

Methicillin-resistant *Staphylococcus aureus* Control in Singapore – Moving Forward

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Abstract

Singapore has a sophisticated healthcare system and is an important referral centre for Asia. Like much of the world, methicillin-resistant *Staphylococcus aureus* (MRSA) is now endemic across its health system. MRSA infection has been associated with considerable attributable mortality, morbidity plus personal and public cost. Nosocomial infections are potentially preventable and need to be considered an unacceptable complication rather than a tolerable by-product of healthcare. Failure to introduce long-term sustainable infection control initiatives is not an option for responsible clinical leaders and managers. Control of MRSA transmission in Singapore is achievable but we need to accept the challenge and acknowledge that it will take perhaps a decade. It requires implementation of many varied infection control measures to be rolled out sequentially and across all health services. Our ambition, in Singapore, should be for hospitals to achieve an inpatient prevalence of <1% MRSA colonised patients. Identified transmission of MRSA should be regarded as a serious breach. Successful control will require extraordinary collaboration, support, resources, accountability and consistency of effort. Currently, efforts are evolving significantly and today, we have a good opportunity to embark on this difficult journey. Implementing infection control initiatives successfully over the next few years will save lives in the future.

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Introduction

The significance of methicillin-resistant *Staphylococcus aureus* (MRSA) is indisputable. Its successful establishment and maintenance as the most important endemic healthcare associated infection (HCAI) results from its reservoir in up to 20% of inpatients and 16% of healthcare workers plus its ability to survive on surfaces for over 12 days.¹⁻⁵ Clinical infection with MRSA represents only 15% of colonised cases.⁶ The remainder have subclinical infection and serve as a “silent reservoir” for MRSA transmission.

Production of biofilm facilitates adherence to prosthetic material making MRSA particularly significant in device-associated infection. Neurosurgical, orthopaedic and cardiac implant infections render a patient incurable without major, often risky, procedures.

MRSA is associated with substantial morbidity and mortality. Clinicians are all too familiar with the poor outcomes of MRSA infection resulting in both substantial financial and non-financial costs to patients.

The knowledge that there are several genetic, phenotypic and epidemiologically varying strains of MRSA complicates an already devastating scenario. The predominant hospital clone in Singapore is changing with the endemic ST 239 clone being progressively replaced by epidemic MRSA-15 (ST 22). With this evolution appears increasing vancomycin resistance heralding a new era in the management of staphylococci. Half of the hospital-acquired MRSA in Singapore have a mean inhibitory concentration (MIC) to vancomycin of 2.0 mg/mL or more.⁷ Furthermore, community-acquired MRSA are increasingly complicating case detection of colonised individuals as high and low risk patients cannot now be so easily defined by past hospital exposure. Now in the US, nearly 50% of hospital-diagnosed MRSA are indeed community acquired.⁸

In Singapore hospitals, 35% of isolates of *S. aureus* are methicillin resistant. It is the dominant hospital-acquired pathogen accounting for 0.31 bacteraemias/1000 inpatient days. This equates to Singapore’s largest hospitals each

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identifying on average, 2 to 3 MRSA bacteraemias per week. In the ICU, the rate is more than 10 fold this (4.48 / 1000 days).⁹

Of MRSA infections, bacteraemia is the most concerning with a high risk of complications including endocarditis, osteomyelitis and deep tissue collections. However, for each of these, there are at least 2 non-bacteraemic infections.¹⁰ Nosocomial MRSA bacteraemia has been associated with nearly 50% thirty-day crude mortality, almost double that of methicillin susceptible *S. aureus* (MSSA) bacteraemia.¹¹ In Singapore's 3 largest hospitals, this equates to almost 1 death, 6 to 9 new clinical infections and up to 60 new individuals colonised per week per hospital. This excessive number of "silently colonised" patients maintains the reservoir and also places those individuals at major risk of future clinical disease.

Interventions to control MRSA are based on early identification of patients colonised with MRSA and subsequent prevention of patient-to-patient spread through infection control measures.¹²

MRSA Control Strategies

Nosocomial transmission of MRSA has been difficult to control in most countries. Countries that have been successful in maintaining a low prevalence of nosocomial MRSA infection have adopted a nationwide and multipronged approach including the so-called "search and destroy" method. It is intuitively sensible; however, it has been difficult to perform well-designed studies to support this approach.¹³⁻¹⁶ The relative contribution of individual infection control approaches has also been difficult to determine, but most agree that the best results are obtained when measures are used together in a concerted manner.¹⁷ Individual components of a proposed approach to nosocomial MRSA infection control in Singapore are discussed below.

