

AN OUTBREAK OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* IN A NEONATAL INTENSIVE CARE UNIT IN SINGAPORE: A 20-MONTH STUDY OF CLINICAL CHARACTERISTICS AND CONTROL

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ABSTRACT

Methicillin resistant Staphylococcus aureus (MRSA) is a major infection control problem in many countries. There have been many reports of outbreaks in neonatal nurseries including, in our part of the world, Australia, Hong Kong and Malaysia.

A recent outbreak of MRSA in the neonatal intensive care unit in the Kandang Kerbau Hospital, Singapore, presented us with the opportunity to study the clinical characteristics of the outbreak and the effects of infection control measures.

Neonates admitted to the neonatal intensive care unit were studied over a 20-month period. They were all screened for nasal colonisation on admission and weekly thereafter. Infections were documented. Over this period there were altogether 2,576 admissions of which 85 infants had nasal colonisation with MRSA (3.3%) and 28 developed infections (1%). Although the majority of infants colonised by MRSA suffered no ill effects, 3 had septicaemia and 2 had septicaemia with osteomyelitis. There were no deaths.

Standard infection control measures with barrier nursing and the use of mupirocin nasal ointment were ineffective, and control was achieved only after strict cohorting together with the use of mupirocin was instituted. This was done without additional costs to the department and without additional nurses or doctors.

Keywords: Methicillin-resistant *Staphylococcus aureus*, neonatal nosocomial infection

SINGAPORE MED J 1994; Vol 35: 277-282

INTRODUCTION

Resistance to methicillin among *Staphylococcus aureus*, rapidly followed its introduction in 1959⁽¹⁾. In recent years, nosocomial outbreaks of methicillin-resistant *Staphylococcus aureus* (MRSA) have become a major infection control problem in many countries⁽²⁻⁴⁾. In our part of the world, outbreaks have been reported in neonatal nurseries in Australia⁽⁵⁾, Hong Kong⁽⁶⁾ and Malaysia⁽⁷⁾. In Singapore, MRSA is present in hospitals⁽⁸⁾.

Much advice is also now available to control these outbreaks^(4,9-11).

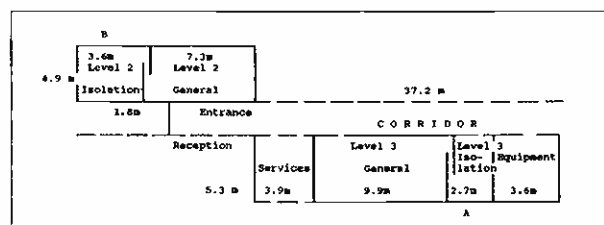
A recent outbreak of MRSA in the neonatal intensive care unit (NICU) of our hospital, a University affiliated teaching hospital, presented the opportunity to study the clinical characteristics of the outbreak and the effects of infection control measures.

The Neonatal Intensive Care Unit

The Kandang Kerbau Hospital (KKH) is the largest maternity hospital in Singapore with 516 beds. From September 1990 to April 1992 there were 24,686 deliveries. There are 2 NICUs serving the hospital on separate floors of one building, each with the same complement of beds but under separate management. The description of the outbreak and its control is confined to one

NICU, the Department of Neonatal Medicine II (henceforth referred to as the department.) The NICU is located on one floor and consists of 8 ventilator (Level 3) beds in a general area and 22 non-ventilator (Level 2) beds in a general area on the same floor. There are isolation areas capable of taking 4 ventilator beds (A) and 6 non ventilator beds (B) Fig 1.

