrointestinal, hepatic or biliary disease (n=25), neurological disease (n=22), acute respiratory failure (n=16), cerebral hypoxia that occurred following cardiopulmonary resuscitation (n=4), severe burn (n=3), and other conditions including poisoning, heat stroke and sepsis (n=6).

There were 33 patients with MRSA during the study period. Twelve had been in other hospitals prior to admission to our facility and 3 had been transferred from another ward within this hospital. There were no significant differences between patients with or without MRSA regarding age, gender, or the mean APACHE III score.

During the study period, MRSA infections were observed in 7 patients with pneumonia, 1 with a surgical wound infection, 1 with both a surgical wound infection and acute cholecystitis, 1 with burn wound infection and sepsis, and 1 with a surgical wound infection and acute colitis. All of the patients with MRSA infections required systemic antibiotic treatment with either arbekacin or vancomycin.

### MRSA isolates from patients

Among the 129 admitted patients, there were 27 (20.9%) nasal MRSA carriers and 102 (79.1%) nasal non-carriers (Figure 1). Of the 27 nasal carriers, 11 (8.5%) were nasal carriers at the time of ICU entry and 16 (12.4%) became nasal carriers after ICU entry. A total of 19 nasal carriers (4 nasal carriers at the time of ICU entry and 15 who became nasal carriers after ICU entry) had MRSA isolates from extra-nasal sites. Specifically, 16 isolates were from the sputum, 6 from surgical wounds, 4 from stool, 3 from blood, 1 from bile, and 1 from urine. Of the 102 nasal non-carriers, 6 had MRSA isolated from sputum. As a result, a total of 25 patients (19 nasal carriers and 6 nasal non-carriers) had MRSA isolates from extra-nasal sites. MRSA was isolated from the sputum in 22 patients, making it the most frequent site of detection. No MRSA isolates were detected in the other 96 patients throughout the course of the study. The detection of MRSA in extra-nasal



**Figure 1.** The nasal carrier state and isolation from extra-nasal sites of methicillin-resistant *Staphylococcus aureus* in intensive care unit patients.

sites was significantly more frequent ( $p < 0.0001$ , Fisher's exact test) in nasal carriers (19/27) than in non-carriers (6/102).

#### MRSA isolates from medical staff

Nasal cultures were obtained from 98 medical staff members, consisting of 33 physicians and 65 nurses. At the first surveillance, 5 physicians and 6 nurses (11.2%, 11/98) were positive for MRSA. Recultures of staff carriers performed 4 weeks after nasal eradication by mupirocin nasal ointment could not be done for 1 staff member who retired and 1 who had been transferred to another hospital. Nasal eradication of MRSA was confirmed for 8/9 (88.9%) staff carriers. Second surveillance nasal cultures were obtained from 91 medical staff, consisting of 27 physicians and 64 nurses. At that time 5 physicians and 7 nurses (12/91 or 13.2%) were positive for MRSA. Among the 12 MRSA positive staff, 2 carriers were positive on both first and second surveillance and the 1 individual who could be treated had eradication that was confirmed by a nasal culture after the first surveillance. The second individual could not tolerate the mupirocin treatment. Thus, 10 medical staff members were newly identified as nasal carriers on second surveillance. None of the staff carriers had a history of skin lesions or any objective evidence of MRSA infection.

#### Comparison of DNA type of MRSA isolated from patients and medical staffs

The PFGE patterns were evaluated for 79 MRSA isolates from 27 patient nasal carriers. The MRSA were from 36 nasal and 26 extra-nasal isolates, 5 sputum isolates from 5 patients who were non-nasal carriers, and 12 nasal isolates from 12 staff carriers who were detected upon second surveillance. The isolates were classified into 12 PFGE types, designated as A to L (Figure 2). Types A, C, D, E, J and K gave PFGE patterns in the isolates from both the patients and the staff carriers, while types B, F, G, H and I were unique, in that they were observed only in patient nasal carriers at the time of ICU entry and not in medical staff (Table 1). Types A ( $n=8$ ) and C ( $n=6$ ) were the most prevalent strains among the patient nasal carriers.

