

Methicillin-resistant *Staphylococcus aureus* in a general intensive care unit

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SUMMARY

Methicillin-resistant *Staphylococcus aureus* (MRSA) has presented special problems in intensive care units (ICUs) because of the difficulties in implementing infection control measures. The prevalence and rate of acquisition of MRSA were studied over thirty months in a nine-bed ICU. Nasal and groin swabs were taken on admission and then weekly, and other cultures as clinically indicated.

Of 1361 admissions 119 were MRSA-positive on arrival. 21 cases had been identified before admission and the remainder were detected by screening; in 57 the positive result was known only after discharge. Of the 1242 admissions initially negative 68 acquired MRSA while in the ICU. The ICU had no known MRSA-positive patients on 185 (20.3%) of 914 days, the longest sequence being 17 days. Positive patients occupied 1387 (16.9%) of the 8226 available bed days. Length of stay predicted the risk of acquiring MRSA. Estimated from patients who completed each weekly screening cycle, the risk was 7.5% per week in the first week and 20.3% per week thereafter. The risk was not influenced by initial APACHE II score, the use of haemofiltration, or the number of MRSA-positive patients in the unit. The data suggest that a further 38 of those discharged between weekly screenings acquired MRSA, giving an incidence of 8.5%. MRSA was grown from blood in 17 patients, and from sputum in 53 (ICU-acquired in 18% and 47%).

This study suggests that nearly 10% of admissions to a general ICU will be MRSA-positive, of whom only half will be identified before discharge. With standard prevention the risk of previously negative patients acquiring MRSA approximates to 1% per day in the first week and 3% per day thereafter, with nearly one-fifth progressing to bacteraemia; one-half will have MRSA in sputum. Patients with longer stays constitute a high-risk minority for whom additional measures such as decontamination with oropharyngeal and enteral vancomycin should be considered.

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA), first described in the 1960s,¹ is now endemic in many hospitals.² Infection and colonization with MRSA may be more frequent in the intensive care unit (ICU) than in general wards.³ The ICU is important in the wider dissemination of MRSA, since patients are admitted from and discharged to many wards and other hospitals.^{3,4} The risk of acquiring MRSA in the ICU is increased by severity of illness,⁵ length of stay,^{5,6} use of intravascular devices,⁷ and the intensity of exposure to infected patients.⁸ Infection control measures include screening,^{9,10} segregation of positive patients,¹¹ attempted eradication of carriage¹² and good standards of general hygiene¹³—in particular, hygienic hand disinfection.¹⁴ This study was undertaken to determine the prevalence of MRSA in patients admitted to our ICU and to estimate the risk, for those initially free of the organism,

of acquiring MRSA while in the unit. One aim was to find a simple method for identifying patients at high risk of acquiring the organism.

PATIENTS AND METHODS

The Medway Maritime Hospital serves a population of 360 000 in urban north Kent. The ICU has nine beds, including two side rooms and a two-bedded bay, and admits adults from all specialties within the hospital (there is no cardiothoracic surgery); it also admits from and transfers to other units in Kent, and on occasion more distant hospitals.

Infection-control practice includes hygienic hand disinfection for all persons entering and leaving ICU and after each patient contact. Basins and alcohol-based preparations (chlorhexidine gluconate in isopropyl alcohol, and ethyl alcohol gel) are widely available. The floor, work surfaces, equipment and curtain rail by each bed are cleaned daily. When a patient is discharged this cleaning process is repeated and the mattress is scrubbed. MRSA-positive

patients are clearly identified as such; whenever possible they are placed in a side room, and separate cohorts of nurses care for positive and negative patients. Staff attending positive patients wear disposable gloves and aprons and hand-wash with triclosan-containing preparations. At discharge the bed curtains are replaced and unused disposables are discarded, in addition to the usual cleaning.