Fig 1 - Floor plan of department of Neonatal Medicine II



Neonates are admitted for Level 2 (L2) or Level 3 (L3) care based on patient acuity and there is free transfer of patients between the 2 main patient areas. All babies are in-born and nurses are fixed for L2 or L3 areas except in times of shortage when temporary cross-coverage occurs. The nurse to patient ratio in L3 was maintained at 1:2.5 and in L2 at 1:5 or 6 on all shifts wherever possible. There are no re-admissions and no inter-hospital transfers into the nurseries. Doctors and other staff are common to all areas. There is a separate room for gowning and hand-washing at the entrance to each nursery and there are 7 sinks in L2 and 5 sinks in L3 nurseries. Gowning with disposable plastic gowns is practised in the Department and there is liberal supply of 4% (w/v) chlorhexidine gluconate (Hibisol ICI), 0.5% (w.v) chlorhexidine in 70% alcohol (Hibisol ICI) and 7.5% (w/v) povidone iodine (Betadine). Umbilical toilet is done by the nurses daily with chlorhexidine. The standard antibiotic therapy for suspected sepsis is ampicillin and gentamicin. Neonates who are recovering are discharged either directly from the L2 nursery or spend some time in L1 nurseries in another part of the hospital prior to discharge.

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The Outbreak

MRSA has been resident in the hospital for many years. Hospital infection control surveillance was practised but no reports had been published.

In 1990, a new Infection Control Committee was formed and surveillance showed a high incidence of MRSA in the department (Fig 2). This was first observed in September 1990 and showed a rising trend in the subsequent 2 months. Consequently it was decided to study the characteristics of the outbreak and the effect of various control measures that were required to achieve a satisfactory outcome. We defined this as absence of new infection and a very low colonisation rate or none at all. The period covered 20 months, from September 1990 to April 1992.

Characteristics of MRSA

During the period of the study, there were 112 isolates of MRSA from staff and patients (Fig 2). All were resistant to methicillin, erythromycin, gentamicin and amikacin and there was a common antibiotic sensitivity to chloramphenicol, clindamycin, vancomycin, fusidic acid and cotrimoxazole.

PATIENTS AND METHODS

For the period of the study the NICU admitted 2,576 neonates. One hundred sixty-five neonates (6.4%) were of very low birth weight (less than 1.5 kg). Staff consisted of 14 doctors and 56 nurses (37 were SRN and 19 assistant nurses). Two thousand, two hundred and seven (86%) of the 2,576 admissions were Level 2 and 369 (14%) were Level 3 cases.

Infection Surveillance

This was carried out by a single Infection Control Nurse using Centers for Disease Control (Atlanta) Guidelines⁽¹²⁾. Surveillance was started under the new Infection Control Committee in September 1990.

Screening consisted of nasal swabs only. Patients were screened for MRSA on admission and then weekly from day 3

onwards. Staff were screened weekly.

The mean hospital infection rate for neonates in 1990 was 0.9% per month. MRSA was a problem only among neonates in the hospital and the MRSA infection rate for the month of September 1990 for the department was 4%.

MRSA Control Measures

The strategy for control of MRSA infection was as follows:

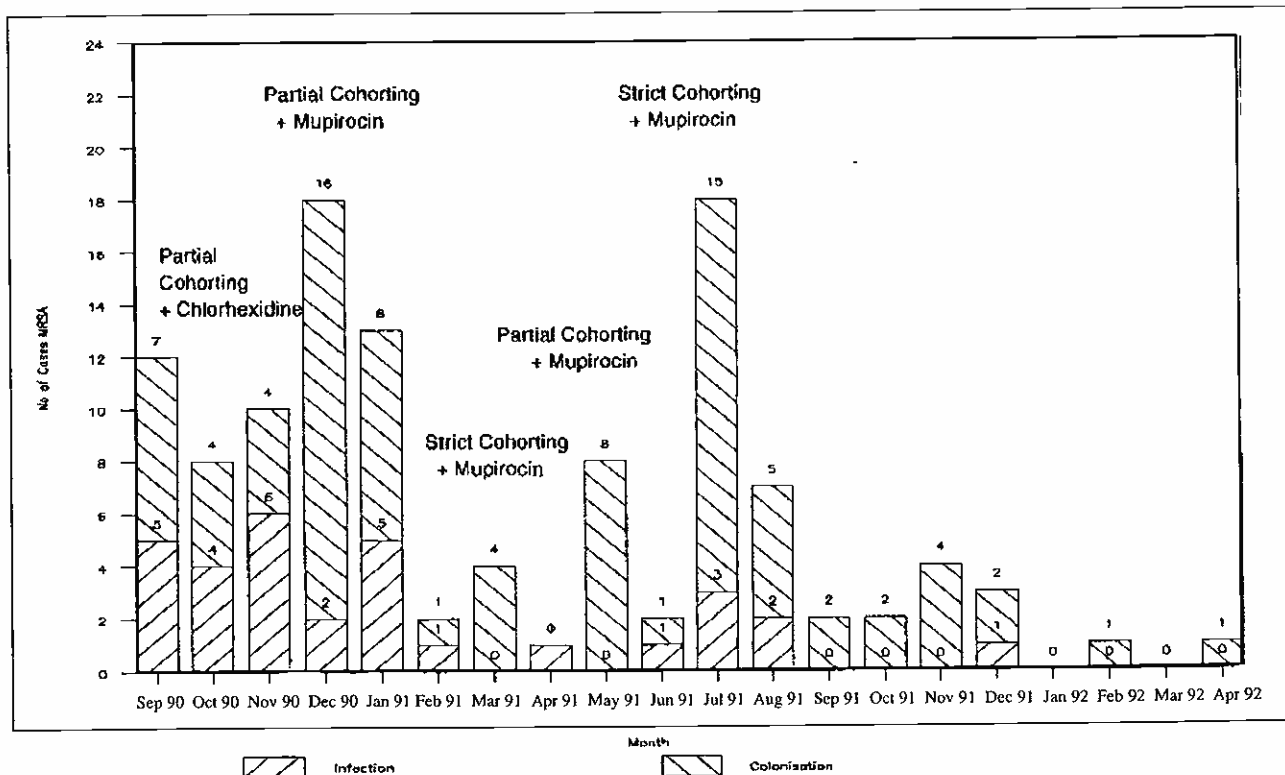
- Patient isolation
- Handwashing before and after contact with patients or their environment to be stressed
- Barrier nursing
- Strict cohorting of nurses on all shifts
- Adequate nurse-patient ratio on all shifts
- Discharge patients early where possible
- Nasal swab surveillance of patients on admission and then weekly from Day 3 onwards
- Staff screening for MRSA carriage weekly
- Treat colonised/infected patients and staff

Isolation of colonised or infected infants

This was carried out in several stages: in November 1990 to February 1991, neonates were segregated into Isolation Areas A and B (Fig 1) but nurses were not (partial cohorting) as there were insufficient numbers of nurses. When segregation of patients alone was deemed to have failed ie persistence of infection and colonisation, or presence of any MRSA infection, a plan for strict cohorting of patients and nurses was put into effect in March 1991 (Fig 2).

In May 1991, owing to shortage of isolation rooms due to other infections, strict cohorting had to be abandoned and segregation or partial cohorting was again practised. This was again revised in mid July 1991 and strict cohorting has been implemented to the present. In September 1991, with fewer

Fig 2 – MRSA Rate Sep 1990 to Apr 1992



numbers of MRSA it was possible to cohort all affected neonates into a single isolation room.

Surveillance of staff, infants and environment

Routine nasal swabbing of infants was done on admission and weekly thereafter. For all staff, weekly nasal swabs were performed in November and December 1990. A repeat screening which included doctors and nurses of the delivery room and operating theatre, was carried out in February and April 1991 (Table I). However, when results showed the nurse carriage to be minimal (Table II) weekly nasal swabs were performed only on doctors, nursing officers and the Infection Control Nurse. These personnel were common to both L2 and L3 nurseries. This routine has been in place from January 1991 to date and mass screening implemented only during further outbreaks if these should occur.

Table I – Results of screening of staff and neonates in February 1991 and April 1991

Nasal Swab Samples	No. (%) Sampled		No. (%) Positive for MRSA	
	February	April	February	April
Nurses	50 (100)	50 (100)	0 (0)	0 (0)
Doctors	14 (100)	14 (100)	1 (7)	1 (7)
Others	49 (100)	–	0 (0)	–
Neonates	136 (100)	184 (100)	1 (1)	0 (0)
Labour ward nurses	87 (100)	–	0 (0)	–
Operating theatre nurses	98 (100)	–	0 (0)	–
Obstetric doctors	31 (100)	–	0 (0)	–

Table II – Results of screening of staff, neonates and environment in November 1990

Nasal Swab Samples	No. (%) Sampled	No. (%) Positive for MRSA
Nurses	44 (100)	1 (2)
Doctors	14 (100)	4 (29)
Others*	49 (100)	0 (0)
Neonates	137 (100)	13 (9)
Environmental swabs+	60	0

* Nursing aides, ward clerks, laboratory technicians, physiotherapists, radiologists, visiting consultants.

