

Community-Acquired Methicillin-Resistant *Staphylococcus aureus*: The New Face of an Old Foe?

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Key Words

Antibiotic resistance · Methicillin-resistant *Staphylococcus aureus*, community-associated · Multilocus sequence typing

Abstract

The burden of infections caused by community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is increasing among different patient populations globally. As CA-MRSA has become established in healthcare facilities, the range of infections caused by them has also increased. Molecular characterization of CA-MRSA isolates obtained from different centers has revealed significant diversity in their genetic backgrounds. Although many CA-MRSA strains are still susceptible to non- β -lactam antibiotics, multiresistance to non- β -lactam agents has emerged in some clones, posing substantial problems for empirical and directed therapy of infections caused by these strains. Some CA-MRSA clones have acquired the capacity to spread locally and internationally. CA-MRSA belonging to ST80-MRSA-IV and ST30-MRSA-IV appear to be the dominant clones in the countries of the Gulf Cooperation Council (GCC). The emergence of pandemic CA-MRSA clones not only limits therapeutic options but also presents significant challenges for

infection control. Continued monitoring of global epidemiology and emerging drug resistance data is critical for the effective management of these infections.

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Staphylococcus aureus: The Old Foe

Staphylococcus aureus is an opportunistic human pathogen, which causes a wide range of infections ranging from superficial skin and soft tissue infections to life threatening pneumonia, bloodstream, bone and joint, respiratory, and gastrointestinal and genital tract infections [1, 2].

In the preantibiotic era, infections caused by *S. aureus* were usually fatal [1]. However, the introduction of penicillin to treat infections caused by *S. aureus* greatly improved the prognosis of patients with severe staphylococcal infections [1–3]. Nevertheless, *S. aureus* strains resistant to penicillin soon appeared [3]. Penicillin resistance is due to the production by the bacteria of an enzyme, i.e. penicillinase, which inactivates the antibiotic, rendering it inactive against the bacteria. Consequently, new antibiotics such as streptomycin, tetracycline, erythromycin, and chloramphenicol were developed in the 1950s [4].

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However, as new antibiotics were developed and put into clinical use, resistance to them appeared, leading to the emergence of strains that were resistant to multiple antibiotics [5, 6].

Emergence of Methicillin Resistance in *S. aureus*

Methicillin resistance was reported in *S. aureus* in 1961 soon after methicillin was introduced for clinical use against penicillinase-producing *S. aureus* [7, 8]. Methicillin-resistant *S. aureus* (MRSA) was subsequently reported in Australia, Europe, the USA, and Japan [9–12]. MRSA is now an important cause of healthcare-associated infections globally. Methicillin resistance in *S. aureus* emerged via the acquisition of the *mecA* gene located on a mobile genomic island designated staphylococcal chromosome cassette *mec* (SCC*mec*) by methicillin-susceptible *S. aureus* [10, 11]. The *mecA* gene is responsible for the synthesis of a novel penicillin-binding protein known as penicillin-binding protein 2a, which has decreased binding affinity for penicillin and cephalosporins [10, 11]. Therefore, MRSA strains are resistant to all β -lactam antibiotics [10, 11].

MRSA strains that were isolated in the 1960s and 1970s were usually susceptible to non- β -lactam antibiotics although they could carry resistance to tetracycline, erythromycin, and chloramphenicol [12]. However, from the late 1970s onwards, new strains of MRSA appeared that were resistant to multi-non- β -lactam agents including aminoglycosides, with only vancomycin left as an antibiotic of last resort for treating MRSA infections. These strains, described as epidemic MRSA (EMRSA), also possessed the capacity to spread extensively and caused serious infections mostly among hospitalized patients worldwide [12–14]. The risk factors for MRSA infections include old age (>60 years), hospitalization in the past 12 months, previous antibiotic use, admission to intensive care units, and catheterization [15].

