Waves of trouble: MRSA strain dynamics and assessment of the impact of infection control

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There has been a sustained decline in bloodstream infections due to methicillin-resistant Staphylococcus aureus (MRSA) throughout the UK. The UK MRSA epidemic, which began in the 1990s, has been dominated by two epidemic MRSA (EMRSA) clones {EMRSA-15, of clonal complex (CC) 22 [sequence type (ST) 22], and EMRSA-16, of CC30 (ST36)}.

It appears that both these clones followed a wave trajectory (initial expansion, relative stasis, then decline). Three recent studies have shown that ST36 has declined faster than ST22, a change that appears to have begun before the recent intensification of intensive control measures in the UK. The biological basis of infectious disease waves, including those of MRSA, is discussed, as are the implications of such waves for the assessment of the impact of infection control measures.

Keywords: ST22, ST36, epidemic

Introduction

Expansion and decline of epidemic clones is a key determinant of isolation rates of clonal microorganisms.1 UK national bacteraemia surveillance has shown substantial, maintained declines in bloodstream methicillin-resistant Staphylococcus aureus (MRSA) isolation throughout the UK.2 Here, we review emerging evidence that the epidemic comprised two waves of different clones3–5 that pursued different kinetics (Figure 1), with changing clone balance evident before the intense focus on infection control that occurred in the UK in the latter part of the last decade.

Decline of MRSA bacteraemia rates in the UK and association with bacterial strains

The UK MRSA epidemic has been dominated by two epidemic MRSA (EMRSA) clones {EMRSA-15, of clonal complex (CC) 22 [sequence type (ST) 22], and EMRSA-16, of CC30 (ST36)}.3 There has been a marked decline in ST36 isolation rates over the last decade, as documented by recent studies in Grampian4 and Oxford5 and by a multicentre study of hospitals participating in the BSAC Bacteraemia Surveillance scheme.6

First a wave of ST36, then of ST22

In the study from the Oxford region, it was first noted that the kinetics of the MRSA epidemic locally were very similar to those of the national outbreak overall.5 Further, it was noted that there was an association between locally determined resistance profiles and ST; from this, the authors were able to estimate ST22 and ST36 isolation rates over time. It appeared that the MRSA epidemic consisted of two ‘waves’ of isolates, with ST36 rising first in the late 1990s, and a subsequent ST22 wave, which became dominant as the ST36 wave declined (Figure 1). This change was not restricted to bacteraemia isolates.2,4,5

Although sampling frames and laboratory methods varied between the three studies, taken together the three papers suggest varying success of ST22 and ST36 clones over time (Table 1), and that waves similar to that described in the Oxford study have occurred more widely. This observation raises obvious questions, which remain unanswered. It is clear that MRSA spreads between hospitals, but there is marked geographical variation in strain prevalence across Europe.7 Did the ST22 and ST36 waves occur simultaneously in all UK hospitals, or were some hospitals affected by one more than the other? To what extent did variants arising during the epidemic contribute to the epidemic’s progression? Did the two waves, both initially noted in southern England,8,9 travel by the same routes?; did they spread across the country? Is there some biological interaction between ST22 and ST36 S. aureus?

Waves of S. aureus

Despite these uncertainties, some things are well established. Firstly, changes in bacterial strains arise due to microbial evolution; consequent changes in clinical impact have been noted for a number of pathogenic organisms, including Clostridium difficile,10 Streptococcus pyogenes,11 Streptococcus pneumoniae12 and Neisseria meningitides13 as well as S. aureus.14,15,16 Secondly, serial displacement of waves of MRSA strains, including ST36, by newer
MRSA variants has been described elsewhere in Europe. Less clear are the factors driving waves of *S. aureus* isolation or those of other microorganisms. Quite small changes in reproduction number can alter the epidemic course, which might be influenced by factors including changes in bacterial genetics, bacterial competition, immune selection and interventions within the human population, including infection control measures such as isolation and the use of antimicrobials.

**Impact of infection control on bacterial waves**

The decline in the huge costs and human burden of disease inflicted by MRSA in the UK is very welcome. However, questions remain as to the main contributions to the decline. Did some poorly understood property of the organism, or an acquisition of immunity in the population in which it was circulating, contribute to the end of the transmission wave? If so, how much ‘help’ did these effects give to infection control programmes at the end of the last decade? We believe this is not easy to determine, but nonetheless needs consideration, since two of the recent studies have noted that the onset of the decline in MRSA strain isolation pre-dated many infection control interventions. Further, a huge UK multicentre intervention study did not demonstrate a clear impact of an infection control package on MRSA bacteraemia. Consequently, it seems possible that strain (‘biological’) behaviour contributed. Equally, a number of infection control measures, particularly those related to intravascular line care, are supported by randomized control trial evidence and are likely to be responsible for some of the decline. That the relative contributions of individual infection control interventions versus intrinsic biological properties of the MRSA strains are unclear is unfortunate. Clear evidence supporting infection control interventions would aid resource targeting. This is particularly apposite to expensive interventions with a contentious evidence base, such as MRSA screening.

**Future actions and preparedness**

If one accepts that it is difficult to work out the relative contributions of both biological strain behaviour and the environment (including infection control measures) to the national decline in MRSA bacteraemia, what are the lessons for the future, given that major threats remain? Much MRSA disease persists, as bacteraemia is only responsible for a fraction of MRSA infections. A second threat comes from methicillin-susceptible *S. aureus*, which is now much more common than MRSA in the clinical setting, and is much more diverse, although this latter point is not discussed here.

A third threat concerns ongoing containment of MRSA. While continuing with evidence-based practice, particularly in areas surrounding surgical practice, intravascular and catheter...
management, we need to be mindful that diverse MRSA strains exist with behaviour very different from that of previous epidemic strains. Transmission of at least one of these MRSA strains (ST239) may be enhanced in settings using chlorhexidine prophylaxis, now widely used in many healthcare environments. Consequently, in settings where MRSA rates deviate from the current downward trajectory, the possibility that lineages with different biological behaviours may be responsible through clonal expansion should be seriously considered. Careful analysis of data from surveillance schemes, integrated with gold-standard typing methods, should provide rapid identification of relevant clones and determine which environmental factors contribute to their spread. Since the expected trajectory of such strains will be unknown and many outbreaks may appear to resolve following ineffective intervention purely by chance, such strains will be unknown and many outbreaks may appear to resolve following ineffective intervention purely by chance,18 confidently identifying effective interventions requires studies with randomized designs rather than depending on studies with interrupted time series designs.

**Transparency declarations**
None to declare.

**References**


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