+ Includes wash basins, liquid soaps, tubings, humidifiers, ultrasound gels, plastic aprons, air samples.

Nasal carriers were initially treated with chlorhexidine (1%) cream applied to the anterior nares three times a day for 5 days and followed up until 3 consecutive weekly cultures were negative. This was effected in mid November 1990 to end December 1990 and was changed to mupirocin (2%) nasal ointment applied three times a day for 5 days and followed up until 3 consecutive weekly cultures were negative. The change to mupirocin was effected at end December 1990 when chlorhexidine cream was found to be ineffective in abolishing nasal carriage.

Environmental cultures were also performed in November 1990.

Infection control talks

Technique and protocol for hand washing was highlighted through posters and regular talks were conducted by Infection Control team members whenever new nurses or doctors joined or when an increase in infection and/or colonisation was observed.

Finger impression plates

The infection control nurse obtained 2 to 3 finger impression plates a day on a random sample of staff during her daily nursery round whenever there was an increase in infection and/or

colonisation until the rate came down. This was used as a reinforcement and reminder to staff of the need for hand-washing.

Bacteriology

Nasal swabs taken from patients and staff were cultured on 5% blood agar plates. Both these plates and the finger impression plates were incubated overnight at 35°C. The presence of *Staphylococcus aureus* was determined by its colonial characteristics and by the formation of a solid clot in the tube coagulation test. Antibiotic susceptibility testing of suspected *Staphylococcus aureus* colonies to oxacillin was performed using the agar disc diffusion method and the method for confirming intrinsic oxacillin resistance as recommended by the National Committee for Clinical Laboratory Standards⁽¹³⁾.

Phage typing and plasmid analysis were not carried out as there were no laboratory facilities for these studies.

RESULTS

For the 20-month period (September 1990 to April 1991) there were a total of 85 nasal colonisations with MRSA (3.3% of admissions) and 28 infections (1% of admissions). One infant had 2 infections (Table III).

Table III – No. of MRSA cases Sep 1990 – Apr 1992

	No. of cases
Infection	28
Colonisation	85

Infections and colonisation

Although the majority of babies colonised by MRSA suffered no ill effects, a number of infections of variable severity occurred (Table IV). None were fatal.

Two infants had septicaemia and osteomyelitis while 3 had septicaemia alone. There were 11 infants diagnosed with pneumonia and treated with vancomycin and fusidic acid. These infants had clinical features of infection plus radiological evidence of pulmonary infiltrates and MRSA in the tracheal aspirate. All responded promptly to treatment.

Clinical features of the neonates with deep or disseminated infections are shown in Table V. All but 3 infants were very low birth weight (under 1.5 kg) and all were premature. All babies were on ventilatory support and over three-quarters had indwelling arterial and/or central venous lines. All but 2 were treated with vancomycin and fusidic acid. Deep or disseminated infections were therefore confined mainly to neonates under 1.5 kg and all 5 neonates with septicaemia were under 1.5 kg. All but 2 survived. These 2 infants died of unrelated causes.

Table IV – Types of MRSA infection

Type of infection	No. of infection	No. of death	Associated problem
Superficial			
Conjunctivitis	7	0	–
Omphalitis	2	0	–
Minor skin	3	0	Hydrocephalus with V-P shunt (1 patient)
Total	12		
Deep or disseminated			
Septicaemia	3	0	–
Sepsis with osteomyelitis	2	0	–
Pneumonia	11	0	–
Total	16		