Emergence of Community-Associated MRSA

MRSA was initially isolated from patients in large or tertiary care hospitals such as teaching hospitals, specialist hospitals, and nursing homes [16] and was described as healthcare-associated MRSA (HA-MRSA). In the 1990s, a new type of MRSA causing infections in the community among individuals who had no history of hospital admission or medical treatment in the previous

year was reported in Western Australia [17]. These types of MRSA strains were described as community-acquired, community-originated, community-associated, or community-onset MRSA (CA-MRSA) [18]. The initial report from Western Australia was followed by reports from New Zealand [19, 20], the USA [21–23], and Europe [24–26]. CA-MRSA is now a major cause of infections in the community as well as in healthcare facilities worldwide [27].

CA-MRSA have genetic and phenotypic characteristics that are different from those of HA-MRSA. CA-MRSA tend to be susceptible to a variety of non- β -lactam antibiotics, whereas HA-MRSA are typically multiresistant to antibiotics. CA-MRSA are more likely than HA-MRSA isolates to encode a putative virulence factor, i.e. Panton-Valentine leukocidin (PVL), a cytotoxin that has been associated with severe pneumonia [28–30], necrotizing fasciitis, and skin and soft tissue infections [11, 25, 30]. Furthermore, CA-MRSA often express lower levels of resistance to oxacillin (MIC: 8–32 mg/l) and multiply faster than HA-MRSA strains with significantly shorter doubling times, which may help CA-MRSA achieve successful colonization by enabling it to outcompete commensal bacterial flora [11]. In addition, CA-MRSA strains harbor SCC*mec* types IV and V, whereas the HA-MRSA carry SCC*mec* types I, II, and III [31, 32]. SCC*mec* types IV and V are smaller in size than SCC*mec* types I, II, and III [32]. Based on SCC*mec* typing, CA-MRSA strains are typically SCC*mec* IV, V, and VI, while HA-MRSA are usually SCC*mec* I, II, and III [32]. Otter and French [24] suggested that using SCC*mec* typing as a marker for CA-MRSA poses a particular problem because of the presence of successful hospital lineages carrying SCC*mec* IV, such as ST22 EMRSA-15-SCC*mec* IV or ST125-SCC*mec*IV, in some parts of the world. The use of SCC*mec* typing may increase the likelihood that these strains will be misclassified as CA-MRSA. Consequently, genotyping based on a combination of multilocus sequence typing (MLST) or Spa typing and SCC*mec* typing has been recommended as criteria for defining CA-MRSA, especially since CA-MRSA has become a major player in healthcare-associated infections [33].

The genetic characteristics, clinical presentations, virulence characteristics, and recommended treatment regimens for CA-MRSA have been reviewed extensively [27, 34–36]. This review focuses on the recent changes in the range of clinical presentations, the emergence of a multi-drug resistance, and the emergence of epidemic clones among recent CA-MRSA strains.

Epidemiological Typing of *S. aureus*

The diversity of *S. aureus* infections and virulence determinants warrant the institution of typing schemes to identify strains with unusual pathogenic abilities, to investigate the source and route of spread of infection, and for the formulation of effective control measures [37]. Over the years, many typing methods, including phage typing, plasmid analysis, pulsed-field gel electrophoresis (PFGE), and DNA sequencing-based methods have been used to type *S. aureus*. The developments and use of these typing methods have coincided with the emergence and dominance of different epidemic *S. aureus* clones. For simplicity, typing of *S. aureus* for epidemiological purposes is divided into three periods, namely pregenetic, genetic, and genomic eras.

The pregenetic era covers the period from 1950 to 1970. Phage typing was the primary method for typing *S. aureus* during this period. Bacteriophage typing is based on the susceptibility of *S. aureus* strains to lysis by specific bacteriophages. Fisk [38] showed that most coagulase-positive staphylococci carried phages that could be detected by cross-culture of pairs of strains and propagated on the sensitive member of the pair. Lysis by these phages was strain specific and was used to characterize isolates from human sources [38]. Phage typing identified the virulent strain of the penicillinase-producing *S. aureus* strain, i.e. phage 80/81, that was responsible for infections in Australian hospitals in the mid-1950s [4]. The phage 80/81 strains were also important causes of epidemics in hospitals in The Netherlands, the USA, and Canada [4]. Leukocidin was a major virulence factor of the 80/81 strains [37, 39].