Nasal and groin swabs were taken from all patients on admission and weekly thereafter. They were incubated in brain–heart infusion broth for 18–24 hours at 37 °C. A loop of the broth was cultured on a OXA-R-*Staph* screen agar (Biomérieux) and incubated for 24 hours. Suspicious colonies were identified by tube coagulase and the VITEK (Biomérieux) automated identification system. Sensitivities and methicillin resistance were tested by VITEK and methicillin strip agar diffusion. Swabs were not taken at discharge. Other cultures were taken as clinically indicated. Patients in whom nasal and/or groin swabs grew MRSA were treated for 5 days with mupirocin and/or triclosan preparations. Those in whom MRSA was grown in blood culture were treated with intravenous vancomycin.

Details of all admissions were entered on a database. The day-one acute physiological and chronic health evaluation score (APII)¹⁵ was calculated, and hospital outcome was recorded. Within the ICU a record was kept of all patients known to be MRSA-positive, and the control-of-infection department prepared monthly returns of all MRSA-positive cultures taken from patients in the ICU. These three sources, plus individual patient records have been used in this study, which includes all admissions from 1 October 2001 to 31 March 2004.

For the sake of brevity the term MRSA-positive is used to describe patients in whom MRSA was grown from any site. Patients were considered to be positive from the date on which the culture that yielded MRSA was taken, and to have remained so for the rest of their admission. Mortality refers to death within hospital.

As swabs were not taken at discharge, the rate of acquisition was estimated by considering those patients who completed each weekly screening cycle. Those at risk were patients who were MRSA-negative at the beginning of that week, and the acquisition rate was the proportion who had a positive screening swab at the end of, or any positive culture during, the week. Results are expressed as mean with standard deviation (SD) or with 95% confidence intervals (CIs).

RESULTS

There were 1472 admissions. 94 were too brief for APACHE II scoring, and 17 had incomplete data; thus 1361 admissions were analysed. The 1361 admissions were of 1252 patients; 86 had two admissions, and 10 had three or

more. Table 1 lists the age, day-one APII score, and length of ICU stay by source of admission.

119 of the 1361 admissions (8.7%, CI 7.2–10.2%) were of patients (total 111) MRSA-positive on arrival in the ICU. Of the 8 readmitted, 7 returned within 28 days, and one 8 months after the initial admission on which MRSA was identified. The 119 admissions had 151 positive cultures—nose 76, groin 40, sputum 21, blood 5, and 9 from other sites. The positive MRSA status was known before admission in 21 of the 119 and detected by initial screening in the remainder. In 57 the positive result was known only after discharge; their length of stay was 3.2 SD 2.4 days.

Table 2 lists the positive admissions by source. MRSA-positive patients from the wards had been there for 8.9 SD 13 days before ICU admission, compared with 5.6 SD 13.2 days for negative patients (not significant). Of the 16 MRSA-positive admissions from the emergency department (A&E), 15 had been inpatients at least once in the preceding year.

In each calendar month there were between 0 and 7 MRSA-positive admissions. There was no seasonal pattern and no increase with time—62 in the first fifteen months, and 57 in the second.

Of the 1242 admissions MRSA-negative on initial screening, 68 (5.5%, CI 4.2–6.8%) subsequently had a positive culture from either a routine weekly swab or some other site. There was no increase with time—33 in the first fifteen months, 35 in the second. The 68 admissions were of

Table 1 Details of admissions

Source	No.	Age (SD)	APII (SD)	LOS (SD)
Wards	504	61.3 (16.0)	17.5 (7.2)	7.7 (9.0)
Theatre	479	65.9 (15.7)	12.0 (6.1)	4.3 (5.6)
A&E	308	53.4 (18.5)	17.0 (7.5)	5.4 (5.8)
Other ICU	70	58.5 (16.6)	14.5 (6.3)	8.2 (6.6)
All	1361	60.9 (17.2)	15.3 (7.3)	6.0 (7.4)

A&E=accident and emergency department; APII=acute physiological and chronic health evaluation score; LOS=length of stay on intensive care unit (ICU); SD=standard deviation

Table 2 Prevalence of MRSA in admissions from each source

Source	No.	MRSA-positive	% positive (CI)
Wards	504	56	11.1 (8.4–13.8)
Theatre	479	33	6.9 (4.0–9.7)
A&E	308	16	5.2 (2.7–7.7)
Other ICU	70	11	15.7 (7.1–24.2)
All	1361	119	8.7 (6.2–10.2)

