Community-associated Methicillin-resistant Staphylococcus aureus: Overview and Local Situation
Limin Wijaya, MBBS (Mel), MRCP (UK), Li-Yang Hsu, MBBS, MRCP (UK), DTMH (Gorgas), Asok Kurup, MBBS, MRCP (UK), FAMS

Introduction

The emergence and spread of methicillin-resistant Staphylococcus aureus (MRSA) isolates from the community that are distinct from their archetypal healthcare-associated counterparts (HA-MRSA), CA-MRSA isolates are usually susceptible to multiple non-beta-lactam antibiotics and cause a distinct spectrum of infections in epidemiologically disparate populations – in particular, cutaneous abscesses, necrotising fasciitis and necrotising pneumonia. They arise from a broader genetic background, and possess differing virulence genes. We aim to describe the distribution of different molecular subtypes of CA-MRSA among various regions and discuss briefly the implications of CA-MRSA from a local perspective.

Methods: Literature review of articles on CA-MRSA, focusing mainly on reports where the genetic background of isolates had been analysed using multi-locus sequence typing (MLST). Singapore data were obtained from the local CA-MRSA database. Results: MLST analysis demonstrated the presence of epidemic subtypes of CA-MRSA within most geographic areas. In parts of the United States, community MRSA infections currently exceed those caused by their methicillin-susceptible counterparts. In Singapore, CA-MRSA infections are increasing, predominantly as a result of the spread of ST30 clones. Conclusion: Available evidence suggests that the emergence of MRSA from the community is not going to be a transient phenomenon. Local guidelines for dealing with this phenomenon at both therapeutic and preventive levels are needed prior to the potential development of a situation mirroring that of meso-endemic HA-MRSA in local hospitals or CA-MRSA epidemics in parts of USA.

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Introduction

The emergence and spread of methicillin-resistant Staphylococcus aureus (MRSA) isolates from the community that are distinct from their archetypal healthcare-associated counterparts (HA-MRSA) marked a critical evolutionary milestone for the organism. In less than 2 decades, particularly in the last 3 years, this initially sporadic phenomenon of community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) has become a global reality, leading to paradigm shifts in the perception and management of staphylococcal infections in countries where CA-MRSA has reached epidemic proportions.1,2

In the past year alone, more than 200 articles on CA-MRSA have been published in the medical literature, of which at least 10 have been review articles. Nevertheless, this is a fast evolving field and the incidence of CA-MRSA infections is increasing at an alarming rate locally. In this article, we aim to provide a brief review of the current state of knowledge regarding this organism, with an emphasis on the implications of this phenomenon in the local context.

The Fundamental Organism

S. aureus is a gram-positive coccoid bacterium named for its tendency to form clusters (“staphyle” is the Greek expression for “bunch of grapes”) and its golden pigmentation (“aureus” is Latin for “golden”) on culture plates. Its importance as a human pathogen has increased in the previous century as a result of the evolution of antimicrobial resistance – to penicillin and subsequently methicillin in particular – and the evolution of medical care resulting in ever-increasing and extensive use of intravascular devices.3 The actual impact was recently estimated by Norskin and co-workers:4 inpatients with
S. aureus infections in US hospitals had approximately 3 times the length of hospital stay, 3 times the total charges (US$48,824 versus US$14,141) and 5 times the risk of in-hospital death when compared to inpatients without infection.

**Methicillin Resistance**

MRSA was first isolated at hospitals in Surrey, UK in 1961, one year after methicillin was introduced. But the mechanism of methicillin resistance was not elucidated until 1981, when Hartman and co-workers discovered altered penicillin-binding proteins (PBP2) in MRSA that had markedly reduced affinity for all currently available beta-lactam antibiotics while maintaining effective cell wall-building activity. PBP2 is encoded by the mecA gene which is carried on a mobile DNA element, the staphylococcal cassette chromosome mec (SCCmec). The other important component of SCCmec, the chromosome cassette recombinase (ccr) genes, encodes for proteins that enable precise integration into and excision from a specific site in the S. aureus chromosome (attBsc). Six SCCmec subtypes have officially been identified to date, varying in size from ~20 kilobase pairs (kb) to 68 kb. SCCmec types I, IV and V possess no antimicrobial resistance determinants other than mecA, whereas SCCmec types II and III possess multiple other resistant determinants such as Tn554 (encodes for macrolide resistance). This partially accounts for the larger sizes of the latter, which is thought to have limited their capability for horizontal transference. It is currently postulated that methicillin resistance did not arise within S. aureus, but was transferred from other staphylococcal species.