The use of phage typing for the study of *S. aureus* outbreaks declined as strains of multiresistant MRSA became nontypeable with the available set of typing phages despite the inclusion of new supplementary phages in the phage typing protocol [40]. This period coincided with the introduction of plasmid analysis for epidemiological typing of *S. aureus*. This signaled the birth of the genetic era. Plasmid contents of bacterial strains and their resistance phenotypes constituted the early genotypic methods used for typing MRSA in the 1970s [40–43]. This was facilitated by the availability of rapid methods for isolating plasmid DNA in *S. aureus* [42, 43]. By combining plasmid content with the location of antibiotic resistance, i.e. on the chromosome or on plasmids in the bacterial strain, Grubb [12] differentiated MRSA that were isolated in the 1960s (classic MRSA) from the epidemic MRSA (EMRSA) strains that were spreading across Australia and Europe in the 1980s.

Epidemiological typing of *S. aureus* was further improved by the introduction of PFGE, MLST, *spa* typing, and SCC*mec* typing [44–47]. This period, the genomic era, witnessed the global expansion of EMRSA and the introduction of CA-MRSA clones.

PFGE enables the resolution of the whole bacterial chromosome. The procedure involves the application of controlled electric fields that change direction at a predetermined angle to samples of DNA that have been embedded in an agarose gel matrix and digested with an infrequent cutting restriction endonuclease. Adjustment of the electrophoretic conditions enables the separation of DNA fragments with lengths from 10 kilobases up to 10 megabases. The banding patterns are used for epidemiological typing [44]. Because of its high discriminatory capacity, PFGE has been regarded as the gold standard for investigating local outbreaks of bacterial infections [48].

MLST is a nucleotide sequence-based approach to the typing and characterization of bacterial isolates. MLST characterizes bacterial isolates using internal fragment sequences of 6–9 housekeeping genes. The fragments are approximately 450–500 bp in length [45]. For each housekeeping gene, the various sequences present within bacterial sequences are specified as distinct alleles. For each of the isolates, the alleles at all loci define the allelic profile or sequence type. MLST allows sequence data to be easily shared electronically between laboratories [45].

Spa typing is a single locus nucleotide sequence-based method that targets the protein A gene of *S. aureus*. The polymorphism in the variable X region in the *spa* gene encoding the staphylococcal surface protein A (*spa*) can be analyzed and used as a determinant to type *S. aureus* [46, 47]. The *Spa* typing method involves sequencing of the 24-bp variable repeat unit in the 3' region of the protein A gene (*spa*) and comparing the pattern of repeats to a public database [46, 47]. The results of *Spa* typing are comparable between laboratories electronically.

SCC*mec* typing characterizes MRSA isolates on the basis of the genetic elements known as SCC*mec*. SCC*mec* vary in size from 21 to 67 Kb [32]. The diversity of SCC*mec* types forms the basis of SCC*mec* typing, which facilitated the genetic differentiation of HA-MRSA from CA-MRSA. Based on SCC*mec* typing, CA-MRSA strains are typically SCC*mec* IV, V, and VI, while HA-MRSA ones are usually SCC*mec* I, II, and III [32]. Collectively, these typing methods are critical for identifying new strains, tracking outbreaks, and monitoring the evolution of *S. aureus*. The continued improvement and expansion

Table 1. Infections associated with CA-MRSA isolates: 2010–2012

Infections	References
Neck abscesses	50
Necrotizing fasciitis	51
Purulent pericardial effusion	52
Bloodstream infections	53, 54
Ocular infections	55–59
Osteomyelitis	60, 61
Epididymitis	62
Infective endocarditis	63
Prostatic abscess	64
Mycotic aneurysm	65
Infections in otolaryngology	66
Scarlet fever	67
Meningitis	68, 69
Liver abscess	70
Epidural abscess	71

of these methods, as well as the development of new diagnostic methods, will ensure that newly emerging *S. aureus* clones are identified quickly [48, 49].

