The significance of MRSA and VRE in chronic wounds

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Summary

Methicillin resistant *Staphylococcus aureus* (MRSA) and Vancomycin resistant enterococci (VRE) are important nosocomial bacteria which are highly resistant to antibiotics and readily transmitted patient to patient. They are significant in chronic wounds in terms of causing infection, especially MRSA, and by constituting an infection control risk.

It is important to distinguish colonisation from infection of chronic wounds, as infection requires specific treatment whereas colonisation does not. If signs of infection (increased purulence, pain, swelling, redness, warmth) are present, local measures to control infection should be instituted and, if these fail, antibiotics should be used. Local measures are more important with these bacteria as the drugs to treat them are not readily available or have to be given parenterally. In terms of infection control, handwashing before and after patient contact is the most important measure. Cleaning of the environment is also important.

Methicillin resistant *Staphylococcus aureus* (MRSA)

Staphylococcus aureus

S. aureus is a pyogenic coccus which exists as a commensal bacterium of humans [1]. It possesses multiple virulence factors and causes a multitude of different infections, either by direct invasion or by liberation of toxins [1]. The organism is noted for its ability to be passed person to person, to evade the host response, and its remarkable ability to acquire resistance to antibiotics.

Emergence of resistance in *S. aureus*

Penicillin was first used in humans in 1942; in the next year, resistance to penicillin was reported. Penicillin resistant *S. aureus* became common initially in the hospital and then in the community setting during the 1960s.

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In 1957, methicillin was released and, in 1961, MRSA was first described [2]. MRSA was uncommon until outbreaks were described in hospitals in the mid 1970s. These strains became endemic throughout hospitals during the 1980s [3]. The 1990s saw the emergence of community MRSA strains which, for the most part, were not derived from hospital strains but emerged *de novo* 3.

Resistance to vancomycin was first reported in 1998 [4]. Fortunately, vancomycin resistant *S. aureus* are extremely rare at this stage.

MRSA strains are currently usually detected in patients that have had association with hospitals or other health care facilities. By definition, MRSA strains are resistant to all beta-lactams and are usually resistant to other drugs. In addition, they readily contaminate the hands of health care workers which is probably the major mode of transmission patient to patient. They also readily contaminate the environment, which can act as an important reservoir. Thus MRSA strains have a high epidemic potential.

'Community acquired' MRSA strains have been reported from multiple parts of the globe [5]. Patients harbouring these strains are often from low socio-economic groups and are often children or young adults [5]. The organism predominantly causes abscesses and cellulitis [6]. The organisms are usually not resistant to non-beta-lactam

antibiotics [6] which is distinct from MRSA strains seen in hospitals.

Transmission of MRSA

MRSA acquisition in the health care setting is a complex interaction between reservoirs of the organism and vectors of transmission [7, 8]. Health care facilities usually acquire MRSA by receipt of a patient colonised with MRSA [9]. This patient acts as the initial reservoir.

MRSA is readily transmitted on the hands of health care workers [8]. If the health care worker does not wash his/her hands before visiting the next patient, transmission of MRSA is likely. Patients with open wounds, endotracheal tubes and other violations of the integrity of the skin readily become colonised with MRSA [10-12] and once it is colonising them, it is very difficult to remove. The anterior nares is usually colonised as well, and sometimes other areas such as the pharynx, the axillae, perineum and gastrointestinal tract are colonised. Colonisation may persist months or even years after discharge from the health care facility [13].

The ward environment is readily contaminated with MRSA [9] and this has been shown to be an important reservoir, especially when cleaning is curtailed due to fiscal pressures. The room itself, and fomites such as sphingmomanometers, thermometers, bed linen etc, all get contaminated, especially if the residing patient is heavily colonised with MRSA.

MRSA is readily moved ward to ward if there is a high circulation of patients, which is the norm in the modern hospital. Health care workers also look after an increasing number of patients and often work in multiple wards. This also helps spread MRSA. In addition, the close proximity of many ill patients, especially in settings such as intensive care units (ICUs) [11] facilitates transmission of MRSA. Patients that have to remain in hospital are more complex, more likely to spend time in the ICU, are more likely to receive broad spectrum antibiotics [10, 11] and, if they become colonised with MRSA, are more likely to remain in the hospital for a long period as a reservoir of MRSA.

