Emer O'Leary

Deborah EA Lockhart and Andrew Smith

This article counts towards one of the five core subjects introduced in 2007 by the GDC.

Coming to a Practice Near You? Community-Acquired Meticillin Resistant *Staphylococcus aureus* (CA-MRSA)

Abstract: Hospital-acquired meticillin resistant *Staphylococcus aureus* (HA-MRSA) arose in the 1960s, but the last decade saw the emergence of a new entity: community-acquired MRSA (CA-MRSA). Unlike HA-MRSA, patients affected by CA-MRSA have no obvious risk factors and may present with recurrent skin and soft tissue infections (SSTI) or, rarely, severe necrotizing pneumonia. This article provides an overview of CA-MRSA and reinforces the standard infection control procedures required to prevent further spread.

Clinical Relevance: The dental team require an awareness of emerging infections, their relevance to dentistry and the infection control procedures necessary to prevent transmission.

Dent Update 2011; 38: 254–260

Introduction

Meticillin resistant *Staphylococcus aureus* (MRSA) is classically associated with healthcare interventions. Consequently, hospital admission represents a prominent risk factor for the acquisition of certain epidemic strains of MRSA, leading to the term 'hospital-acquired infection' (HAI). This was modified to 'healthcare associated infection' acknowledging patient movement between healthcare and community settings, despite the MRSA strains remaining identical.

New strains termed community-associated MRSA (CA-MRSA), with distinct phenotypic and genotypic characteristics, emerged in the last ten years and are now widespread in the USA. As cases have been reported in the UK and the incidence is likely to increase,[1] the dental team should have an understanding of this emerging pathogen and their role in preventing further spread. This article provides a background on the origins of this bacterium, discusses its occurrence in the oral cavity and highlights current treatment and prevention strategies. Dental healthcare workers should have sufficient knowledge to manage patients colonized or infected with any strain of MRSA competently.

Emer O'Leary, BDS, MFDS RCS(Glas), Senior House Officer, **Deborah EA Lockhart**, BSc(DentSci), BDS(Hons), MFDS RCSEd, Specialist Registrar and Honorary Clinical Teacher Microbiology and **Andrew Smith**, BDS, FDS RCS(Edin), FRCPath, PhD, Senior Lecturer and Honorary Consultant Microbiologist, Glasgow Dental School, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow.

Background

Staphylococcus aureus is a Gram-positive coccus that colonizes the nose, skin and oral cavity of approximately 20–30% of healthy individuals. Although *S. aureus* may exist as a commensal, it is responsible for a variety of infections, ranging from superficial skin infections to invasive life-threatening conditions, including septicaemia, endocarditis, osteomyelitis, pneumonia and toxic shock syndrome. There is political pressure to reduce the incidence of this important nosocomial pathogen[2] and Figure 1 demonstrates an overall reduction in the number of *S. aureus* bacteraemias reported in Scotland between 2005 and 2009 as part of a mandatory surveillance scheme.[3]

Emerging resistance

Prior to the 1940s, virtually all *S. aureus* isolates were susceptible to penicillin. Following the introduction of this therapeutic agent in the mid 1940s, widespread resistance appeared as a result of the enzyme penicillinase hydrolysing the beta-lactam ring, rendering the drug inactive. Meticillin, a semi-synthetic penicillinase stable derivative, became