Spectrum of Diseases Caused by CA-MRSA

Although CA-MRSA initially caused infections of the skin and soft tissues in young and healthy individuals [27], they have become more widespread in healthcare facilities. In addition, the spectrum of diseases associated with CA-MRSA has also increased over time. While infections of the skin and soft tissues such as furuncles, carbuncles, abscesses, cellulitis, and pneumonia are still the dominant clinical manifestation of CA-MRSA [14, 16, 27], other less common types of infections associated with CA-MRSA in recent years are presented in table 1.

Involvement of CA-MRSA in Outbreaks

There is a growing number of reports from different countries detailing the establishment of CA-MRSA as the dominant MRSA in healthcare facilities with some of the strains causing outbreaks of infections [72–77]. O'Brien et al. [77] first described an outbreak of infection in a Western Australian metropolitan hospital involving a CA-MRSA clone that was indistinguishable from a clone circulating in a remote community in the state. This was followed by reports of outbreaks caused by CA-MRSA in France [78]. Outbreaks caused by CA-MRSA now occur

worldwide [27], with increasing reports of outbreaks in neonatal units [79–82].

Transmission of CA-MRSA strains within healthcare facilities by some identified epidemic clones has resulted in the displacement of the previously endemic HA-MRSA clones [83]. In Germany, nonmultiresistant MRSA, including CC45-MRSA-IV and CC22-MRSA-IV clones, replaced the previously dominant multiresistant MRSA with the HA-MRSA genotype ST239-MRSA-III [84]. In the United Arab Emirates, MRSA with the HA-MRSA genotypes ST239-MRSA-III and ST22-MRSA-IV, which were the dominant strains in 2003, were replaced by CA-MRSA genotypes ST80-MRSA-IV and ST5-MRSA-IV in 2008 [85]. The ST30-MRSA-IV clone emerged in Singapore in 2004 and by 2005 had become the dominant MRSA clone in their hospitals [76]. Similarly, infections caused by CA-MRSA clone USA300 have surpassed those caused by the traditional HA-MRSA isolates in parts of the USA [27].

Emergence of Multiantibiotic Resistance in CA-MRSA

The earlier community MRSA isolates were generally susceptible to commonly used non- β -lactam antibiotics and were consequently described as nonmultiresistant MRSA [18, 86]. The absence of multiresistance in the early CA-MRSA isolates was likely due to a lack of exposure to many antibiotics rather than an inability to acquire multiantibiotic resistance determinants. In 2004, Munckhof et al. [87] showed that CA-MRSA isolates, when exposed to antibiotics in vitro over time, readily acquired resistance to these antibiotics. Soon after, multiresistance to non- β -lactams began to appear in CA-MRSA strains isolated in different centers. In North America, the USA300 CA-MRSA clone acquired multiantibiotic resistance via the acquisition of the multiresistant conjugative plasmid pUSA03 [88, 89, 90] or pSK41-like plasmids [91]. The conjugative plasmid pUSA03 encodes resistance to erythromycin, clindamycin, and high-level mupirocin. USA300 also express resistance to tetracycline and fluoroquinolones. High-level mupirocin resistance has also been reported in strains belonging to the ST80-SCC*mec*-IV CA-MRSA clone that was also resistant to tetracycline, fusidic acid, gentamicin, and streptomycin and cadmium acetate [92]. In Brazil, CA-MRSA strains belonging to the lineage ST1-SCC*mec* IV were reported to be resistant to erythromycin, clindamycin, ciprofloxacin, gentamicin, trimethoprim-sulfamethoxazole, and tetracycline [93]. Some strains belonging to the ST59 clone obtained from patients

