Sirs,

Although community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) have distinct microbiological, epidemiological and molecular characteristics different from those of healthcare-associated MRSA (HA-MRSA), currently, there are no validated definitions for CA-MRSA. We read with interest the newly proposed definitions published by Millar et al. In their article, comparing the differences between CA-MRSA and HA-MRSA, the authors also reviewed all published cases of CA-MRSA endocarditis to date.

There are several errors in the article by Millar et al. First, of the 23 patients with infective endocarditis due to CA-MRSA, 2 of the 7 cases in the Haque series (Cases 3 and 7) were in fact healthcare-associated, although all 7 cases were Panton–Valentine leucocidin (PVL)-positive and carried the SCCmec type IV gene. In Taiwan, the most common SCCmec types in CA-MRSA infections were types IV and V. MRSA colonized a substantial proportion of healthy children and accounted for 25% to 75% of the childhood CA-MRSA infections. However, SCCmec type IV can also be hospital-acquired and accounted for 40% to 43% of MRSA infections in two studies. This suggests that SCCmec type IV alone is not sufficient to indicate community acquisition and should not be the only criterion for CA-MRSA.

Secondly, in the table comparing clinical characteristics and outcome for patients with meticillin-susceptible *S. aureus* (MSSA) native valve endocarditis with those of MRSA and CA-MRSA native valve endocarditis (Table 3), it is unclear why only 81% of the CA-MRSA was community-acquired. What then is the definition of CA-MRSA if it does not satisfy the criteria of ‘community acquisition’?

We concur with the authors that emergence of CA-MRSA infection impacts significantly on the outcome and management of infective endocarditis. However, a comprehensive definition of CA-MRSA is still currently lacking, reflecting the complexity of this pathogen in its clinical, epidemiological and microbiological characteristics. We caution that a combination of characteristics, rather than a single one (such as SCCmec type IV genotype), should be used to define CA-MRSA.

**Transparency declarations**

None to declare.

**References**


**Letters to the Editor**

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Although community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) have distinct microbiological, epidemiological and molecular characteristics different from those of healthcare-associated MRSA (HA-MRSA), currently, there are no validated definitions for CA-MRSA. We read with interest the newly proposed definitions published by Millar et al. In their article, comparing the differences between CA-MRSA and HA-MRSA, the authors also reviewed all published cases of CA-MRSA endocarditis to date.

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**Transparency declarations**

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**References**


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**Community-associated MRSA (CA-MRSA): an emerging pathogen in infective endocarditis—authors’ response**

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**Keywords:** *Staphylococcus aureus*, CDC criteria, hospital-acquired MRSA

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Sir,

We read with interest the comments made by Tsai et al., in response to our recently published Leading article. These comments primarily serve to reiterate the importance of definitions for community-associated MRSA (CA-MRSA), regardless of whether such infections have been acquired in the community or healthcare setting. Such definitions are applicable to all CA-MRSA infections, not only those resulting in infective endocarditis (IE). Indeed, the comments made by these authors do not directly address any issues *per se* relating to IE, but how CA-MRSA is defined within the 23 reviewed cases of IE.

As reiterated by Tsai et al., there is no unique characteristic (for example, SCCmec type IV) that is attributed to all CA-MRSA isolates, and in order to help define CA-MRSA, we have previously proposed definitions based on a combination of characteristics. Furthermore, there appears to be confusion with regard to the terminologies ‘associated’ and ‘acquired’. These terms are not synonymous or interchangeable. ‘Associated’ represents where the isolate originated, whereas ‘acquired’ identifies where the patient acquired the isolate.