MRSA=methicillin-resistant *Staphylococcus aureus*; CI=95% confidence interval. See Table 1 for key to other abbreviations

Table 3 Details of those MRSA-negative on admission who did and did not acquire the organism while on intensive care unit

All admissions at risk	Acquired MRSA	Did not acquire MRSA
No.	68	1174
Male/female	1/1	1.3/1
Age (SD)	59.3 (16.3)	61.0 (17.4)
APII (SD)	19.0 (6.5)	14.9 (7.4)*
LOS (SD)	21.1 (11.7)	4.9 (7.1)*
Length of stay 8 days or less		
No.	6	985
APII (SD)	19.5 (11.3)	12.5 (7.3)
Length of stay > 8 days		
No.	62	189
APII	19.7 (6.4)	17.9 (6.5)

**P* < 0.001; other comparisons *P* > 0.05. See Tables 1 and 2 for key to abbreviations

67 patients. One patient first acquired MRSA while in the ICU but on admission 2 years later her initial cultures were negative; she then reacquired MRSA. These 68 admissions had 112 positive cultures—nose 26, groin 23, sputum 32, blood 12, and 19 from other sites. The time from admission to first positive culture was 12.8 SD 7.7 days (range 4–62).

Table 3 compares the 68 known to have acquired MRSA with the 1174 at risk who did not. Those who acquired MRSA had a higher day-one APII score and greater length of stay. Of the 991 staying in the ICU for 8 days or less only 6 (0.6%, CI 0.1–1.1%) previously negative were known to acquire the organism. Of the 251 at risk and staying longer than 8 days 62 (24.7%, CI 19.4–30.0%) acquired MRSA.

Table 4 focuses on admissions for whom each weekly screening cycle was completed. Of the 1361 admissions 1047 remained for less than a week, so the 314 completing the first screening cycle constitute a 23% sample of those entering it. The comparable figures for the second, third and fourth weeks are 50%, 58% and 63%. In the first week 7.5% (CI 4.4–10.6%) of those at risk acquired MRSA. The combined results for the second, third and fourth weeks suggest that the risk of acquiring MRSA was 20.3% (CI 14.3–26.3%) per week. The small difference in APII between those who did and did not acquire MRSA was not statistically significant.

In 170 admissions haemofiltration was required. Of these, 11 were MRSA-positive on admission and 19 were known to acquire it while in the ICU. Thus 19 of 159 at risk (11.9%, CI 6.9–16.9%) acquired MRSA. Day-one APII was 21.2 SD 6 in these 19 and 22.2 SD 6 in the remainder, and respective lengths of stay were 28.8 SD 14 and 10.3 SD 10.5 days (*P* < 0.001). Time from admission to first positive culture was 17.1 SD 10.1 days. The estimated acquisition

rates were 5.6% (CI 0.1–11.1%) in the first week and 22.6% (CI 11.4–33.9%) per week thereafter.

Blood culture was positive for MRSA in 17 admissions (Table 5). In 13 of the 17 (76.5%, CI 56.3–96.7%) MRSA was first grown from another site. Neither day-one APII score nor length of stay differed significantly between those with MRSA in blood and those with the organism in other cultures. The incidence of MRSA in either sputum or blood was higher in those acquiring MRSA in the ICU than in those positive on admission. In those acquiring MRSA in the ICU and progressing to bacteraemia, the interval between initial detection of MRSA and positive blood culture was 5.2 SD 5.1 days (range 1–14). Of the 30 MRSA-positive patients who received haemofiltration 4 became bacter-aemic (13%, CI 0.1–25).