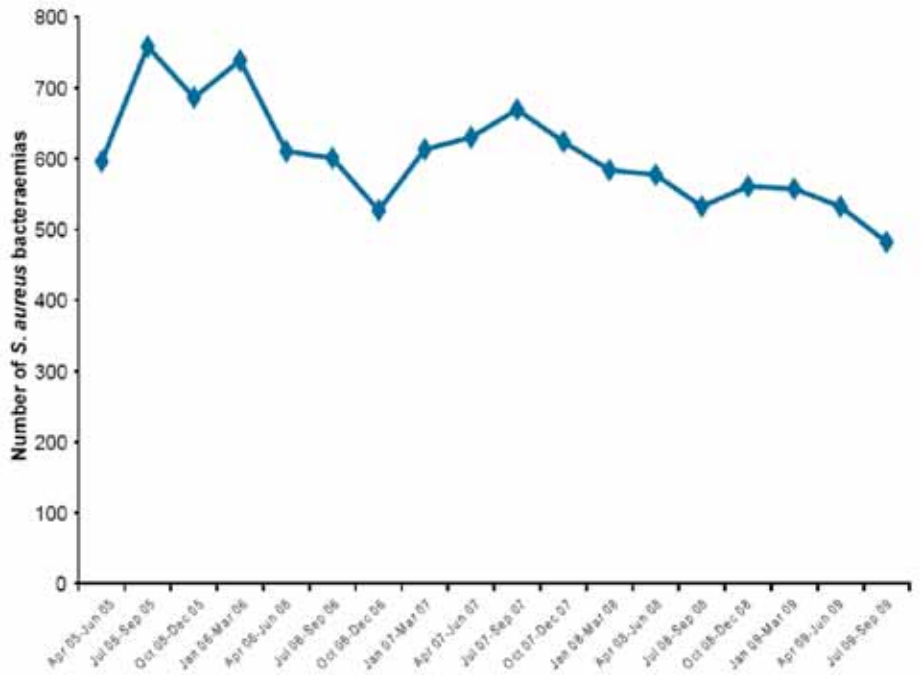

Figure 1. Quarterly numbers of *S. aureus* bacteraemias (including MRSA) in Scotland from April 2005 to March 2009.[3]

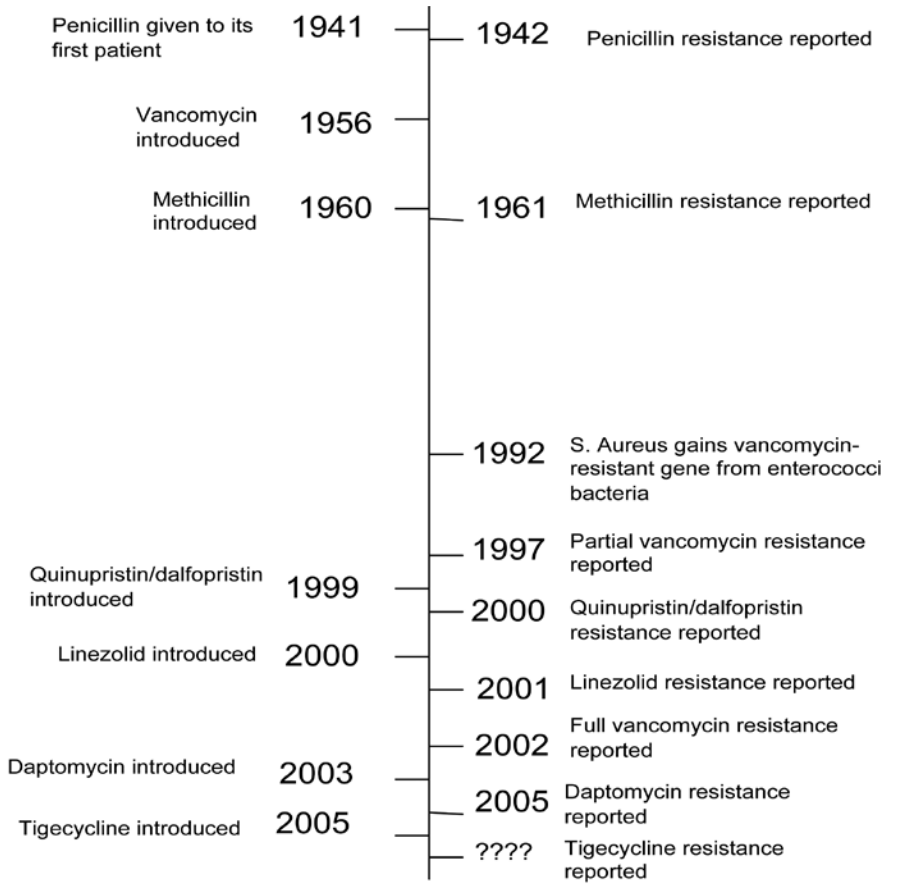

Figure 2. Time-line of emergence of resistance in *S. aureus*.