Table 2. Epidemic CA-MRSA clones and their geographical distribution obtained from Udo et al. [81] and Mediavilla et al. [99]

Sequence types	SCC <i>mec</i>	Countries where they have been reported
ST1	IV	Australia, Brazil, Canada, China, Denmark, Egypt, Finland, France, Germany, Greece, Ireland, Italy, Japan, Kuwait, Pakistan, Romania, Samoa, Singapore, South Korea, Switzerland, United Arab Emirates, UK, USA
ST5	IV/V/VI	Algeria, Argentina, Australia, Austria, Azores, Cameroon, Canary Islands, China, Egypt, France, Germany, Iceland, Italy, Japan, Kuwait, Morocco, Nigeria, Samoa, Senegal, Spain, Switzerland, UK
ST8	IV/V/VI	Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Cameroon, Canada, Canary Islands, China, Colombia, Costa Rica, Cuba, Czech Republic, Denmark, Ecuador, Finland, France, French Polynesia, Gabon, Germany, Greece, Hong Kong, Iceland, India, Iraq, Ireland, Italy, Japan, Kuwait, Madagascar, Mexico, The Netherlands, New Zealand, Nigeria, Norway, Pakistan, Peru, Poland, Portugal, Romania, Russia, Samoa, South Korea, Spain, Sweden, Switzerland, Trinidad and Tobago, United Arab Emirates, UK, USA, Uruguay, Venezuela
ST30	IV/V	Australia, Austria, Brazil, Canary Islands, China, Czech Republic, Denmark, Egypt, Finland, France, French Polynesia, Germany, Hong Kong, Ireland, Italy, Japan, Kuwait, Latvia, Madagascar, Malaysia, The Netherlands, New Zealand, Pakistan, Peru, Philippines, Poland, Romania, Russia, Samoa, Singapore, South Korea, Spain, Sweden, Switzerland, Taiwan, Turkey, United Arab Emirates, UK, USA, Uruguay
ST45	IV/V/VI	Australia, Azores, Belgium, Germany, Hong Kong, Switzerland
ST59	IV/V	Australia, China, Denmark, Finland, Germany, Hong Kong, The Netherlands, Singapore, Sweden, Taiwan, UK, USA, Vietnam
ST72	IV/V	Czech Republic, Germany, Portugal, South Korea, Sweden, United Arab Emirates, USA
ST80	IV	Algeria, Australia, Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Egypt, Finland, France, Germany, Greece, Ireland, Italy, Jordan, Kuwait, Lebanon, Libya, Malta, The Netherlands, Norway, Poland, Portugal, Romania, Saudi Arabia, Singapore, Slovenia, Spain, Sweden, Switzerland, Tunisia, United Arab Emirates, UK
ST88	IV/V	Angola, Cameroon, China, Gabon, Italy, Japan, Madagascar, Mali, The Netherlands, Niger, Nigeria, Portugal, Senegal, Spain, Sweden, United Arab Emirates, UK
ST93	IV	Australia, Czech Republic, Finland, Italy, The Netherlands, Samoa, UK
ST97	IV/V	Brazil, Canary Islands, Denmark, Egypt, Germany, Kuwait, Lebanon, The Netherlands, Sweden, United Arab Emirates, UK, USA
ST152	V	Austria, Canary Islands, Denmark, Germany, Kosovo, Macedonia, Slovenia, Sweden, Switzerland
ST772	IV/V	Australia, Bangladesh, Finland, Germany, Hong Kong, India, Ireland, Italy, Japan, The Netherlands, UK

in Vietnam were resistant to the macrolides, lincosamide, streptogramin, gentamicin, tetracycline, chloramphenicol, and trimethoprim-sulphamethoxazole [94–97].