Surveillance, Audit Measures, Education and Feedback

Surveillance of health data and auditing outcomes of interventions is important for a number of reasons. It maps and quantifies patterns of infection and enables early detection of epidemiological changes. Trends and effectiveness of interventions can be monitored with areas for further investigation identified. Surveillance and reporting therefore must be performed with consistency to allow benchmarking of results across sites and through time.¹⁸ Standardisation of definitions, laboratory methods, interventions, data maintenance and outcome measures is essential in the monitoring process.

Feedback of transmission and prevalence data to clinical staff is obviously an important component of surveillance yet is often lacking in infection control programmes. Regular

feedback of results from interventions provides motivation for optimal compliance with these measures (be they process or outcome measures) and provides the opportunity for continued education on other standard infection control measures, such as hand hygiene. Hospitalwide feedback of surveillance data was associated with a 50% reduction in the rate of MRSA acquisition in 1 study and a greater than 20% reduction in hospital-acquired infection in another.^{19,20}

The best method of engaging the public and the lay media is debatable. Ideally, if the information is provided constructively and objectively, informing the public of their risks as well as the efforts of healthcare providers, then such education should be helpful for families and possibly add impetus to infection control efforts at the bedside. Any information should be up-to-date and site specific. If information is outdated or reflecting the whole hospital, for instance, then the impact of any information falls considerably.

Screening with Isolation or Cohorting

The British guidelines recommend that samples for screening be taken from the anterior nares, skin lesions, wounds, insertion sites of devices, catheter urine, perineum and sputum (in patients with a productive cough). They recommend screening of all high-risk patients for MRSA carriage at admission as well as screening all inpatients on high-risk units at regular intervals.¹⁸ What constitutes a high-risk patient and unit is determined by local epidemiology.

No studies to date have reported screening as the primary intervention, most have included screening as an additional intervention to contact precautions (either isolating or cohorting MRSA colonisers). Studies assessing universal screening and implementation of contact precautions have produced conflicting results.^{12,21} However, when these interventions have been assessed in areas with high endemic rates of MRSA (which is the case in Singapore) or targeted to use in high-risk units (such as intensive care units) they have been shown to be of substantial benefit, eliminating nosocomial MRSA transmission in 1 ICU study.²¹⁻²⁴

Isolation and cohorting of patients can potentially reduce the bed capacity of a hospital by restricting a patient's type of bed allocation. Rapid diagnostic tests (RDT) utilising molecular methods can determine colonisation status within a few hours compared to conventional microbiological cultures (the gold standard), which can take up to 5 days in practice. Culture for MRSA using selective and differential media results in a shorter turn-around time (24 to 48 hours) and equivalent sensitivity and specificity when compared with conventional culture.^{25,26} It also requires limited training and is relatively inexpensive when compared to molecular methods.²⁵ These methods are now commonly used in most

microbiology laboratories in Singapore. Introduction of RDT could lead to faster determination of MRSA colonisation status and potentially reduce unnecessary pre-emptive isolation. Sensitivity and specificity of RDT in high endemicity settings has been reported to be >90%, and its use in this setting has been predicted to reduce isolation needs by 20%.^{27,28} Use of molecular diagnostic tests in practice, however, does not carry the benefits one might expect. Testing is undertaken in the laboratory which, in general, will mean that they are batched and run during working hours making the result time potentially days. Furthermore, the costs can be several times greater than that of conventional culture. A cheap, fast and accurate point of care test would be ideal.

Whatever surveillance is used, one must be reminded that they are not 100% sensitive; therefore, additional measures, such as hand hygiene, are required to help overcome the less than perfect sensitivities and specificities of these tests.