The nasal MRSA isolates from the patient had 11 PFGE types (A to K). The PFGE patterns of the nasal isolates from the index nasal carriers that were initially detected during the study were identified not only at the time of ICU entry (types A, B, C, F, G, H, I and J), but also after ICU entry (types D, E and K) (Figure 1). The 3 index nasal carriers identified after ICU entry had the first positive nasal culture between days 4 to 15 (mean 8.7) of ICU hospital stay. Among the 16 non-index nasal carrier patients with PFGE types identi-

**Table 1.** Pulsed-field gel electrophoresis (PFGE) determination of DNA types of nasal isolates obtained from patients and medical staff at second surveillance.

DNA type by PFGE	Study subjects		Total
	Patients (n=27)	Medical staff (n=12)	
A	8	1	9
B	1	—	1
C	6	3	9
D	3	1	4
E	1	1	2
F	1	—	1
G	1	—	1
H	1	—	1
I	1	—	1
J	2	4	6
K	2	1	3
L	—	1	1

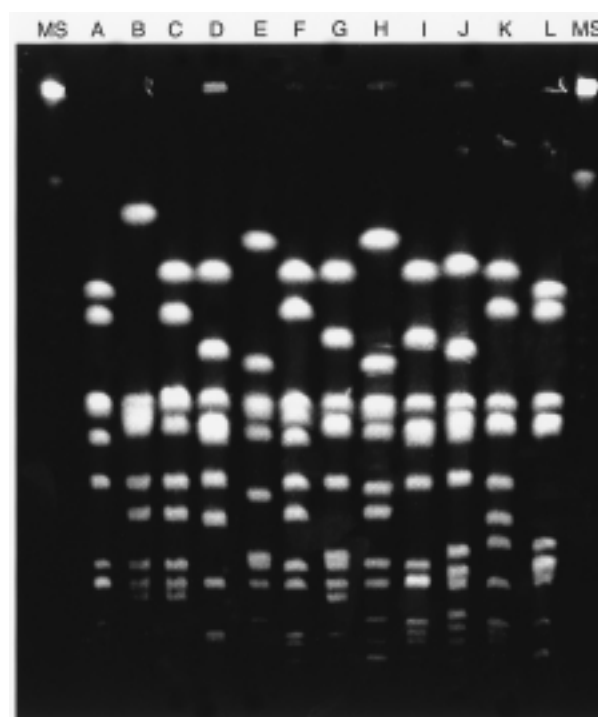
cal to those of the index nasal carriers, 3 were the nasal carriers of types A, C, and D at the time of ICU entry and 13 became nasal carriers of types A, C, D, J, and K after ICU entry. The 13 non-index nasal carriers after ICU entry had their first positive nasal cultures between days 6 to 24 (mean 12.5) of their ICU hospital stay.

The extra-nasal isolates from 14/19 nasal carriers and 5/6 nasal non-carriers were available for PFGE analysis and types A, C, D, E, J, and K were identified. Of the 6 PFGE types identified, type A was the most common (n=9) for the extra-nasal isolates (Table 2). The extra-nasal isolates from both the 10 non-index nasal carriers and 5 nasal non-carriers had PFGE types identical to those of the index nasal carriers (types A, C, D, J and K). The PFGE types of the extra-nasal isolates from all 14 of the nasal carriers were identical to their nasal isolates.

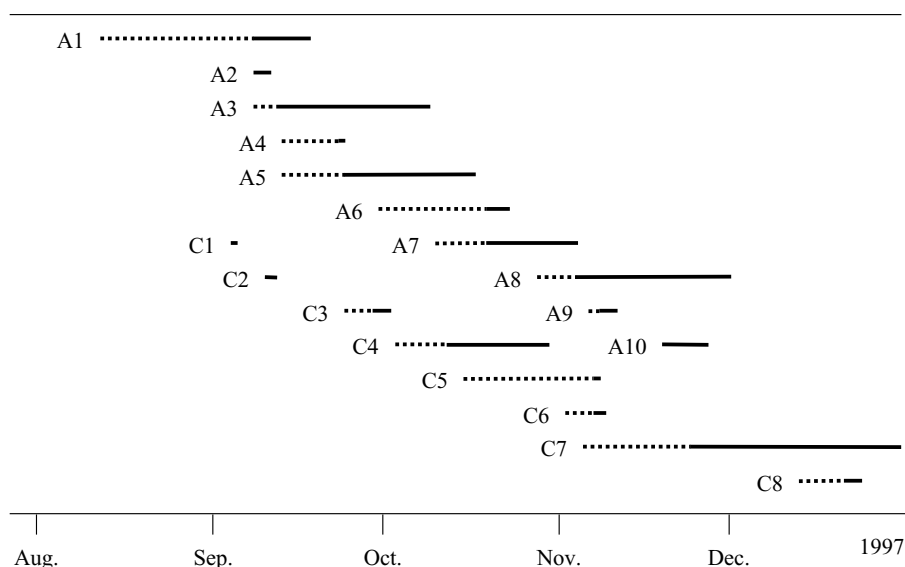
Twelve nasal isolates from the staff carriers on second surveillance exhibited types A, C, D, E, J, K and L (Table 1). These 7 PFGE types, with the exception of type L, were also observed in the patient isolates. Type J (n=4) prevailed among the staff carriers. The first surveillance nasal isolates of 2 staff carriers who were positive at both surveillance times were also evaluated by PFGE. The isolates from 1 staff carrier who could not use mupirocin had PFGE type D on both surveillances. However PFGE type M was obtained at