Emergence of Epidemic CA-MRSA Clones

Several studies have shown that specific clones of CA-MRSA with diverse genetic backgrounds have emerged in different geographical areas, suggesting that these strains acquired SCC*mec* elements independently on multiple occasions [33, 36]. However, an increasing number of CA-MRSA clones have been reported to have attained epidemic status in recent years. These include

USA300, ST80, ST30, ST59, ST93, and ST772 [27, 36, 49, 98, 99]. The widely recognized epidemic CA-MRSA clones and their geographic distributions are summarized in table 2.

The USA300 clone is the dominant CA-MRSA clone causing infections in the USA [90, 99] and Canada [100]. The USA300 (PFGE-based designation) corresponds to MLST sequence type 8 (ST8). Outside of North America, USA300 has been isolated in Western Europe [101], Japan [71, 98], and Australia [102, 103]. The USA300 clones carry the SCC*mec* IV genetic element and produce PVL, and some carry the genes for ACME [30]. Surprisingly, USA300 is rare in the Middle East and Gulf Cooperation Council (GCC) countries.

ST80-MRSA has remained the dominant CA-MRSA clone in European countries [36, 99, 101, 103], North Africa, and the Middle East [85, 104, 105–110]. It has also been reported in Malaysia [111] and Australia [27, 112, 113]. The ST80-MRSA clones carry the SCC mec IV genetic element and belong to the accessory gene regulator (*agr*) type 3, and the majority of the strains produce PVL [99, 110]. Curiously, the ST80-MRSA clone does not seem to be successful in North America.

The ST30-MRSA clone, also known as the Southwest Pacific (SWP) clone, emerged in Oceania [20, 113] but has become a pandemic clone reported from many parts of the world, including the USA, Japan, Latin America, Turkey, the Middle East, Egypt, and many countries in Western Europe [36, 96, 109, 112, 113]. ST30 isolates are known as PFGE type USA1100 in the USA [114].

The ST59-MRSA clone emerged in Asia and is the dominant CA-MRSA clone prevalent in Taiwan [94, 115]. However, it has also been isolated in Australia [116, 117], China [95, 118], Hong Kong [119], Japan [120, 121], Europe [103], and the USA, where it is known as PFGE type USA1000 [114]. ST59-MRSA has also been isolated from cats and dogs in Malaysia, suggesting that cats and dogs are potential reservoirs of CA-MRSA [122].

The ST93-MRSA clone, also known as the Queensland MRSA clone, was first identified in Queensland and New South Wales, Australia, in 2000 [123]. It was soon reported in other parts of Australia [124, 125], though it was rarely reported in other countries. ST93-MRSA is highly virulent and has been associated with severe infections, including necrotizing pneumonia [125, 126], although it harbors very few known virulence determinants [126, 127].

The ST772-MRSA clone, also known as the Bengal clone, was first reported in Bangladesh [128]. It has since been reported in India [56, 129, 130], Ireland [82], Australia, Germany, Hong Kong, the United Arab Emirates, and Saudi Arabia [112, 128]. The ST772 clone is rapidly becoming the dominant CA-MRSA clone in Indian hospitals [56, 129, 130]. Interestingly, PVL-producing strains of ST772 isolated in India are relatively susceptible to antimicrobial agents compared to ST772 clones isolated in Western Australia that appear to be more resistant to antibacterial agents [112].

CA-MRSA in the GCC Countries

CA-MRSA strains have emerged as important causes of infections in healthcare facilities in the GCC as in other parts of the world. CA-MRSA have been reported in

Saudi Arabia, the United Arab Emirates, Kuwait, and Bahrain. In Saudi Arabia, CA-MRSA was first reported among patients at the King Fahd Hospital in the Eastern Province of the country in 1998 [131]. Since then, CA-MRSA have been reported in other areas of the kingdom with increasing prevalence, and their antibiotic susceptibility patterns have also changed with increasing levels of resistance to erythromycin, tetracycline, clindamycin, ciprofloxacin, and gentamicin [132]. Genetic analysis of CA-MRSA isolates obtained in a hospital in Riyadh revealed that they belonged to different clones [108].