CA-MRSA is predominately acquired within the community setting; however, there are increasing reports of CA-MRSA infections acquired within the healthcare setting, whereby a community strain has entered into the healthcare environment and has subsequently been transmitted nosocomially, similar to the transmission of healthcare-associated MRSA (HA-MRSA). As such, in Table 3 of our article, although the isolates had characteristics of CA-MRSA, in four cases, the infection was acquired within a healthcare setting.
Letters to the Editor

Haque et al.\textsuperscript{7} described two of their seven cases of IE, due to USA300 MRSA, as healthcare-associated; however, they did not clarify how they defined community-associated. It may be presumed that, due to the fact that these two patients had a prior hospital admission, the authors deemed the MRSA to be hospital-acquired as per the CDC criteria (http://www.cdc.gov/ncidd/dhqp/ar_mrsa_ca_clinicians.html#4). This further highlights the inadequacies of the CDC criteria, which do not take into account the microbiological characteristics of the isolates but focus largely on the epidemiological characteristics of the patient.

Overall, the emergence of CA-MRSA over the last decade and its relative difference from HA-MRSA in terms of its epidemiology, microbiology and treatment now require proper categorisation so that authors and readers are clear as to the nature of the MRSA isolate being described. Therefore, when MRSA isolates are being reported, further microbiological work should be undertaken to ensure that a correct classification of the isolate as CA-MRSA/HA-MRSA is given.

Transparency declarations

None to declare.

References


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Comment on: Therapy for Whipple’s disease

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Keywords: Tropheryma whippeli, MICs, failure

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Sir,

We read with much interest the article by Knaapen and Barrera\textsuperscript{1} recently published in \textit{JAC} on Whipple’s disease treatment. It is fascinating as it shows, in this intriguing and rare disease, how successive deductive opinions finally came to be considered as established facts. There are no comparative studies on therapy of Whipple’s disease and, until recently, treatment recommendation was empirical, based on anecdotal reports of failures or relapses.\textsuperscript{2} We believe that this is confusing.

Relapse rates depend on the length of treatment and follow-up. As tetracyclines have been used for many years before co-trimoxazole in the treatment of Whipple’s disease, there are more reports on failures with the tetracyclines than with co-trimoxazole.\textsuperscript{2} There is no published evidence of the superiority of any regimen in terms of relapse rate during 5 years post-treatment follow-up.

The situation is also confusing for primary treatment failure. Whipple’s disease can exacerbate when treated, as during leprosy with lepromatous reaction or as in immune reconstitution. These immediate ‘failures’ are not antibiotic failures and when they are excluded, the only difference in failure rates between treatment regimens in the single published comparative study (tetracycline versus co-trimoxazole)\textsuperscript{3} is observed in patients with initial neurological manifestations. In these patients, doxycycline is poorly effective. In addition, treatment with co-trimoxazole is associated with failures caused by acquired resistance\textsuperscript{3} and, in our clinical experience, has a frequency of \~{}3%\textsuperscript{2}.

We should base our recommendations on objective information such as \textit{in vitro} data, genome analysis and clinical trials. Antibiotic susceptibility testing \textit{in vitro} demonstrated that doxycycline alone was bacteriostatic rather than bactericidal, against \textit{Tropheryma whippeli}, although the addition of hydroxychloroquine makes doxycycline bactericidal. \textit{T. whippeli} is intrinsically resistant to trimethoprim (the gene coding for the target enzyme of this compound is missing in the genome of \textit{T. whippeli}),\textsuperscript{4,5} and it has been confirmed \textit{in vitro} that trimethoprim is ineffective.\textsuperscript{6} Thus, only the sulphonamide component of co-trimoxazole is active against \textit{T. whippeli}, and there is no objective reason to prescribe co-trimoxazole instead of a sulphonamide compound alone.

The antibiotic susceptibility of \textit{T. whippeli} to sulfadiazine has never been evaluated \textit{in vitro}. We therefore determined the MICs of sulfadiazine for \textit{T. whippeli} Twist and Neuro 20 strains using quantitative real-time PCR with methods as previously described.\textsuperscript{5} Experiments were conducted in 24-well plates. Cultures were centrifuged at 7500 rpm for 10 min. Pellets were resuspended to 1/100 in axenic medium. Antibiotics were diluted in culture medium at the concentrations of 0.25, 0.5, 1 and 2 mg/L. Antibiotic-free wells served as growth controls and experiments were performed in triplicate. During the experiments, cultures were harvested at day 0, day 14 and day 21 and frozen at \textminus{}20°C, until DNA extraction for quantitative PCR.