Table 6 shows that the ICU was free from MRSA-patients on only 185 of the 914 days of the study, the longest sequence being 17 days. Of the 68 admissions identified as having acquired MRSA on ICU, 12 (17.6%) did so when there were no known positives in the ICU (20.2%

Table 4 Acquisition of MRSA in admissions completing each weekly screening cycle

	At risk	Acquired MRSA	Did not acquire MRSA	Rate % (CI)
First cycle	279	21	258	7.5 (4.4–10.6)
APII (SD)		17.7 (5.9)	17.4 (6.6)	
Second cycle	98	21	77	21.4 (12.2–30.6)
APII (SD)		18.9 (7.5)	16.9 (6.8)	
Third cycle	45	7	38	15.6 (5.6–20.6)
APII (SD)		19.6 (3.2)	18.0 (8.1)	
Fourth cycle	29	5	24	17.2 (4.2–30.2)
APII (SD)		22.0 (6.5)	16.1 (9.2)	

At risk=those admissions completing the screening cycle who were MRSA-negative at the beginning of that cycle. See Tables 1 and 2 for key to abbreviations

Table 5 Incidence of positive blood and sputum cultures in MRSA-positive patients

	All MRSA-positive	MRSA-positive on admission	MRSA acquired in ICU
No.	187	119	68
Positive blood culture	17	5	12
Per cent	9.1	4.2	17.7
95% CI	5.0–13.2	0.6–7.8	8.6–26.7
Positive sputum culture	53	21	32
Per cent	28.3	17.6	47.1
95% CI	21.8–34.8	10.8–24.4	35.2–59.0

See Tables 1 and 2 for key to abbreviations

Table 6 Beds occupied by MRSA-positive patients

No. of beds	0	1	2	3	4	5	6	7
No. of days	185	347	226	112	20	10	10	4
Total days (%)	20.2	38.0	24.7	12.3	2.2	1.1	1.1	0.4

of the study period). Of the 8226 bed-days in the study period, 1387 (15.7%) were taken by MRSA-positive patients. There was no correlation between the number acquiring MRSA in each month and the number of positive admissions or the number of bed days occupied by positive patients, or with bed occupancy. Bed occupancy was 103% over the 30 months, and the lowest monthly figure was 87%.

The hospital mortality for all ICU admissions was 27.9% (CI 25.5–30.3%). Table 7 shows hospital mortality in those with MRSA. It was 58.8% (CI 35.4–82.2%) in those with positive blood cultures, which was not significantly different from the 31.7% (CI 25.2–38.9%) in other MRSA-positive patients. 8 of the 10 with MRSA bacteraemia who died were treated with intravenous vancomycin. In the other 2 the positive blood culture result was known only after death. One patient died sixteen weeks after positive blood culture, but the other 9 all did so within 28 days, mean 9.9 SD 7.0 days, range 1–23.

DISCUSSION

This study illustrates the size of the problem posed by MRSA in the ICU, the practical difficulties of implementing infection control measures, and their limited effectiveness.

The 8.7% prevalence of MRSA in our admissions is comparable to that reported in other studies with routine screening.^{9,10} As our protocol did not include screening cultures at discharge, the 5.5% of previously negative patients with positive cultures in ICU underestimates the true incidence. The fact that those acquiring MRSA had greater length of stay in ICU than the remainder suggests that duration of exposure to the ICU environment determines risk. The weekly screening cycle was used to

estimate the acquisition rate as a function of time. Only those completing each weekly screening cycle were considered: the acquisition rate is the proportion of those MRSA-negative at the start of that week who are positive at the end of that week. Many patients had short stays so only one-quarter of admissions completed the first cycle. The estimate for the first week might not therefore be truly representative, whereas more than half those entering completed each of the later cycles.

According to this method, the risk of acquiring MRSA was approximately 1% per day in the first week and 3% per day thereafter. The reason for this difference is not clear. The APII of those completing the first cycle was not significantly lower than that in the longer staying patients. Shorter staying patients may have had fewer invasive procedures, but the same phenomenon was seen in patients undergoing haemofiltration. Application of these estimates to those discharged between weekly screenings suggests that a further 27 short-stay and 11 longer-stay patients acquired MRSA, increasing the incidence from 5.5% to 8.5%, approaching the 11% reported in studies with discharge screening.¹⁶

Those who acquired MRSA had greater length of stay and higher day-one APII scores than the remainder. However, APII did not differ significantly between those acquiring MRSA and the remainder, either in those staying on the ICU for longer than eight days or in the cohorts completing each screening cycle. Although vascular intervention may be associated with increased risk,⁷ the rate of acquisition was no greater in our patients who required haemofiltration. The risk of acquiring MRSA while in intensive care is largely a function of length of stay; within our population other patient characteristics are of less importance.