In the United Arab Emirates, a study conducted at Tawam Hospital showed that the prevalence of CA-MRSA increased from 38.5% of all MRSA isolated at the hospital in 2003 to 73.1% in 2008 [85]. These strains consisted mostly of ST80-MRSA-IV, ST5-MRSA-IV, and ST1-MRSA clones. The study also revealed that only one third of the CA-MRSA infections were actually acquired in the community, indicating that CA-MRSA clones had entered and spread within the hospital [85].

In Bahrain, a study conducted at the Salmaniya Medical Complex in 2005 revealed that 13.3% of their MRSA strains were CA-MRSA. These strains were nonmultiresistant to non- β -lactam antibiotics, belonged to different genetic backgrounds, and were isolated mostly from skin and soft tissue sources [133].

In Kuwait, CA-MRSA was first identified in 2001 [134]. The prevalence of CA-MRSA increased from 1.7% of all MRSA in 2001 to 17% in 2005 [135]. Molecular characterization of CA-MRSA obtained between 2006 and 2007 showed that ST80-SCC mec -IV (51.1%), ST30-SCC mec -IV (22.2%), and ST5-SCC mec -IV (14.1%) were the dominant CA-MRSA clones in the country [110]. The ST80-SCC mec -IV strains obtained in Kuwait hospitals belonged to diverse PFGE backgrounds and resistance patterns. Some strains had resistance patterns similar to that of the European clone obtained in Denmark [101].

There are currently no published data on the prevalence of CA-MRSA in Qatar and Oman, although MRSA has been reported in these countries.

Relation of the Current CA-MRSA to the Pandemic *S. aureus* Phage 80/81 Clone

Similarities were observed between the infections and spread of some CA-MRSA clones and the patterns of infections associated with those of the pandemic phage 80/81 MSSA clones. For example, the phage 80/81 clone caused a wide range of syndromes including skin infec-

tions (boils, carbuncles, and pustules) and fatal sepsis or pneumonia [136] similar to the spectrum of infection caused by CA-MRSA [27]. The phage 80/81 clone emerged rapidly in Australia before being reported in the UK, Canada, and the USA in the 1950s, similar to the pattern of emergence of CA-MRSA strains. In addition, outbreaks of infections caused by the phage 80/81 clone occurred initially among newborns, young children, and nursing mothers. This mirrors the initial association of CA-MRSA infections in the young healthy and outbreaks among neonates [137]. These observations, together with the emergence and successful spread of EMRSA-16 in the UK and ST30 globally, prompted a comparison of these clones with strains belonging to the phage 80/81 MSSA to establish their relatedness [114]. To clarify the relationship between phage 80/81 and contemporary CA-MRSA clones, DeLeo et al. [114] sequenced representative isolates belonging to the phage 80/81, SWP CA-MRSA (ST30-MRSA), and EMRSA-16 genomes and compared their virulence determinants. The study revealed that phage 80/81 and EMRSA-16 belonged to the same clonal complex 30 (CC30), suggesting that they may have a common ancestor. The study also suggested that there was a coincident divergence of these clones from a common ancestor but, unlike the suggestion by Robinson et al. [138], the SWP clone was not a descendant of the phage 80/81 clone.

Conclusions

There is significant diversity in MRSA arising in communities worldwide. As CA-MRSA has become established in healthcare facilities, the range of infections caused by them has also increased. Although many CA-MRSA still maintain a nonmultidrug resistant antimicrobial profile, multiresistance to non- β -lactam agents has emerged in some clones, posing substantial problems for empirical and directed therapy of infections caused by these strains. The emergence of pandemic CA-MRSA clones not only limits therapeutic options but also presents significant challenges for infection control. Continued monitoring of global epidemiology and emerging drug resistance data is critical for the effective management of these infections.

Disclosure Statement

The author declares no conflict of interest.

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