Table V – Clinical features of neonates with deep or disseminated infections

Patient No.	Birth Weight (gm)	Gestation in weeks	Ventilatory Support	Central Lines	Peripheral Arterial Lines	Diagnosis	MRSA Infection	Day of Infection	Treatment	Outcome
1	1305	30	Nil	Nil	Nil	Premature	Sepsis	11	Vancomycin Fusidic Acid	Discharged well D.54
2	875	27	Yes	Yes	Yes	Premature	Pneumonia	13	Vancomycin	Died D124
3	1430	36	Yes	Yes	Yes	Premature RDS	Pneumonia	15	Vancomycin	Discharged well. D52
4	1380	28	Yes	Yes	Yes	Premature RDS	Pneumonia Sepsis with OM (Lt elbow)	32	Vancomycin	Discharged well. D80
5	1055	26	Yes	Yes	Yes	Premature RDS	Sepsis	34	Vancomycin Fusidic Acid	Discharged well. D82
6	1305	27	Yes	Yes	Yes	Premature RDS	Pneumonia	14	Vancomycin	Still in nursery (with chronic lung disease)
7	1640	33	Yes	Nil	Yes	Premature RDS	Pneumonia	11	Vancomycin Fusidic Acid	Discharged well D36
8	1515	28	Yes	Yes	Yes	Premature	Pneumonia	10	Vancomycin Fusidic Acid	Discharged well D59
9	1200	30	Yes	Yes	Yes	Premature RDS	Sepsis with OM (Lt radius & ulnar)	9	Vancomycin	Discharged well D63
10	925	29	Yes	Yes	Nil	Premature	Pneumonia	22	Vancomycin Fusidic Acid	Discharged well D53
11	2220	31	Yes	Yes	Yes	Premature RDS	Pneumonia	9	Vancomycin	Discharged well D104
12	770	29	Yes	Yes	Yes	Premature RDS	Sepsis	34	Vancomycin Fusidic Acid	Discharged well D104
13	1260	26	Yes	Yes	Yes	Premature RDS	Chest tube site	5	Vancomycin	Died D8
14	755	24	Yes	Yes	Yes	Premature RDS	Pneumonia	21	Clavulanic Acid (Augmentin)	Discharged well D93
15	1045	28	Yes	Yes	Yes	Premature RDS	Pneumonia	21	Vancomycin	Discharged well D 78
16	1240	28	Yes	Yes	Yes	Premature RDS	Pneumonia	19	Vancomycin	Discharged well D98

Abbreviations: RDS: Respiratory Distress Syndrome

D: Day

Screening of staff, neonates and environment

The results of screening in November 1990 showed that among staff the majority of the carriers in the Department were doctors (Table II). Nurses were relatively free of MRSA. Environmental cultures were all negative for MRSA.

The repeat screening in February and April 1991 again showed the nurses to be clear of MRSA, while there was a single positive isolate from a doctor and a neonate (Table I). This was the same doctor who had repeated nasal colonisation in all 3 mass screening examinations. After the last treatment in April 1991 his nasal carriage was eradicated. Delivery and Operating Theatre staff were clear of MRSA.

Infection control measures

Earlier measures with segregation of patients and chlorhexidine nasal cream for carriers in November and December 1990 were

found to be ineffective and the outbreak peaked in mid December 1990. Mupirocin nasal ointment and segregation of patients (partial cohorting) that followed showed some promise initially in that colonisation decreased dramatically although infection increased. However, colonisation rose again in March 1991.

Strict cohorting reduced colonisation to zero and infection to only a single case in April 1991.

In May through July 1991, colonisation peaked again and infections rose as a result of partial cohorting.

The effect of the re-implementation of strict cohorting in July 1991 together with mupirocin treatment was dramatic and since December 1991 there has been only isolated incidences of colonisation without any infection.

DISCUSSION

This is the first report of an outbreak of MRSA in a Neonatal

Intensive Care Unit in Singapore and the institution of measures necessary for its control.

Although the majority of the colonised neonates suffered no ill effects, 5 babies had septicaemia with 2 complicated by osteomyelitis. The morbidity is not as high as that reported in one study⁽¹⁴⁾ but higher than that reported in a 2-year study of 4 neonatal units in Australia⁽⁵⁾. Like the latter study there were no deaths from MRSA infection.