Maintaining a Database/Collaboration and Information Sharing between Institutions

Many countries in Europe have created national systems for the surveillance of healthcare associated infections (HCAI). The Hospitals in Europe Link for Infection Control through Surveillance (HELICS) has provided a standardised approach to surveillance of HCAI and formed a “network of networks” to enable data from hospitals contributing to national networks also to be submitted to the HELICS database. A significant proportion of patients in Singapore are admitted to institutions more than once and often receive care in more than 1 institution.

There is no specific evidence to support the need for collaboration and information sharing although it is (like most interventions) intuitively obvious. It is cited as crucial by the World Health Organization (WHO).²⁹ The time to achieve MRSA control is directly linked to isolation and cohorting “efficiency”.²⁷ This is clearly linked to knowledge of a patient’s MRSA status. Thus, a central database is crucial in decreasing the need for repeat swabbing (and thus cost) and also instituting early isolation and minimising unnecessary pre-emptive isolation; so called “isolation efficiency”. Any such database would need to find a balance between respecting patient privacy and facilitating information flow to triage and outpatient areas as well as bed management units.

Decolonisation Strategies

Decolonisation of MRSA refers mainly to the use of topical agents (mupirocin intranasally and antiseptic body wash and shampoo) to reduce nasal and skin carriage. Asymptomatic colonisation with MRSA often precedes clinical infection, thus the rationale for decolonisation is to

reduce the risk of clinical infection and the reservoir of MRSA for subsequent spread.¹⁰ A Cochrane systematic review of trials assessing topical decolonisation of MRSA concluded that there was insufficient evidence to support widespread use of this intervention.³⁰ Furthermore, despite initial nasal eradication after mupirocin use, subsequent recolonisation in the longer term is common.^{31, 32} There are also concerns that widespread use and repeated courses of mupirocin could contribute to development of antimicrobial resistance.³³

Although widespread decolonisation remains controversial, in selected groups it is beneficial. Nasal carriage of MRSA has been associated with increased risk of surgical site infections after cardiac surgery and orthopaedic implant surgery. Regimens eradicating nasal carriage perioperatively have resulted in a significant reduction in surgical site infections without selecting for mupirocin resistance.^{34,35}

In Singapore, our reservoir of MRSA carriage is very large. It may be worth considering widespread decolonisation but not until we are confident that in-hospital transmission, and thus the risk of recolonisation, is well controlled. Without eventually tackling the reservoir, it would seem unlikely that the risk of transmission can be sustainably decreased.

Antibiotic Stewardship

The rationale of antibiotic stewardship is to reduce the selection pressure brought about by inappropriate antibiotic use in hospitals and prevent the emergence of resistance. Previous exposure to broad spectrum antibiotics has been identified as a risk factor for MRSA colonisation and infection.^{5,36-39} Some studies have shown reduced rates of MRSA colonisation and infection associated with implementation of antibiotic stewardship programmes.^{40,41} Systematic reviews of the literature, however, have concluded that there is insufficient evidence to support antibiotic stewardship as a means for reducing the prevalence of resistant gram-positive bacteria.^{42,43} Antibiotic stewardship is also very labour intensive, and in the setting of high endemic prevalence of multidrug-resistant organisms, difficult to implement effectively without significantly increasing the number of specifically-dedicated medical staff.

Environmental Cleaning

Environmental cleaning has been described as a component in controlling MRSA transmission. An observational study involving increased cleaning hours and adherence to a comprehensive cleaning protocol concluded that increased cleaning in addition to other infection control measures was associated with a reduction in MRSA colonisation. The increased cost of cleaning was

thought to be less than one third of the estimated cost saved in treatment of MRSA infection.⁴⁴ Evidence regarding the value of enhanced environmental cleaning alone is lacking. Enhanced environmental cleaning may serve as an adjunct to other infection control measures, however, should not receive priority over the other interventions discussed.

Current MRSA Control Activities in Singapore

Infection control units within all hospitals encourage standard infection control measures with the use of hand hygiene posters and audits. These audits are not standardised amongst institutions at present, and feedback of the results to the clinical interface is unusual.