Tracking of infections with MRSA is much more difficult with earlier discharge, and devolvement of most of the post-operative care to facilities outside the control of hospitals. Many post-operative infections now presenting to the GP are not recorded in the infection control statistics of hospitals.

Antibiotic use, particularly heavy use of third generation cephalosporins and quinolones, exerts pressure to select out resistant bacteria such as MRSA.

The significance of *S. aureus* in chronic wounds

The significance of *S. aureus* in a patient's wound needs to be assessed for each patient. The organism may be colonising the wound or may be causing infection [1]. Colonisation means that the organism is present but is not invading the tissues and is not inciting acute inflammation. Infection denotes tissue invasion and damage from toxins and the host's immune response. Colonisation does not require treatment, infection does.

The fact that a *S. aureus* strain is MRSA does not necessarily mean that infection is present, it may just be colonising the wound. However, its presence may retard wound healing, as the multiple toxins liberated may incite an ongoing inflammatory response [14]. It also is of infection control significance (see below).

It is difficult, if not impossible, to clear MRSA presence in a chronic wound, even if appropriate antibiotics are given. Presumably this is because most of the non-beta-lactam antibiotics are bacteriostatic i.e. do not kill the bacteria. Vancomycin, the usual parenteral antibiotic used for MRSA, only acts slowly on MRSA and does not penetrate well into secretions on the surface of ulcers and other chronic wounds. This results in the paradoxical finding of positive swabs for MRSA despite the patient being on vancomycin.

Signs of infection include redness, pain, swelling, heat and purulence. If the bacteria invade lymphatics or blood, the patient may exhibit systemic features; fever, rigors, tachycardia, hypotension. Patients with wounds exhibiting signs of infection will require antibiotic treatment. If the inflammation is minor, topical measures may suffice. This is worth noting as the drugs to treat MRSA (such as rifampicin and fusidic acid) are often difficult to obtain outside of the teaching hospital setting or have to be given parenterally.

Diabetic and decubitus ulcers are wounds that are particularly likely to become infected [15]. These lesions are likely to penetrate deeply to bone. Consequently, bacteria can readily invade bone and set up osteomyelitis. Paradoxically, most cases of osteomyelitis, complicating diabetic and decubitus ulcers do not exhibit systemic signs of sepsis. However, they may have raised markers of infection, such as

Erythroate Sedimentation Ratio and C. Reactive Protein, which should always be performed in this setting.

A technetium bone scan, coupled with either a gallium or labelled white cell scan, is very useful in this setting to make the diagnosis of osteomyelitis [16]. MRI scanning is also useful – despite the expense – as it shows the information that a bone and white cell scan give together with anatomical information [17] which is useful for the surgeon. If osteomyelitis is diagnosed, a prolonged course of intravenous followed by oral antibiotics needs to be given.

Infection control issues

Specific measures dealing with this are described in state department of health documents [18]. The general principles are as follows [8]. A patient with a chronic wound colonised or infected with MRSA acts as a heavy reservoir of MRSA infection. If the patient is in a health care facility, the earlier he/she is discharged the better. The patient should be isolated or cohorted with other MRSA patients. Universal precautions should be followed.

Health care workers dealing with the wound should wear a new pair of gloves which are discarded after dealing with that patient. Hand antisepsis before and after the contact with the wound has been shown to decrease MRSA transmission [19] – this paper showed compliance with hand asepsis was improved by providing antiseptic hand rubs. Compliance with hand rubs increased, but compliance with handwashing remained stable during the study period. Compliance with hand rubs was enough to reduce transmission of MRSA.

After wounds have been dressed, all the equipment used should be disposed of. The room should be terminally cleaned before a patient without MRSA is cared for in the room. The reason for this is that the MRSA will disperse to colonise the room – transmission to the next patient, especially one with a wound, can occur if the environment is contaminated with MRSA.