It was not surprising that deep or disseminated infections were confined to neonates under 1.5 kg. These neonates have numerous host defence problems because of their extreme prematurity and these have been reviewed recently⁽¹⁵⁾. The technological improvement in neonatal care with the use of invasive procedures in such patients also meant that these infants were exposed to higher infection risks. Whereas the relative contribution of each of these factors to infection risk remains unknown, low birth weight alone has been conclusively linked to infection rate in several studies^(16,17). Within the department doctors were more frequently and consistently found to be carriers than nurses. This finding is contrary to that found in one report⁽³⁾ where the authors found both nurses and doctors were carriers in about equal proportions. The reasons are not obvious as both groups of staff are frequently overworked and nurses had more close patient contact time. However, 8 of the doctors (57%) were residents who rotate through the department every 6 months and were probably less committed to nursery routines than permanent staff.

Our experience at control of the outbreak showed some interesting findings.

Chlorhexidine nasal cream (1%) together with patient segregation (partial cohorting) proved ineffective. Moreover, the majority of neonates continued to be colonised despite the application of the cream.

This was not the experience of an earlier study⁽¹⁸⁾ where the authors found that chlorhexidine nasal cream was effective in a neonatal outbreak. In a recent review⁽¹⁹⁾, however, other authors noted that 1% chlorhexidine nasal cream is less effective than mupirocin in eradicating MRSA.

Mupirocin treatment of the nose and umbilicus of affected neonates and the use of hexachlorophane powder together with patient segregation was successful in the control of one recent outbreak⁽¹⁰⁾. However, it is known that hexachlorophane use in neonates poses some risks⁽²⁰⁾. In our experience, mupirocin nasal ointment (2%) was highly effective in eradication of nasal carriage of MRSA. However, despite this and the use of partial cohorting, the outbreak continued. It is possible that the affected neonates and other undetected carriers could have continued to spread the organism through sites that were not sampled or treated, eg the umbilicus^(10,21) and rectum⁽²²⁾.

In our study, the outbreak was controlled only where strict cohorting of patients and nurses was introduced. It is possible that strict cohorting of patients and all grades of staff alone could control an MRSA outbreak as reported in one study⁽²³⁾. However, this method is costly and requires many nurses, doctors and ancillary staff, which we could not afford. We did not therefore adopt this approach.

Another consideration was whether we should aim for eradication of MRSA or containment of the problem. Our initial goal was eradication but owing to high patient admissions and staff constraints, this goal had to be abandoned for a more practical one of control of spread of MRSA. A similar experience was reported recently⁽²⁴⁾.

We did not aim to trace the source of the outbreak as it was well established before control measures were taken. Moreover, there are no readily available facilities for phage typing or

plasmid analysis in Singapore although the antibiogram of all the isolates suggested a common strain.

Our study, as mentioned earlier, was done at little cost as staff surveillance was limited to periods of outbreaks and routine surveillance was reduced to fortnightly intervals, confined to shared staff – in the latter part of the study. Moreover, we found nasal swabs alone to be effective and no additional nurses were required for our programme. Finally, we were also able to combine isolation facilities into a single isolation room when the outbreak was controlled and this again allowed for optimal use of staff.

Our 20-month experience with an outbreak of MRSA and attempts at control reinforced the principle that with limited resources and at little additional cost, control of the outbreak was still possible. Mupirocin was effective in eradication of nasal carriage in all our cases but this alone was not sufficient to control the outbreak. Our experience reinforces the view that outbreaks are best controlled by having all colonised patients physically isolated and nursed by staff members especially allocated to these patients⁽⁹⁾.

ACKNOWLEDGEMENTS

The authors thank the Chief Executive Officer and the Chairman, Medical Board, Kangar Kerbau Hospital for their support. We also thank Mrs K A Nathan, Secretary, Department of Neonatal Medicine II for typing this manuscript. This study was partly financed by a grant from the Singapore Totalisator Board.

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MOH - CLEVELAND CLINIC FOUNDATION UPDATE

organised by the Ministry of Health

Theme : Diabetas

Date: 3-4 September 1994

Venue: Auditorium
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