available in the late 1950s and the first MRSA was described around the same time.[4] Meticillin is no longer used clinically with flucloxacillin, the preferred agent for a meticillin sensitive *S. aureus* (MSSA). This pattern of emerging resistance has been repeated following the introduction of other antibiotics (Figure 2).[5]

MRSA refers to a strain of *S. aureus* that has acquired the *mecA* gene coding for an altered penicillin-binding protein (PBP2A) that renders the organism resistant to all current beta-lactam antibiotics, including penicillin, amoxicillin, flucloxacillin and the cephalosporins. Many HA-MRSA isolates demonstrate resistance to other antibiotic classes, such as the macrolides (eg erythromycin), lincosamides (eg clindamycin) and fluoroquinolones (eg ciprofloxacin). Serious infections with MRSA are treated with intravenous glycopeptides, such as vancomycin or teicoplanin. Newer oral agents, such as linezolid, have a role in special circumstances, although there are concerns regarding bone marrow toxicity.

Types of MRSA

Understanding the evolution of MRSA has improved with a range of phenotypic and genotypic (fingerprinting) techniques that can trace the spread of successful clones. There are thought to be five major lineages that spread throughout the world following the introduction of meticillin.[6] The main HA-MRSA strains in the UK are epidemic (E) MRSA15 and EMRSA16.

Advances in the sequencing of bacterial housekeeping genes has led to the use of a technique called multi-locus sequence typing (MLST) that assigns a unique 'sequence type' to identify a particular *S. aureus* strain accurately. Common MLST types are ST22 (EMRSA15) and ST36 (EMRSA16), for hospital-acquired strains, and ST8 (USA 300) and ST1 (USA 400), for those originating in the community.

Hospital and community-acquired MRSA – what is the difference?

In 1999, one of the first cases of CA-MRSA was reported in the USA, causing the death of four previously healthy children.[7] Cases of CA-MRSA have continued

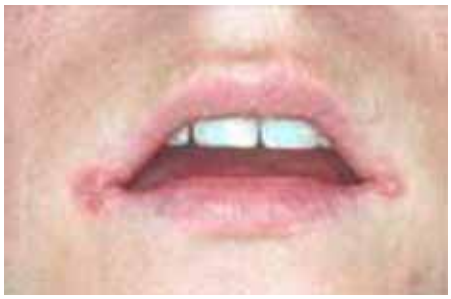

Figure 3. Clinical photograph of patient with angular cheilitis.

to increase in the USA, particularly amongst young people; often running a rapid and devastating course. Worldwide prevalence, however, remains low.[8] There are important phenotypic and genotypic differences between HA- and CA-MRSA, which are used to distinguish them (Table 1). Skin and soft tissue infections are among the most common manifestations of CA-MRSA and patients may report recurrent abscesses. Less common, but more severe, infections include necrotizing pneumonia and severe sepsis.

An array of pathogenic determinants may facilitate host colonization and disease in *S. aureus*, including:

- Surface proteins (eg fibronectin binding protein A/B);
- Antiphagocytic polysaccharide capsules;
- Cytotoxins;
- Superantigens; and
- Enzymes facilitating spread (eg proteases and hyaluronidase).

Panton-Valentine Leucocidin (PVL) toxin production is an important virulence factor in CA-MRSA, causing destruction of white blood cells and leading to massive tissue necrosis. The precise role of PVL in disease remains unresolved, although epidemiologically associated with SSTI and believed to have a role in the pathogenesis of severe necrotizing. While almost all CA-MRSA strains carry the PVL toxin, it is also found in MSSA.[9]

Staphylococcus aureus in the oral cavity

Colonization

There is sufficient evidence that *S. aureus* is an oral commensal, although its role in oral mucosal disease in immunocompetent hosts is unclear. The carriage rate in healthy adults ranges from 24–36%.[10] Prosthetic materials, such as acrylic dentures, increase the incidence of *S. aureus*, with one study reporting colonization in 23–48% of denture wearers, with 10% MRSA positive. Owing to the formation of biofilms, MRSA is difficult to eradicate using conventional denture cleansers, with some requiring heat sterilization or even re-making.[11,12] Another study suggested that 19% of institutionalized veterans were MRSA positive in the oral cavity.[13]