Treatment of MRSA

If an ulcer is deemed to be infected, treatment may consist of local measures, such as anti-infective dressings, topical antibiotics, oral antibiotics or parenteral antibiotics [1]. Local measures assume greater importance because of the difficulty of procuring the MRSA drugs and their toxicity, and should be used in the first instance. Most MRSA isolates are susceptible to mupirocin (Bactroban®). However, use of topical agents may result in the emergence of resistance, especially with MRSA, and is to be discouraged.

The exact susceptibility profile of the MRSA dictates what oral or parenteral antibiotics can be used. Most of the hospital associated MRSA strains in eastern Australia are multi-resistant, and usually are only susceptible to vancomycin, rifampicin and fusidic acid [20]. However, we are seeing the emergence of new hospital MRSA strains, such as EMRSA-15 ('epidemic' MRSA strain 15), which are susceptible to a wider range of antibiotics [21]. The community acquired MRSA strains are usually susceptible to drugs such as erythromycin, clindamycin, tetracyclines, ciprofloxacin, trimethoprim etc [6] and these drugs could be used in treating infections with these strains. The take home message is that it is essential to take swabs to determine the bacterial flora of an ulcer and, if *S. aureus* is isolated, for the susceptibility pattern to be reported in full.

Eradication of MRSA carriage

This only works if endogenous reservoirs can be cleared. This is impossible in the presence of actively infected lesions, as the organism load is high and the bacteria can be sequestered beyond the reach of antibiotics. A regimen to eradicate MRSA carriage is only indicated if a patient has recurrent infections but has no active lesions at the time.

One regimen consists of four arms – oral rifampicin, oral fusidic acid, nasal mupirocin and showering daily using a medicated anti-staphylococcal soap. The regimen is continued for 2 weeks, then repeated a month later. Alternatively, it can be given for 4 weeks. The success rate is >90 per cent if all four measures are complied with *and* the patient does not have active lesions at the time treatment is started.

Vancomycin resistant enterococci (VRE)

Enterococci

Enterococci, which used to be grouped with the streptococci, are part of the normal gastrointestinal and genital flora of animals and humans [22]. They do not possess many virulence factors, unlike *S. aureus*, and hence usually only cause problems in the immunocompromised [22]. In general, their presence represents colonisation rather than infection. The two species of enterococci of most importance in human infection are *Enterococcus faecalis* and *Enterococcus faecium*.

Emergence of resistance in enterococci

Enterococci are intrinsically resistant to antibiotics [22] i.e. the resistance is innate and not acquired. Whilst microbiology reports generally call them susceptible to penicillins, they are in fact much less susceptible to penicillins than, say, group A streptococci. In fact, no antibiotic alone (in clinical doses) will kill them, and it requires a combination of either a penicillin or vancomycin plus an aminoglycoside to kill them. Enterococci are completely resistant to cephalosporins. *E. faecium* isolates are often resistant to amoxycillin and gentamicin.

Resistance to vancomycin emerged in Europe in the late 1980s [23] but really had a major impact in 1990s, such that they are common in Europe and the USA [24]. Isolation of VRE was first reported in Australia in 1994, and has steadily increased since [25]. By 1999, 60 per cent of teaching hospitals were reported to have VRE, 3.5 per cent of enterococci were VRE, and 10 per cent of *E. faecium* in blood cultures were VRE [Jan Bell, personal communication].

Transmission of VRE

The reservoirs and vectors of transmission of VRE are essentially the same as with MRSA [24], with some differences as highlighted below. VRE, like other enterococci, are colonisers and tend to reside in the usual sites enterococci are found – the gastrointestinal and genital tracts [24]. Of note; diarrhoea or faecal incontinence can disperse VRE throughout a ward [26]. The administration of antibiotics will eradicate most of the normal flora of the gastrointestinal and genital tracts and facilitate colonisation with VRE. VRE disseminate widely in the environment [26].

Patient risk factors for VRE acquisition include: exposure to antibiotics, especially vancomycin, but also quinolones and third generation cephalosporins; having a prolonged hospitalisation; spending time in ICU or the haematology ward; and undergoing dialysis or transplantation [24].