**From Hospital to the Community, Worldwide**

Since 1961, successive waves of epidemic MRSA have spread throughout hospitals and other chronic healthcare facilities worldwide to the extent that it is now the most commonly isolated antimicrobial-resistant pathogen in many countries. Despite the apparent success of MRSA in the nosocomial setting, it was originally hardly ever isolated from the community. This observation was attributed to the much slower growth rates of earlier MRSA isolates (probably a result of the fitness costs of SCCmec I to III) compared to methicillin-susceptible S. aureus (MSSA) isolates, a factor which may be of crucial ecological importance in settings where antibiotic selection pressure is not the main evolutionary imperative.

The initial description of sporadic cases of CA-MRSA infections in patients without the usual risk factors for nosocomial MRSA acquisition did not generate much attention. However, the deaths of 4 children in North Dakota and Minnesota from severe CA-MRSA infections dramatically highlighted the potential threat of these organisms, and drummed in the concept that CA-MRSA had evolved separately from HA-MRSA, and possessed a distinct virulence profile. These concerns have only escalated with the subsequent profusion of reports from all around the world.

In a predictable but unpleasant development, the latest reports suggest that in parts of the USA, the problem of CA-MRSA has reached epidemic proportions. This occurred initially in situations where conditions of overcrowding and poor sanitation prevail, such as among the homeless in San Francisco, within US correctional facilities, or among players of contact sports. Subsequent sobering analyses have demonstrated that CA-MRSA currently accounts for almost 50% of all outpatient staphylococcal infections in some states, and are starting to replace HA-MRSA as a cause of nosocomial infections. These developments have rendered prophetic the comment that the evolution of methicillin resistance in S. aureus may in time reprise that of penicillin resistance.

The reason for the recent steep upsurge in CA-MRSA cases worldwide is not well understood. Experts have attributed this to the relatively new SCCmec subtypes – in particular SCCmec IV – which had probably been introduced into S. aureus only in the recent 2 or 3 decades, but which are now present in more clones of S. aureus than the earlier 3 SCCmec subtypes. The small size of SCCmec IV (20-25 kb) probably allows for greater promiscuity in horizontal transference, and importantly, does not confer a replicative disadvantage compared to MSSA. Circumstantial corroborative evidence is provided by the simultaneous expansion of new healthcare-associated MRSA (HA-MRSA) clones bearing SCCmec IV within various hospitals internationally.

**Differentiating CA-MRSA from HA-MRSA**

A plethora of differing definitions of CA-MRSA in the early literature led to confusion and non-comparability of some of these reports. Most authors had initially used the isolation of MRSA from a clinical specimen obtained as outpatient or within 48 to 72 hours of hospitalisation as a yardstick. However, it is known that patients may be colonised with HA-MRSA for years before developing infection. Similarly, nosocomial outbreaks of CA-MRSA have been reported, and the experience of a single institute in Atlanta, USA suggest that these lines are likely to be blurred further in the future. For these reasons, any attempt at distinguishing CA-MRSA from HA-MRSA using purely epidemiologic criteria will neither be sensitive nor specific.

Investigators from Lyon had highlighted 2 potential molecular markers for CA-MRSA: the Panton-Valentine leukocidin (PVL) genes and SCCmec IV.
genes are present in the majority of CA-MRSA isolates reported in the literature, their absence alone in any MRSA isolate is not proof against a community origin. This can be seen from the example of Australia, where the majority of CA-MRSA isolates lack PVL genes.\textsuperscript{52} SCC\textsubscript{mec} IV has also been well described in HA-MRSA isolates.\textsuperscript{47,48}

What is clear is that CA-MRSA isolates at present have different genetic backgrounds compared to HA-MRSA isolates. Using molecular methods such as pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing (MLST) – the latter being a PCR-based method for characterising organisms based on differences between the internal fragments of highly-conserved housekeeping genes – a picture of a globally diverse though regionally conserved distribution of CA-MRSA clones has emerged.\textsuperscript{18-40,51} These facts debunk the misconception that CA-MRSA had initially originated from HA-MRSA that had adapted to survival in the community, and suggest that the horizontal transference of methicillin resistance had occurred separately and nearly-simultaneously in different parts of the world.