**Table 2.** Pulsed-field gel electrophoresis (PFGE) determination of DNA types of extra nasal isolates in the nasal carriers and non-nasal carriers.

DNA type by PFGE	nasal carrier		nasal non-carrier	total
	index	non-index		
A	1	5	3	9
B	—	—	—	—
C	—	2	1	3
D	—	1	—	1
E	1	—	—	1
F	—	—	—	—
G	—	—	—	—
H	—	—	—	—
I	—	—	—	—
J	1	1	—	2
K	1	1	1	3
L	—	—	—	—
total	4	10	5	19

**Figure 2.** The pulsed-field gel electrophoretic patterns of methicillin-resistant *Staphylococcus aureus* isolates from patients and medical staff.

Lanes A to L show the PFGE patterns of types A to L of DNA digested with *Sma*I. Molecular size standards are in Lane MS.



**Figure 3.** The temporal relationships of consecutive hospital stays of the patients with epidemic methicillin-resistant *Staphylococcus aureus* (MRSA) strains. A 1 to 10 : patients with type A strain ; C 1 to 8 : patients with type C strain. Hospitalization without MRSA strains in specimens (···) Hospitalization with MRSA strains in specimens (—).

first surveillance and type J at second surveillance in the staff carrier with confirmed nasal eradication after mupirocin treatment. The type M strain was not detected in any of the patients during the study period (data not shown).

Figure 3 shows the length of ICU stay and time course of isolation of MRSA from the patients with type A and C strains. There were some periods during which patients with type C strain had no detectable MRSA, although the patients with type A strains were consecutively observed. Similarly, some periods with no detection were seen among the patients with type D, E, J and K strains.

The type A strain was also detected from 1 staff carrier on second surveillance, but this individual had relocated in December to the ICU from another ward within this hospital and had no known subsequent direct contact with any ICU patients with type A strain. However, type C strain was detected from 3 staff carriers on second surveillance. All 3 staff carriers had a history of contact with patients who yielded the identical strain. Similarly, type D, J and K strains were also detected in 1 to 4 staff carriers. Each of these staff carriers had contact with patients, from whom the corresponding strain was subsequently

isolated.

### Discussion

Based on the results, strains were classified as (1) those which were isolated from only index nasal carriers and not from other patients or medical staff (types B, F to I), (2) those which were isolated from patients but not from medical staff members (type A), and (3) those which were isolated from both patients and medical staff members (types C to E and J to K).

The following important findings were obtained by PFGE analysis, done in conjunction with prospective isolation of epidemic MRSA strains from both patients and medical staff. First, among the 27 nasal carriers, nasal isolates of 16 non-index nasal carriers showed the identical PFGE strains as those of the previously admitted index carriers (Figure 1). In addition, the extra-nasal isolates of 15/19 patients including 10 nasal carriers and 5 nasal non-carriers also revealed the presence of a strain identical to those of the previously admitted patients (Table 2). As a result, more than half (16 of 27) of the patient nasal carriers and more than three-quarters of the patients with extra-nasal isolates (15 of 19) were infected by nosocomial

transmission. Moreover, all of the extra-nasal isolates from the patient nasal carriers had PFGE types that were identical to their nasal isolates. These results suggest that a majority of the patient nasal carriers had acquired MRSA by nosocomial transmission, with subsequent transmission to other sites or vice versa.