Currently, screening for MRSA infection does occur in Singapore; however, practices vary. No hospital in Singapore currently practises universal screening of all admissions. Cohorting and isolation policies and efforts are also inconsistent between and within hospitals. Enforcing cohorting has been difficult without policies in place. All hospitals in Singapore have infection control practitioners that collect and report data on MRSA according to international guidelines and monitor for colonisation and infections. This information is collected on an individual institution basis and is currently not linked to a central database for the access of others. Furthermore, definitions of “new cases” are not uniform with variable efforts applied to establishing past culture results. It is difficult to differentiate new cases of MRSA colonisation or infection when information on previous patient status is not readily available. The Ministry of Health (MOH) requires that hospitals report new cases of MRSA per 1000 deaths and discharges and also per 1000 bed days. This information is not collected uniformly and as a broad hospitalwide measure has no impact at the individual clinician or departmental level. It is important that information to be reported reflects transmission in a way that is useful and encourages improvement. It should identify changing epidemiology perhaps for instance the effects of an intervention.

Hospitals, nursing homes and outpatient settings have various strategies and policies regarding control of MRSA transmission. They are not negotiated together and there is only ad hoc potential for learning from each other’s successes and failures. Different policies may also exist within individual institutions because there is often variable communication between management (in the broad sense) and the clinical level. Also, data sharing of outcomes between the 2 levels is ad hoc.

In Singapore, a collaborative group has been formed specifically to oversee the implementation of the above strategies in 3 hospitals. While it is a good start, it is essential that all of Singapore’s health providers are engaged and collaborating for the long term.

Motivation to Improve

There is public outrage over hospital-acquired MRSA overseas. Patients and their families no longer have the same respect for the hospital “fiefdom” where nosocomial infection is an “acceptable complication”. The lay press of Europe and the US are proactive in promoting this unacceptability and highlights the threat of funders and insurers refusing to meet the costs of such “preventable expense” in the future. In the US, at least 2 states have legislated infection control measures.⁴⁵

In Singapore, it is now increasingly common for individuals to formally complain about their infection and its ramifications in terms of morbidity, mortality and added financial, social and emotional costs. They will seek to have fees waived and furthermore, seek financial compensation.

In addition, *Singapore Medicine* is a product in which medical services are promoted within the region and foreign individuals will attend for diagnostic opinions, services and therapies (such as elective surgery and oncology treatment). From a pure marketing point of view, MRSA infections or any other hospital-linked complications are obviously unacceptable.

Can MRSA Control be Achieved?

Control of MRSA is possible even in high endemicity settings. Modelling based on real life institutions predicts that with implementation of all MRSA control measures discussed above, a reduction of endemic prevalence to less than 1% is possible within 6 to 12 years.²⁷ The drawbacks of doing this are that it involves substantial up front expense, can reduce hospital admission capacity in a setting where bed occupancy is already very high, and it increases demands on infection control resources that may already be limited. The alternative to universal implementation of interventions simultaneously is a gradual roll out. Mathematical modelling still predicts success with this approach, while substantially reducing demands on local resources.²⁷

Scandinavian countries and Australia have been able to control outbreaks and maintain persistently low MRSA prevalence rates with comprehensive infection control measures.⁴⁶ Sustained success in Singapore is possible although the efforts in controlling MRSA when starting from such a high endemic level cannot be overstated. Economic and clinical benefits will surely arise from infection prevention and control in the long term. Success will depend on development of nationwide policies, cooperation and collaboration between health institutions, constant review of processes and clinical outcomes, and the understanding that significant results may only be appreciated in the long term.

Conclusion

Our target should be to have an MRSA hospital inpatient prevalence of <1%. Patient care areas should be aiming for zero transmission with any new cases regarded as an infection control failure. Breaches should be investigated and explained just as they were so successfully addressed in Singapore's SARS outbreak.

Successful control of MRSA is very difficult. Having systems in place to sustain control are even harder. Indeed, while people talk in terms of unrealistic time frames with no specific dedication of resources we cannot overcome the first hurdle. To roll out the many processes, across all hospitals as well as to other healthcare settings, dialysis units, specialist outpatient areas, nursing homes, polyclinics etc will take years. It is only some years after the processes are in place that we can begin to consider a prevalence <1%. Where processes are implemented smoothly and isolation efficiency is good, realistic time frames remain in excess of 10 years.

Changing processes and mindsets are the greatest challenge in hospital management and infection control. Singapore is a very successful country built on an axiom of long term planning. It is this ability to engage the long-term view together with strong collaboration and commitment of stakeholders that can bring about MRSA control.

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