Children may have a higher incidence of *S. aureus* carriage compared to older dentate patients, with one study reporting 64% of children having *S. aureus* in the oral cavity.[14] Studies examining MRSA carriage in the oral flora of children revealed much lower incidence rates of up to 1.6%.[15]

Infection

Staphylococcus aureus is implicated in a spectrum of oral diseases, including angular cheilitis (Figure 3), parotitis, osteomyelitis and mucositis

Parameter	HA-MRSA	CA-MRSA
Patient group	Chronically or critically ill and/or immunocompromised patients in healthcare settings or with recent healthcare exposure. Nursing home residents.	Generally young healthy individuals with no healthcare exposure. Often occurs in settings where people are crowded, frequent skin to skin contact, lack adequate hygiene, share personal items and may have open cuts/abrasions on their skin.
Infection site	Variable including bacteraemia, surgical site, IV lines, bone/joint, pneumonia and catheter urines.	Predilection for recurrent skin and soft tissue infections (abscess, cellulitis). Rarely necrotizing pneumonia.
Transmission	Within healthcare settings. Often prior colonization.	Community-acquired. Spreads in sports teams and household contacts.
Panton-Valentine Leucocidin (PVL)	Usually absent.	Often present.
Antibiotic susceptibility	Often multi-resistant to several classes of antibiotics, eg macrolides, licosamides, fluoroquinolones, Treatment options may be limited.	Often resistant only to beta-lactam antibiotics. More treatment options.
Lineage	ST 22 (EMRSA 15). ST 8 (USA 300).	ST 36 (EMRSA 16). ST 1 (USA 400).

Table 1. Differences between HA-MRSA and CA-MRSA.[8]

(especially in the immunocompromised).

A 3-year study of laboratory data from Glasgow found a 5% incidence rate of MRSA from the 5,005 specimens analysed. Patients with MRSA were more commonly seen in primary care settings, such as nursing homes, hospices and general dental practice, rather than the dental hospital where the majority of MSSAs were isolated.[16]

Diagnosis

Diagnosis of suspected oral infections should be confirmed by appropriate specimens submitted to a diagnostic microbiology laboratory for culture, identification and susceptibility testing. This is particularly important for recurrent and/or difficult to treat infections that have not responded to first-line therapy. For example, intra- and peri-oral mucosal lesions should be swabbed, alongside other potential reservoirs of infection, such as the anterior nares and dentures. An oral rinse is also useful for angular cheilitis as *S. aureus* has been implicated in 63% of cases.[17]

General dental practitioners are advised to contact their local microbiology laboratory that will provide advice and supply specimen collection materials. The poor uptake of diagnostic microbiology facilities in general dental practice probably underestimates the role of *S. aureus* in oral disease.

Treatment

The successful treatment of any suspected infection, including MRSA, depends on an accurate diagnosis and removing the source of infection. Severe infections with systemic involvement require admission to tertiary referral centres and will not be discussed further here, aside from commenting that intravenous antibiotics are usually required guided by appropriate susceptibility results.

For more minor infections, including angular cheilitis, the use of topical miconazole (primarily an anti-fungal agent but with some anti-staphylococcal properties) or topical naseptin (a combination of neomycin and chlorhexidine) may suffice. Prolonged courses of topical fusidic acid monotherapy must be avoided as this leads to the emergence of resistance, thereby reducing the availability of a useful oral anti-MRSA agent in more severe infections.

Other infections, including mucositis and parotitis, often require systemic antibiotics, and these must be guided by susceptibility testing, as the resistance pattern of oral anti-MRSA agents is difficult to predict. Specific advice should be sought from a microbiologist, however, treatment usually involves combination therapy, eg doxycycline and fusidic acid to minimize resistance. Flucloxacillin is advocated for MSSA infections. Treatment of MRSA colonization is generally not advocated.