The significance of VRE in chronic wounds

VRE, like other enterococci, are of low virulence and are unlikely to invade tissues and establish an infection [24]. Their presence is primarily an infection control issue. They are almost impossible to eradicate, as they will colonise the gut as well as the wound. If a wound colonised with VRE is clinically infected, exhibiting the signs described above with MRSA, then local measures assume greater importance as the organism is very difficult to treat with antibiotics. It is mostly not necessary to give antibiotics to patients with VRE isolated from wounds.

Infection control issues

When VRE first occurred, draconian infection control measures were instituted in many centres. Subsequently, these recommendations have been scaled back to parallel those for MRSA [18]. Again, handwashing is the most important control measure.

Antibiotic control measures are important in controlling VRE [27]. The use of vancomycin is related to the emergence of VRE, and it is no surprise that since vancomycin is used to treat MRSA, if MRSA rises then the likelihood of also developing a VRE problem also rises.

Vancomycin is also used to treat coagulase-negative staphylococci, which are usually methicillin resistant. Infections with coagulase-negative staphylococci (such as *Staphylococcus epidermidis*) are on the rise. It is recommended to only use vancomycin for proven infections with methicillin resistant staphylococci (both *S. aureus* and coagulase-negative staphylococci), and to avoid empiric or prophylactic use if possible. Similarly, drugs such as cephalosporins and quinolones exert selection pressure and their use should be curtailed.

Environmental hygiene is very important. Cleaning of wards goes a long way in controlling VRE [28]. Rooms that harboured a VRE colonised patient need to be terminally cleaned before the next patient takes up residence.

Treatment of VRE

Treatment of VRE will necessarily be done on the recommendation of a medical microbiologist or infectious diseases physician using experimental drugs obtained under the special access scheme. Drugs used include linezolid, pristinomycin and quinupristin/dalfopristin.

Eradication of VRE carriage

This is entirely experimental, there are no defined regimens. None of the agents with good mucosal penetration are active against VRE. Avoiding any antibiotic use is important at facilitating the clearing of VRE.

Conclusions

The presence of MRSA or VRE in chronic wounds is mostly of infection control significance. Sometimes the presence of MRSA may prolong wound healing. Occasionally MRSA may cause overt infection and antibiotic treatment is required

should local measures fail. It is very important to adhere to infection control recommendations when dealing with patients whose chronic wounds harbour MRSA or VRE.