Second, at least 2 distinct modes of transmission were recognized among the patients and staff carriers. In the first mode, involvement of staff nasal carriers was likely, based on the existence of a period during which no patients with MRSA were detected, as has been documented for the transmission of the type C strain. The second mode of transmission does not involve staff nasal carriers. This is exemplified by the lack of type A strain staff nasal carriers and a period of non-detection of MRSA between consecutive hospital stays of the patients with type A strain. These findings differ from those for type J strain, which was the most prevalent among the staff carriers but was detected in only 2 patients. These observations suggest that variability exists in the ability of different strains to colonize the nares or to undergo transmission to other persons. Specifically, some cases which occur due to nosocomial transmission, such as those for type A strain, appear to be the result of direct contact with transiently contaminated hands of the medical staff during various medical procedures rather than as a result of the staff nasal carrier status. The different modes of transmission of type C and type A strains among the patients may partially explain the conflicting results regarding the role of nasal carriage status of medical staff in patient outbreaks.

The origins of the nasal isolates from the 3 non-index nasal carriers at the time of ICU entry and the 3 index nasal carriers after ICU entry could not be identified. The 3 cases of non-index nasal carriage might be the result of transmission by medical staff during the interval between admission to our department and ICU entry. Alternatively, nosocomial transmission might have occurred in these patients in other facilities prior to ICU entry. The latter 3 index nasal cases identified after ICU entry might be related to an increase in the number of colonies in the nares after positive selection following the administration of antibiotics

without anti-MRSA effects. Indeed, broad-spectrum cephalosporins or carbapenems had been used after ICU entry for these 3 patients. Another possibility is a failure to detect MRSA by nasal sampling. In this study, nasal swabs were obtained only once at the time of ICU entry to discriminate between those who became nasal carriers before ICU entry and those who became nasal carriers after entry. It is possible that MRSA was not detected by this initial screening, since nasal sampling may give false negative results.<sup>1)</sup> Similarly, screening by nasal cultures alone at the time of ICU entry may have missed some patients with MRSA, who subsequently served as reservoirs inside the ICU.

Our data provide important clues regarding controversial aspects of infection control for MRSA outbreaks in the ICU. The identification of multiple strains in such outbreaks in patients and medical staff makes infection control more difficult than for outbreaks that are caused by a single predominant strain. Outbreaks involving multiple strains may be caused by the introduction of patients from other facilities. Our finding that all but 1 of the index nasal carriers had been hospitalized at other hospitals and subsequently were transferred to our institution supports this idea. As a result, eradication of nasal carriage in patients on admission may be justified in the ICU setting when patients are admitted from other facilities. In addition, our observation that a majority of patients who became nasal carriers after ICU entry were the result of nosocomial transmission and may subsequently have suffered further transmission to other sites. These data point to the importance of eradicating nasal carriage, not only at ICU entry, but also during prolonged ICU stays.

The incidence of nasal MRSA carriage in the ICU medical staff ranged from 11.2 to 13.2% , which is similar to that of a previous study.<sup>28)</sup> There is epidemiological evidence that medical staff who happened to be nasal carriers are responsible for the transmission of MRSA to patients, especially during epidemic strain outbreaks.<sup>9), 15)-18)</sup> These findings suggest that the screening and eradication in staff nasal carriers may be necessary to either prevent or limit an outbreak with an epidemic MRSA

strain. However our study shows that there are some limitations to the effectiveness of nasal eradication in medical staff, given the absence of involvement in transmission of staff that carries the prevalent type A strain in the nares. However, nasal eradication may be of value for preventing outbreaks of such strains as type C. In a recent study, Tammelin et al.<sup>29)</sup> reported that half of the health care workers acquire *S. aureus* on the hands probably via self-inoculation from the nose. In addition, treatment with topical mupirocin, which eliminates nasal carriage, is also known to be associated with a decrease in hand carriage.<sup>8)</sup> Therefore, the eradication of nasal carriers in medical staff should be considered as an additional infection control measure for MRSA outbreaks to supplement control by contact precautions based on thorough handwashing and hand hygiene.

#### Acknowledgments

We are indebted to Noriyuki Murakami and Fumiyoshi Era in the department of clinical laboratory of Fukuoka University Hospital for their technical assistance with the microbiological analyses of the screened specimens and all of the medical staff who participated in this study.