Antibiotic prescribing and MRSA

An important role in the control of MRSA by dentists is responsible prescribing of antibiotics. Frequent antibiotic use has been linked to increased MRSA acquisition.[18] One study showed that, among professional football players, the risk of contracting MRSA was almost eight times higher if players had taken antibiotics in the previous year versus those who had not.[19] A study of general dental practitioners in England found that, of the 2,951 prescriptions issued over a time period, only 29% were considered justifiable using published guidelines.[20] Another study,[21] examining prescribing practices of general dental practitioners in England, found 69% of dentists prescribed antibiotics prior to drainage and 45% when it was established, despite research demonstrating that drainage of an infection is the only treatment necessary for the majority of infected swellings without systemic symptoms. As *S. aureus* may colonize various body sites, systemic antibiotics prescribed inappropriately for other conditions will affect the endogenous flora and potentially drive resistance.

Prevention of MRSA transmission

The dental team has a responsibility for the prevention of spread of MRSA. Therefore, it is essential that high standards of infection control are adhered to for every patient in the practice, as most patients are unaware of their MRSA status.

The nine elements of standard infection control procedures

1. Hand hygiene
2. Personal protective equipment
3. Cleanliness of care equipment
4. Cleanliness of environment
5. Prevention of occupational exposure
6. Management of blood and body fluid spillage
7. Safe handling of uniforms
8. Safe disposal of waste
9. Patient placement (applicable in secondary care facilities)

Table 2. Standard infection control procedures.

Furthermore, it is not feasible to screen for MRSA carriage in dental practice. Table 2 outlines the standard infection control procedures (SICPs) that must be followed. No additional precautions are required to manage a patient known to have MRSA in the dental setting.

There have been documented cases of MRSA oral infection transmitted by a dentist.[22] A study in Japan[23] of nosocomial transmission of MRSA, via the surfaces of the dental surgery, found that 6% (8/140) of patients treated in an oral and maxillofacial surgery were found to be colonized after treatment, after identical strains were isolated on the dental chair and air syringe. A further study of *S. aureus* environmental contamination in an 89 chair dental clinic in a dental hospital in Brazil identified MRSA colonized surfaces in the emergency dental clinic and that clinical procedures increased the dispersal of *S. aureus* into the environment.[24] Both these studies highlight the need for strict adherence to SICPs in dental settings.

Conclusions

CA-MRSA is a significant problem in the USA and is of growing concern in the UK. These new strains appear to have a predilection for damaged skin and airways, and may be PVL toxin positive. CA-MRSA strains are transmissible, especially amongst family members, staff/children in nurseries and in sports teams. Therefore, it is essential that the dental team follow SICPs, practise prudent

antimicrobial prescribing and do not discriminate against MRSA positive patients.

The incidence of documented oral *S. aureus* infections is low, but this may be masked by an equally low number of diagnostic samples taken by dentists. We strongly encourage all dentists to consider using diagnostic microbiology laboratories to facilitate in the diagnosis of oral infections.

Acknowledgements

1. Figure 1 by kind permission of Health Protection Scotland.
2. Figure 2 by kind permission of Elsevier.
3. Figure 3 kindly donated by Professor David Wray, Oral Medicine Department, Glasgow Dental Hospital.