References

1. Waldvogel FA. *Staphylococcus aureus* (including Staphylococcal Toxic Shock). In: Mandell GL, Bennett JE & Dolin R (Eds). Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. New York: Churchill Livingstone, 2000: 2069-2092.
2. Jevons MP. "Celbenin"-resistant staphylococci. Br Med J 1961; **1**:124-125.
3. Pearman JW. MRSA: the pathogen hospitals dread. Microbiol Aust 1996; 29-31.
4. Hiramatsu K, Aritaka N, Hanaki H *et al.* Dissemination in Japanese hospitals of strains of *Staphylococcus aureus* heterogeneously resistant to vancomycin. Lancet 1997; **350**:1670-1673.
5. Collignon P, Gosbell I, Vickery A, Nimmo G, Stylianopoulos T & Gottlieb T. Community acquired meticillin-resistant *Staphylococcus aureus* in Australia. Australian Group on Antimicrobial Resistance. Lancet 1998; **352**:145-146.
6. Gosbell IB, Mercer JL, Neville SA *et al.* Non-multiresistant and multiresistant methicillin resistant *Staphylococcus aureus* in community acquired infections. Med J Aust 2001; **174**:627-630.
7. Weber DJ & Rutala WA. Environmental Issues and Nosocomial Infections. In: Wenzel RP (Ed). Prevention and Control of Nosocomial Infections. Baltimore: Williams and Wilkins, 1993: 420-449.
8. Mayhall CG. Surgical Infections Including Burns. In: Wenzel RP (Ed). Prevention and Control of Nosocomial Infections. Baltimore: Williams and Wilkins, 1993: 614-664.
9. Haley RW, Hightower AW, Khabbaz RF *et al.* The emergence of methicillin resistant *Staphylococcus aureus* infections in United States hospitals. Possible role of the house staff-patient transfer circuit. Ann Intern Med 1982; **97**:297-308.
10. Wenzel RP, Nettleman MD, Jones RN & Pfaller MA. Methicillin resistant *Staphylococcus aureus:* implications for the 1990s and effective control measures. Am J Med 1991; **91**:221S-227S.
11. Thompson RL, Cabezudo I & Wenzel RP. Epidemiology of nosocomial infections cuased by methicillin resistant *Staphylococcus aureus.* Ann Intern Med 1982; **97**:309-317.
12. Haley RW, Cushion NB, Tenover FC *et al.* Eradication of endemic methicillin resistant *Staphylococcus aureus* infections from a neonatal intensive care unit. J Infect Dis 1995; **171**:614-624.
13. Frenay HME, Vandenbroucke-Gauls CMJE, Molkenboer MJCH & Verhoef J. Long-term carriage and transmission of methicillin resistant *Staphylococcus aureus* after discharge from hospital. J Hosp Infect 1992; **22**:207-215.
14. Yamada Y, Sugai M, Woo M, Nishida N & Sugimoto T. Acquired subglottic stenosis caused by methicillin resistant *Staphylococcus aureus* that produce epidermal cell differentiation inhibitor. Arch Dis Child Fetal Neonatal Edition 2001; **84**:F38-F39.
15. Tentolouris N, Jude EB, Smirnof I, Knowles EA & Boulton AJ. Methicillin resistant *Staphylococcus aureus*: an increasing problem in a diabetic foot clinic. Diab Med 1999; **16**:767-771.
16. Becker W. Imaging osteomyelitis and the diabetic foot. Q J Nuc Med 1999; **43**:9-20.
17. Spaeth HJ Jr & Dardani M. Magnetic resonance imaging of the diabetic foot. Mag Res Imag Clin Nor Am 1994; **2**:123-130.
18. NSW Health Department Circular 99/87. Infection Control Policy. Sydney, Australia, NSW Health Department 1999.
19. Pittet D, Hugonnet S, Harbarth S *et al.* Effectiveness of a hospital wide programme to improve compliance with hand hygiene. Infection Control Programme. Lancet 2000; **356**:1307-1312.
20. Vickery AM, Australian Group for Antimicrobial Resistance. Strains of methicillin resistant *Staphylococcus aureus* isolated in Australian hospitals from 1986 to 1990. J Hosp Infect 1993; **24**:139-151.
21. Pearman JW, Coombs GW, Grubb WB & O'Brien F. A British epidemic strain of methicillin resistant *Staphylococcus aureus* (UK EMRSA-15) in Western Australia. Med J Aust 2001; **174**:662-662.
22. Fuchs PC, Jones RN, Barry AL & Gavan TL. Ofloxacin susceptibility testing quality control parameters for microdilution and disk diffusion, and confirmation of disk diffusion interpretive criteria. J Clin Microbiol 1989; **27**:49-52.
23. Uttley AH, Collins CH, Naidoo J & George RC. Vancomycin resistant enterococci. Lancet 1988; **1**:57-58.
24. Cetinkaya Y, Falk P & Mayhall CG. Vancomycin resistant enterococci. Clin Microbiol Rev 2000; **13**:686-707.
25. Bell J, Turnidge J, Coombs G & O'Brien F. Emergence and epidemiology of vancomycin resistant enterococci in Australia. Comm Dis Intel 1998; **22**:249-252.
26. Boyce JM, Opal SM, Chow JW *et al.* Outbreak of multidrug resistant *Enterococcus faecium* with transferable vanB class vancomycin resistance. J Clin Microbiol 1994; **32**:1148-1153.
27. Quale J, Landman D, Saurina G, Atwood E, DiTore V & Patel K. Manipulation of a hospital antimicrobial formulary to control an outbreak of vancomycin resistant enterococci. Clin Inf Dis 1996; **23**:1020-1025.
28. Armstrong-Evans M, Litt M, McArthur MA *et al.* Control of transmission of vancomycin resistant *Enterococcus faecium* in a long-term care facility. Infect Control Hosp Epidemiol 1999; **20**:312-317.

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