In this study some patients acquired MRSA when there were no known positive patients in the unit. Perhaps there were sufficient MRSA-positive patients not identified by weekly nasal and groin swabs¹⁰ to account for this, or perhaps persistence of the organism in the environment was the explanation.¹⁷ Clearly, general infection control measures must not be relaxed when the ICU is apparently free of MRSA.

Table 7 Hospital mortality in MRSA-positive patients

	Patients	APII (SD)	Deaths	Mortality (95% CI)*
MRSA-positive on admission	111	17.7 (7.4)	38	34.2 (25.4–43.0)
MRSA acquired	67	18.9 (6.5)	23	34.3 (22.9–45.7)
Sputum positive	49	18.5 (6.6)	14	28.6 (16.0–41.2)
Blood culture positive	17	18.5 (6.0)	10	58.8 (35.4–81.2)
Blood culture negative	161	18.1 (6.8)	51	31.7 (24.9–38.9)

*Calculated by patients, not admissions. See Tables 1 and 2 for key to abbreviations

MRSA bacteraemia is usually preceded by colonization or superficial infection.^{3,18} In this study the organism had been found earlier at another site in most of those with a positive blood culture. Those acquiring MRSA in the ICU had the highest incidence of positive blood culture. Within this group no additional risk factor for bacteraemia was identified.

The relative failure of our infection control measures has multiple causes.^{19,20} Eradication of a resistant organism requires exclusion of infected patients from the ICU.²¹ Since nearly 10% of our admissions are MRSA-positive the reservoir of infection is constantly refreshed. Identification, segregation, and treatment of infected patients can reduce spread,⁹ but each has practical difficulties.²⁰ Only a minority of positive patients are known before admission, it takes time to identify the remainder, and nasal and groin swabs will not detect all colonized patients.¹⁰ Side rooms and the separate cohort of nurses are not always available, and the agents used to treat colonization and superficial infection are only partly effective.²⁰ Good basic hygiene, hygienic hand disinfection in particular, will reduce cross-infection rates,^{13,22} but in practice compliance is imperfect.²³

The spread of MRSA has two broad consequences. Commonly the organism does little harm to the patient but adds to the pool of MRSA carriers. In a minority there is progression to septicaemia, pneumonia, or other deep-seated infection causing serious morbidity or death.^{24,25} Our patients can be divided by length of stay. The majority remain for a few days and have a small risk of acquiring MRSA and a low incidence of bacteraemia. The minority staying for longer than a week have a higher and continuing risk of acquiring the organism, with almost one-fifth of those who do acquire it progressing to MRSA bacteraemia and one-half to positive sputum cultures. Currently the low-risk majority and the high-risk minority are managed with the same infection control protocol. Protective isolation for the longer-staying patients is an attractive but impractical idea. This minority occupy more than half the total available bed days and our ICU does not have the capacity to isolate these patients in addition to those who are MRSA-positive.

Two research groups have suggested another approach.^{26,27} Where MRSA was endemic a careful policy of surveillance cultures and enteral and oropharyngeal vancomycin reduced progression from carriage to bacteraemia and the incidence of ventilator-acquired MRSA pneumonia,^{26,27} and the overall incidence of MRSA within the ICU fell.²⁷ The use of enteral vancomycin was not associated with the appearance of resistant or insensitive staphylococci or enterococci.²⁷ It has been suggested that this strategy should be employed in high-risk ICU patients.²⁸

Current measures to prevent spread of MRSA and progression to bacteraemia enjoy limited success, and their

ever more vigorous application might be neither practicable nor beneficial.^{29,20,28} Length of stay greater than one week identifies a group at high and continuing risk of both acquiring MRSA and progressing from carriage to serious infection. There is now evidence that in these high-risk patients treatment of MRSA carriage with enteral vancomycin in addition to standard control-of-infection practice is effective and safe.^{25–27} Clinicians responsible for patients in intensive care need expert advice on the wider application of this promising treatment.

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