Therefore molecular typing, complemented by patient epidemiology, is the most sensitive and specific method for differentiating CA- from HA-MRSA. While this adds costs in terms of resources and manpower (not forgetting that HA-MRSA have to be typed as well), it allows for an accurate depiction of the problem of CA-MRSA, and for timely and directed infection control intervention if required.

A summary of current predominant CA-MRSA clones in various countries as typed via MLST is shown in Table 1. It is to be cautioned that this list is transient and subject to change over time. For example, ST1-MRSA-IV (USA400) was the initial CA-MRSA reported from the USA but this was quickly overtaken by the more stable and highly transmissible ST8-MRSA-IV (USA300) clone. Furthermore, with the ease and frequency of travel, CA-MRSA clones may be transplanted across the world, an event that has already been documented several times.\textsuperscript{22,53}

### Risk Factors for CA-MRSA

CA-MRSA clusters have been described in various population groups such as participants of contact sports,\textsuperscript{27} military personnel,\textsuperscript{29} intravenous drug abusers (IVDA),\textsuperscript{14,29,40} prison inmates,\textsuperscript{41} aboriginal groups,\textsuperscript{15,19,20} and people belonging to a lower socio-economic stratus.\textsuperscript{18,48} In each of these settings, perhaps with the exception of IVDA, overcrowded facilities, close contact and lack of sanitation had contributed to the spread of MRSA. The majority of published cases have occurred, however, in patients who do not belong to these population groups, are young, immunocompetent, and lack traditional risk factors for MRSA infection such as recent hospitalisation, presence of indwelling medical devices or catheters, dialysis and residence in chronic healthcare facilities.\textsuperscript{16,21,22,24}

### Clinical Presentation

The archetypal presentation of CA-MRSA infection is a young, healthy outpatient with a cutaneous abscess.

In one of the earliest comparison studies between CA- and HA-MRSA, Naimi and co-workers\textsuperscript{49} found that skin and soft tissue infections were far more common among patients with CA-MRSA (75%) than those with HA-MRSA (37%). Cutaneous infections, particularly in the form of furuncles or abscesses, have thus far consistently remained as the most commonly reported manifestation of CA-MRSA.\textsuperscript{16,18-40} This is probably a consequence of the

### Table 1. Summary of Predominant Community-associated Methicillin-Resistant Staphylococcus aureus (CA-MRSA) Clones According to Geographic Region as Classified by Multi Locus Sequence Typing (MLST), Staphylococcal Chromosome Cassette mec (SCC\textsubscript{mec}) Subtype and Presence of Panton-Valentine Leukocidin (PVL) Genes

<table>
<thead>
<tr>
<th>Country*</th>
<th>Sequence Type†</th>
<th>SCC\textsubscript{mec}†</th>
<th>PVL†</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>8</td>
<td>IV</td>
<td>Positive</td>
<td>27, 29, 36</td>
</tr>
<tr>
<td>Canada</td>
<td>1</td>
<td>IV</td>
<td>Positive</td>
<td>34</td>
</tr>
<tr>
<td>Brazil</td>
<td>30</td>
<td>IV</td>
<td>Positive</td>
<td>25</td>
</tr>
<tr>
<td>Uruguay</td>
<td>30</td>
<td>IV</td>
<td>Positive</td>
<td>39</td>
</tr>
<tr>
<td>Belgium</td>
<td>80</td>
<td>IV</td>
<td>Positive</td>
<td>31</td>
</tr>
<tr>
<td>Denmark</td>
<td>80</td>
<td>IV</td>
<td>Positive</td>
<td>26</td>
</tr>
<tr>
<td>France</td>
<td>80</td>
<td>IV</td>
<td>Positive</td>
<td>18, 51</td>
</tr>
<tr>
<td>Germany</td>
<td>80</td>
<td>IV</td>
<td>Positive</td>
<td>24</td>
</tr>
<tr>
<td>Greece</td>
<td>80</td>
<td>IV</td>
<td>Positive</td>
<td>32</td>
</tr>
<tr>
<td>Holland</td>
<td>80</td>
<td>IV</td>
<td>Positive</td>
<td>33</td>
</tr>
<tr>
<td>Latvia</td>
<td>30</td>
<td>IV</td>
<td>Positive</td>
<td>37</td>
</tr>
<tr>
<td>Norway</td>
<td>8</td>
<td>IV</td>
<td>Positive</td>
<td>36</td>
</tr>
<tr>
<td>Sweden</td>
<td>30</td>
<td>IV</td>
<td>Positive</td>
<td>37</td>
</tr>
<tr>
<td>Switzerland</td>
<td>80</td>
<td>IV</td>
<td>Positive</td>
<td>51</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>80</td>
<td>IV</td>
<td>Positive</td>
<td>35</td>
</tr>
<tr>
<td>Taiwan</td>
<td>59</td>
<td>V</td>
<td>Positive</td>
<td>21</td>
</tr>
<tr>
<td>China - Hong Kong SAR</td>
<td>30</td>
<td>IV</td>
<td>Positive</td>
<td>30</td>
</tr>
<tr>
<td>Australia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Queensland</td>
<td>93</td>
<td>IV</td>
<td>Negative</td>
<td>51</td>
</tr>
<tr>
<td>- Western Australia</td>
<td>1</td>
<td>IV</td>
<td>Negative</td>
<td>38</td>
</tr>
<tr>
<td>New Zealand/West Samoa</td>
<td>30</td>
<td>IV</td>
<td>Positive</td>
<td>51</td>
</tr>
</tbody>
</table>