#### References

- 1) Weinstein, H. J. : The relation between the nasal-staphylococcal-carrier state and the incidence of postoperative complications. *N. Engl. J. Med.*, 260 : 1303-1308, 1959.
- 2) Williams, R. E. : Healthy carriage of *Staphylococcus aureus* : its prevalence and importance. *Bacteriol. Rev.*, 27 : 56-71, 1963.
- 3) Thompson, R. L., Cabezudo, I., Wenzel, R. P. : Epidemiology of nosocomial infections caused by methicillin-resistant *Staphylococcus aureus*. *Ann. Intern. Med.*, 97 : 309-317, 1982.
- 4) Sewell, C. M., Clarridge, J., Lacke, C., Weinman, E. J., Young, E. J. : Staphylococcal nasal carriage and subsequent infection in peritoneal dialysis patients. *J. Am. Med. Ass.*, 248 : 1493-1495, 1982.
- 5) Yu, V. L., Goetz, A., Wagener, M., Smith, P. B., Rihs, J. D., Hanchett, J., Zuravleff, J. J. : *Staphylococcus aureus* nasal carriage and infection in patients on hemodialysis. Efficacy of antibiotic prophylaxis. *N. Engl. J. Med.*, 315 : 91-96, 1986.
- 6) Casewell, M. W., Hill, R. L. : The carrier state: methicillin-resistant *Staphylococcus aureus*. *Antimicrob. Chemother.*, 18 Suppl A : 1-12, 1986.
- 7) Luzar, M. A., Coles, G. A., Faller, B., Slingenyey, A., Dah, G. D., Briat, C., Wone, C., Knefati, Y., Kessler, M., Peluso, F. : *Staphylococcus aureus* nasal carriage and infection in patients on continuous ambulatory peritoneal dialysis. *N. Engl. J. Med.*, 322 : 505-509, 1990.
- 8) Reagan, D. R., Doebbeling, B. N., Pfaller, M. A., Sheetz, C. T., Houston, A. K., Hollis, R. J., Wenzel, R. P. : Elimination of coincident *Staphylococcus aureus* nasal and hand carriage with intranasal application of mupirocin calcium ointment. *Ann. Intern. Med.*, 114 : 101-106, 1991.
- 9) Boyce, J. M., Opal, S. M., Potter-Bynoe, G., Medeiros, A. A. : Spread of methicillin-resistant *Staphylococcus aureus* in a hospital after exposure to a health care worker with chronic sinusitis. *Clin. Infect. Dis.*, 17 : 496-504, 1993.
- 10) Sanford, M. D., Widmer, A. F., Bale, M. J., Jones, R. N., Wenzel, R. P. : Efficient detection and long-term persistence of the carriage of methicillin-resistant *Staphylococcus aureus*. *Clin. Infect. Dis.*, 19 : 1123-1128, 1994.
- 11) Wenzel, R. P., Perl, T. M. : The significance of nasal carriage of *Staphylococcus aureus* and the incidence of postoperative wound infection. *J. Hosp. Infect.*, 31 : 13-24, 1995.
- 12) Kluytmans, J. A., Mouton, J. W., Ijzerman, E. P., Vandembroucke-Grauls, C. M., Maat, A. W., Wagenvoort, J. H., Verbrugh, H. A. : Nasal carriage of *Staphylococcus aureus* as a major risk factor for wound infections after cardiac surgery. *J. Infect. Dis.*, 171 : 216-219, 1995.
- 13) von Eiff, C., Becker, K., Machka, K., Stammer, H., Peters, G. : Nasal carriage as a source of *Staphylococcus aureus* bacteremia. Study Group. *N. Engl. J. Med.*, 344 : 11-16, 2001.
- 14) Perl, T. M., Cullen, J. J., Wenzel, R. P., Zimmerman, M. B., Pfaller, M. A., Sheppard, D., Twombly, J., French, P. P., Herwaldt, L. A. : Mupirocin And The Risk Of *Staphylococcus aureus* Study Team. Intranasal mupirocin to prevent postoperative *Staphylococcus aureus* infections. *N. Engl. J. Med.*, 346 : 1871-1877, 2002.
- 15) Rodrigues, J. N., Amaral, J. L., Leme, I. L., Pignatari, A., Wey, S., Hollis, R., Pfaller, M. A., Jones, R. N. : Molecular epidemiology and antimicrobial susceptibility testing. Testing of quinolone-resistant *Staphylococcus aureus* strains isolated in Brazil. *Diagn. Microbiol. Infect. Dis.*, 16 : 9-16, 1993.
- 16) Sheretz, R. J., Reagan, D. R., Hampton, K. D., Robertson, K. L., Streed, S. A., Hoen, H. M., Thomas, R., Gwaltney, J. M. Jr. : A cloud adult : the