References

1. Elston JW, Barlow GD. Community-associated MRSA in the United Kingdom. *J Infect* 2009; **59**: 149–155.
2. The Scottish Government. *NHS Scotland Chief Executive's Annual Report 2007/08*. Edinburgh: web only, 2008. **http://www.scotland.gov.uk/Publications/2008/11/28081831/10**
3. Health Protection Scotland. *Staphylococcus Aureus Bacteraemias Report – January 2010*. **http://www.documents.hps.scot.nhs.uk/hai/sshaip/publications/mrsa-quarterly-reports/sab-2010-01.pdf**
4. Jevons MP. "Celbemom"– resistant staphylococci. *Br Med J* 1961; **14**: 113–114.
5. Lubelchek RJ, Weinstein R. Antibiotic resistance and nosocomial infections. In: *The Social Ecology of Infectious Diseases*. Mayer KH, Pizer HF, eds. London: Academic Press, 2008; p243.
6. Oliveira DC, Tomasz A, de Lencastre H. Secrets of success of a human pathogen: molecular evolution of pandemic clones of meticillin-resistant *Staphylococcus aureus*. *Lancet Infect Dis* 2002; **2**: 180–189.
7. Centers for Disease Control and Prevention. Four pediatric deaths from community-acquired methicillin-resistant *Staphylococcus aureus*: Minnesota and North Dakota, 1997–1999. *MMWR Morb Mortal Wkly Rep* 1999; **48**: 707–710.
8. Nathwani D, Morgan M, Masterton RG *et al*. Guidelines for UK practice for the diagnosis and management of methicillin-resistant *Staphylococcus aureus* (MRSA) infections presenting in the community. *J Antimicrob Chemother* 2008; **61**: 976–994.
9. Que Y, Moreillon P. *Staphylococcus aureus* (including Staphylococcal toxic shock). In: *Principles and Practice of Infectious Disease* 7th edn. Mandell GL, Bennett JE, Dolin R, eds. Philadelphia: Churchill Livingstone, 2010; pp2543–2578.
10. Jackson MS, Bagg J, Gupta MN, Sturrock RD. Oral carriage of staphylococci in patients with rheumatoid arthritis. *Rheumatology* 1999; **38**: 572–575.
11. Dahlen G, Linde A, Moller AJR, Ohman A. A retrospective study of microbiologic samples from oral mucosal lesions. *Oral Surg Oral Med Oral Pathol* 1982; **53**: 250–255.
12. Tawara Y, Honma K, Naito Y. Methicillin-resistant *Staphylococcus aureus* and *Candida albicans* on denture surfaces. *Bull Tokyo Dent Coll* 1996; **37**: 119–128.
13. Owen MK. Prevalence of oral methicillin-resistant *Staphylococcus aureus* in an institutionalized veterans population. *Spec Care Dentist* 1994; **14**: 75–79.
14. Jackson MS, Bagg J, Kennedy H, Mitchie J. Staphylococci in the oral flora of healthy children and those receiving treatment for malignant disease. *Microb Ecol Health Dis* 2000; **12**: 60–64.
15. Miyake Y, Iwai M, Sugai M, Miura K, Suginaka H, Nagasaka N. Incidence and characterization of *Staphylococcus aureus* from the tongues of children. *J Dent Res* 1991; **70**: 1045–1047.
16. Smith AJ, Robertson D, Tang MK, Jackson MS, Mackenzie D, Bagg J. *Staphylococcus aureus* in the oral cavity: a three-year retrospective analysis of clinical laboratory data. *Br Dent J* 2003; **195**: 701–703.
17. Ohman S-C, Dahlen G, Moller A, Ohman A. Angular cheilitis: a clinical and microbial study. *J Oral Pathol* 1986; **15**: 213–217.
18. Tacconelli E, De Angelis G, Cataldo MA, Pozzi E, Cauda R. Does antibiotic exposure increase the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) isolation? A systematic review and meta-analysis. *J Antimicrobial Chemother* 2008; **61**: 26–38.
19. Kazakova SV, Hageman JC, Matava M *et al*. A clone of methicillin-resistant *Staphylococcus aureus* among professional football players. *N Engl J Med* 2005; **352**: 468–475.
20. Chate RA, White S, Hale RO *et al*. The impact of clinical audit on antibiotic prescribing in general dental practice. *Br Dent J* 2006; **201**: 635–641.
21. Palmer NA, Pealing R, Ireland RS, Martin MV. A study of therapeutic prescribing in National Health Service general dental practice in England. *Br Dent J* 2000; **188**: 554–558.
22. Martin MV, Hardy P. Two cases of oral infection by methicillin resistant *Staphylococcus aureus*. *Br Dent J* 1991; **10**: 63–64.
23. Kurita H, Kurashina K, Honda T. Nosocomial transmission of methicillin-resistant *Staphylococcus aureus* via the surfaces of the dental operatory. *Br Dent J* 2006; **201**: 297–300.
24. Motta RH, Groppo FC, Bergamaschi Cde C, Ramaciatto JC, Baglie S, de Mattos-Filho TR. Isolation and antimicrobial resistance of *Staphylococcus aureus* isolates in a dental clinic environment. *Infect Control Hosp Epidemiol* 2007; **28**: 185–190.

CPD ANSWERS

April 2011

1. B, D
2. A, B, D
3. C, D
4. B, C, D
5. A, B
6. A, D
7. A, C, D
8. A, B, D
9. B, D
10. A, D