* Based on articles available on PubMed until January 2006. Countries that have reported CA-MRSA cases but without MLST being performed on the isolates (India, Nigeria) are not listed.
† Only one predominant CA-MRSA clone from each country is listed, unless different regions or states within a country have differing major clones. Note that most countries (in particular, Australia and Switzerland) have reported multiple unrelated CA-MRSA clones.
association of PVL genes with CA-MRSA.

PVL is an extracellular bicomponent toxin that targets and induces leukocyte death with release of cytokines and intracellular proteases by creating pores in the cell membrane. Its production is practically deterministic of the ensuing infection — either cutaneous furuncles/abscesses or, more rarely, necrotising pneumonia. The latter condition is rare perhaps because other virulence factors are required.

As mentioned, more fulminant presentations such as septicaemia and necrotising pneumonia have been described, and new, severe manifestations not commonly associated with staphylococcal infections such as Waterhouse-Friderichsen syndrome and necrotising fasciitis have emerged. Miller and co-workers reported 16 cases of the latter condition over a 2-year period in Los Angeles.

Curiously, nosocomial infections attributed to PVL-producing CA-MRSA appear to be less distinctive and are similar from those caused by HA-MRSA. These include wound infections, septicemia, and implant infections. The reason for this is not clear at present, although it is possible that the portal of entry (open wounds and lines in nosocomial cases) may play a part in determining the type of infection subsequently arising.

PVL-negative CA-MRSA infections are less commonly reported. Infections attributed to these organisms are not distinct from other MSSA or even HA-MRSA infections, although they also occur in young patients without the usual risk factors for HA-MRSA infection.

Whether CA-MRSA is more virulent than HA-MRSA is not a question that is easily answered. On the whole, CA-MRSA isolates possess a greater array of known virulence factors than their healthcare-associated counterparts, and USA300 has been associated with several spectacular and fulminant presentations. However, the vast majority of cases have been cutaneous abscesses, resulting in...
Table 2. Distribution of Local Community-associated Methicillin-Resistant *Staphylococcus aureus* According to Multi Locus Sequence Type, Patient Ethnicity and Types of Infection Caused