- Staphylococcus aureus*-virus interaction revisited. Ann. Intern. Med., 124 : 539–547, 1996.
- 17) Meier, P. A., Carter, C. D., Wallace, S. E., Hollis, R. J., Pfaller, M. A., Herwaldt, L. A. : A prolonged outbreak of methicillin-resistant *Staphylococcus aureus* in the burn unit of a tertiary medical center. Infect. Control. Hosp. Epidemiol., 17 : 798–802, 1996.
  - 18) Cetinkaya, Y., Kocagoz, S., Hayran, M., Uzun, O., Akova, M., Gursu, G., Unal, S. : Analysis of a mini-outbreak of methicillin-resistant *Staphylococcus aureus* in a surgical ward by using arbitrarily primed-polymerase chain reaction. J. Chemother., 12 : 138–144, 2000.
  - 19) Ahmed, A. O., van Belkum, A., Fahal, A. H., Elnor, A. E., Abougroun, E. S., VandenBergh, M. F., Zijlstra, E. E., Verbrugh, H. A. : Nasal carriage of *Staphylococcus aureus* and epidemiology of surgical-site infections in a Sudanese university hospital. J. Clin. Microbiol., 36 : 3614–3618, 1998.
  - 20) Mueller-Premru, M., Muzlovic, I. : Typing of consecutive methicillin-resistant *Staphylococcus aureus* isolates from intensive care unit patients and staff with pulsed-field gel electrophoresis. Int. J. Antimicro. Agents., 10 : 309–312, 1998.
  - 21) Lessing, M. P., Jordens, J. Z., Bowler, I. C. : When should healthcare workers be screened for methicillin-resistant *Staphylococcus aureus*? J. Hosp. Infect., 34 : 205–210, 1996.
  - 22) Knaus, W. A., Zimmerman, J. E., Wagner, D. P., Draper, E. A., Lawrence, D. E. : APACHE—Acute physiology and chronic health evaluation : A physiologically based classification system. Crit. Care Med., 9 : 591–597, 1981.
  - 23) Garner, J. S., Jarvis, W. R., Emori, T. G., Horan, T. C., Hughes, J. M. : CDC definitions for nosocomial infections. Am. J. Infect. Control., 16 : 128–140, 1988.
  - 24) Garner, J. S. : Guideline for isolation precautions in hospitals. The hospital infection control practices advisory committee. Infect. Control. Hosp. Epidemiol., 17 : 53–80, 1996.
  - 25) National Committee for Clinical Laboratory Standards. 2000. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically ; approved standard — fifth edi., M7-A5, National Committee for Clinical Laboratory Standards, Villanova, Pa.
  - 26) Yasunaka, K., Kono, K. : Epidemiological study of methicillin-resistant *Staphylococcus aureus* at Fukuoka University Hospital. Microb. Drug. Resist., 5 : 207–213, 1999.
  - 27) Tenover, F. C., Arbeit, R. D., Goering, R. V., Mickelsen, P. A., Murray, B. E., Persing, D. H., Swaminathan, B. : Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis : criteria for bacterial strain typing. J. Clin. Microbiol., 33 : 2233–2239, 1995.
  - 28) Aoki, Y., Kashiwagi, H. : Significance of nasal carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) by medical staff in nosocomial infection. Kansensyogaku Zasshi., 64 : 549–556, 1990.
  - 29) Tammelin, A., Klotz, F., Hambraeus, A., Stahle, E., Ransjo, U. : Nasal and hand carriage of *Staphylococcus aureus* in staff at a Department for Thoracic and Cardiovascular Surgery : endogenous or exogenous source? Infect. Control. Hosp. Epidemiol., 24 : 686–689, 2003.

(Received on November 10, 2003,

Accepted on December 24, 2003)