<table>
<thead>
<tr>
<th>Sequence type</th>
<th>SCC_mec</th>
<th>PVL</th>
<th>Patient ethnicity (No. of cases)</th>
<th>Type of infection (No. of cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>V</td>
<td>Positive</td>
<td>Chinese (1)</td>
<td>Cutaneous abscess (1)</td>
</tr>
<tr>
<td>7</td>
<td>V</td>
<td>Negative</td>
<td>Chinese (1)</td>
<td>Exfoliative dermatitis (1)</td>
</tr>
<tr>
<td>8</td>
<td>V</td>
<td>Positive</td>
<td>Caucasian (1)</td>
<td>Cutaneous abscess (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chinese (1)</td>
<td>Wound infection (1)</td>
</tr>
<tr>
<td>30</td>
<td>IVa</td>
<td>Positive</td>
<td>Malay (1)</td>
<td>Cutaneous abscess (1)</td>
</tr>
<tr>
<td></td>
<td>IVc</td>
<td>Positive</td>
<td>Caucasian (1)</td>
<td>Cutaneous abscess (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chinese (14)</td>
<td>Cutaneous abscess (13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Malay (6)</td>
<td>Bacteremia (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cutaneous abscess (5)</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>V</td>
<td>Positive</td>
<td>Chinese (1)</td>
<td>Cutaneous abscess (1)</td>
</tr>
<tr>
<td>59</td>
<td>V</td>
<td>Positive</td>
<td>Chinese (2)</td>
<td>Cutaneous abscess (2)</td>
</tr>
<tr>
<td>78</td>
<td>IVa</td>
<td>Negative</td>
<td>Chinese (1)</td>
<td>Bacteremia/Endocarditis (1)</td>
</tr>
<tr>
<td>80</td>
<td>IVa</td>
<td>Positive</td>
<td>Filipino (1)</td>
<td>Cutaneous abscess (1)</td>
</tr>
<tr>
<td>88</td>
<td>V</td>
<td>Positive</td>
<td>Malay (1)</td>
<td>Cutaneous abscess (1)</td>
</tr>
<tr>
<td>188</td>
<td>V</td>
<td>Negative</td>
<td>Chinese (1)</td>
<td>Cutaneous abscess (1)</td>
</tr>
<tr>
<td>524</td>
<td>V</td>
<td>Positive</td>
<td>Indian (1)</td>
<td>Bacteremia/Pneumonia (1)</td>
</tr>
<tr>
<td>571</td>
<td>IVa</td>
<td>Negative</td>
<td>Chinese (1)</td>
<td>Osteomyelitis (1)</td>
</tr>
<tr>
<td>573</td>
<td>V</td>
<td>Negative</td>
<td>Chinese (2)</td>
<td>Cutaneous abscess (2)</td>
</tr>
</tbody>
</table>

PVL: Panton-Valentine leukocidin; SCC\_mec: staphylococcal chromosome cassette *mec*

estimated attributable morbidity and mortality rates that are much lower than that quoted for HA-MRSA infections, although this has to be balanced against the fact that patients who develop HA-MRSA infections tend to be older and have more co-morbidities. More longitudinal data are required before the truth can be determined, but it is probably fair comment to state that at this point in time, CA-MRSA is not more virulent than HA-MRSA according to conventional measures.

**Local Context**

A search through the microbiology archives of the Singapore General Hospital (SGH) from January 2001 to April 2004 yielded 8 possible CA-MRSA cases, of which only 5 isolates remained available for typing. These were found to be completely unrelated to each other, and based on strain typing and patient epidemiologic data, at least 3 were likely to have been imported from other countries.²²

Between May 2004 and June 2005, however, a further 37 CA-MRSA isolates were confirmed by molecular typing. Although a reporting bias is evident (many isolates had been contributed by hospitals other than SGH), this nevertheless marks a real and progressive increase in CA-MRSA cases locally (Fig. 1). 70.3% (26 of 37) of the new isolates had identical PFGE patterns and belonged to ST30 on MLST. This is highly suggestive that local transmission had occurred, and that ST30 clones have become the predominant CA-MRSA in Singapore.⁶⁰ ST30 clones currently form perhaps the most globally widespread clonal group among CA-MRSA, and it is interesting but worrying to note these isolates have probably evolved from the pandemic phage type 80/81 penicillin-resistant MSSA that had caused considerable morbidity and mortality in the 1950s, particularly during the global outbreak of Asian influenza.⁶¹

The distributions of CA-MRSA according to the sequence type, infections caused, and ethnicity of the patients is shown in Table 2, and the residential addresses of the patients (only 23 available) is depicted in Figure 2. A significant proportion had been isolated from Filipino expatriates working as maids or construction workers locally, but it is not clear whether they had imported their CA-MRSA isolates or had been infected while working in Singapore. Despite a slight congregation of cases in the eastern part of the island, it is apparent that CA-MRSA – including ST30 isolates – has spread island-wide. The mean age of patients was 34.9 years (range, 1 to 74), and cases were almost equally distributed between the sexes (male-to-female ratio = 1.1:1).
Cutaneous abscesses had accounted for the vast majority of local CA-MRSA infections (35 of 42 cases), which is consistent with global reports. Three cases with cutaneous abscesses had experienced at least 1 relapse. There have only been 2 cases with severe infections to date—a diabetic who had necrotising pneumonia in 2001, and an IVDA with tricuspid valve endocarditis and septic pulmonary embolism in 2004. Both survived. Two patients had wound infections post surgery where CA-MRSA (demonstrated by molecular typing) was isolated from wound cultures, reinforcing the lack of sensitivity of epidemiologic criteria alone in the identification of such organisms.

While the number of local cases appears to be relatively small, this figure is biased by the fact that only hospitalised patients and CA-MRSA isolates submitted to public hospital microbiology laboratories are likely to be detected. The actual prevalence and incidence of CA-MRSA infections locally is not known, but is probably much higher than reported.

**Therapy and Control**

The current approach towards a suspected *S. aureus* infection from the community involves the use of beta-lactam antibiotics along with removal of foci of infection, e.g., abscess drainage. Severe community-acquired infections such as pneumonia or septicaemia are treated with broad-spectrum intravenous beta-lactam antibiotics in the majority of cases. While uncomplicated cutaneous abscesses caused by CA-MRSA are often cured by incision and drainage alone, the delay in initiating appropriate antibiotic therapy for severe MRSA infections might prove costly.

In regions where CA-MRSA incidence is high, empiric antimicrobial therapy guidelines have been changed to reflect this. Intravenous vancomycin is now given empirically for selected septicaemic patients in Northern Territory, Australia, and oral clindamycin and trimethoprim/sulfamethoxazole are now first-line drugs for the treatment of cutaneous infections in parts of the USA. However, although CA-MRSA infections—in contrast to the majority of HA-MRSA—are generally susceptible to most non-beta-lactam antibiotics, resistance to various older non-beta-lactam antibiotics may be relatively easily acquired. Widespread use of clindamycin had resulted in a small but significant rise in resistance within 2 years in northeast USA.

The recent and impending release of new antibiotics targeting gram-positive organisms such as linezolid, daptomycin, tigecycline and newer glycopeptides appears to blunt the impact of CA-MRSA. But it has to be kept in mind that the newer antibiotics come at an initially prohibitive price (the cost of a 1-day supply of linezolid is >100 times the cost of cloxacillin and >15 times the cost of vancomycin in the SGH formulary), particularly for outpatient therapy of mild-to-moderate infections.

Control of the spread of CA-MRSA is an issue for which no solution looks to be readily available. Time-honoured infection control measures that have proven important in preventing the spread of antibiotic-resistant organisms within institutions, such as isolation and contact precautions, can hardly be applied in the open community without creating a backlash of public outrage against the authorities or ostracism towards those who are isolated. And once a state is reached where both CA- and HA-MRSA rates are high—a situation that is analogous with that of penicillin resistance in *S. aureus*—it might no longer be cost-effective or even possible to control MRSA.

Active contact tracing and de-colonisation of carriers were successful in ending a CA-MRSA outbreak in Denmark. This is an extension of part of the “search and destroy” policy practised by most Scandinavian, Dutch and Western Australian healthcare institutions. But whereas such a policy is feasible within the limited confines of hospitals, it would be daunting to reproduce and operate such a programme indefinitely in open democratic societies, and careful consideration of the costs and resources required to perpetuate such a programme should be undertaken prior to implementation.

In Singapore, we are at the ascending phase of the CA-MRSA outbreak. The small number of cases to date does not justify any alteration in antibiotic prescription guidelines. However, a more rigorous surveillance programme, especially at the primary healthcare level, would be ideal in order to gauge the situation more accurately, and guidelines should be drawn up to prepare for the eventuality where community MRSA infections outnumber those caused by their methicillin-susceptible counterparts.

**Conclusion**

The phenomenon of CA-MRSA has swept worldwide within a couple of decades. The crux of the matter is whether this is an immutable evolutionary process following on the steps of penicillin resistance, or if it can potentially be reversed or contained. Current evidence favours the former theory, although there may be a window period for collaborative human efforts to halt the process. To draw a parallel from the development of penicillin resistance in *S. aureus*, it may take years to decades before methicillin resistance becomes as prevalent as penicillin resistance worldwide.

While there is a clear need locally to keep track of the CA-MRSA situation and to formulate guidelines for empirical therapy and for minimising spread of CA-MRSA should the situation worsen, it is equally important to focus on
antibiotic stewardship both in Singapore and elsewhere in order to reduce the evolutionary pressure for the generation of yet more resistant pathogenic organisms.

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