A review on methicillin-resistant *Staphylococcus aureus*: public health risk factors, prevention, and treatment

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In the United States, the Centers for Disease Control and Prevention estimated that 80 461 invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infections and 11 285 related deaths occurred in 2011. In the United Kingdom, around 190 people passed away from MRSA disease in 2021. Australia, Hong Kong, Singapore, Japan, and Greece also have MRSA infections, along with the whole world. MRSA caused less than 2% of bacterial diseases in the United States in 1974, while the percentage rate increased up to 64% in 2004 only 10 years to increase the infection rate to 300%. In the United States, MRSA killed almost 18 000 more people in the United States in 2005 than the HIV. MRSA is classified as either community-acquired or health-related. Both are community-acquired MRSA or health-related MRSA, and both can be transmitted through skin contact. CA-MRSA, like severe pneumonia, septic conditions, and necrotizing fasciitis, can contaminate soft tissue, causing bubbles and skin abscesses. MRSA influences patients in medical clinic settings like nursing homes, medical clinics, and dialysis centers, as a rule, bringing about blood diseases, careful cut contamination, or pneumonia. The MRSA disease is exceptionally dangerous for newborn children, the elderly, and the debilitated.

Keywords:
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Introduction

Staphylococcus aureus is a human normal flora [1,2]. It possesses the ability to cause diseases like meningitis, sepsis, pneumonia, endocarditis, and osteomyelitis [3]. The accumulation of microorganisms in the human body causes increased contamination levels. It can happen in the skin, perineum, throat, gastrointestinal system, as well as the vagina [4]. According to the bacterial ability to resist methicillin, it was identified as methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *Staphylococcus aureus* (MSSA). Resistance to all beta-lactam antibiotics is conferred by the organism's methicillin resistance [5].

MRSA was first identified as a source of patient disease in clinical offices in the 1960s, and it is now the leading cause of localized skin and soft tissue contamination in many American cities [6,7]. MRSA is a common microorganism of postpregnancy maternal disease [8], and contamination in the neonatal emergency unit is frequent [9]. Transmission through clinical staff, relatives, guests, and surrounding surfaces, for example, has been widely established [10]. All of these factors increase the risk of MRSA colonization or disease [11].

Researchers estimated that antimicrobial resistance in bacteria caused an estimated 1.27 million deaths in 2019 [12]. An unmistakable clone of the MRSA bacterium connected with the cow-like host has been found locally starting around 2003 [13]. This nonprinting (NT) clone was at first known as NT-MRSA as it was found by beat-gel electrophoresis using the SmaI limitation chemical [14]. All strains are individuals from clonal complex 398 (CC398), as indicated by multisite sequencing [15]. Right now, it is obvious that the transmission pace of MRSACC398 among people who have regular contact with pigs or calves is a lot higher than in everybody else (25–35 vs. 0.1% in the Netherlands) [16].

S. aureus, like most different diseases, is classified into three sorts depending on the source of contamination: medical services, community, and livestock. Accordingly, MRSA strains are isolated into three categories: healthcare-associated MRSA (HA-MRSA) [17], community-associated MRSA (CA-MRSA) [17,18], and livestock-associated MRSA

(LA-MRSA) [19]. Noncrisis cases, past hospitalization, ongoing hemodialysis, past infection medication, past MRSA disease or colonization, past admission to the critical care unit, and HIV infection of the human-resistant framework have all been recognized as *S. aureus* risk factors just like diabetes [20].

A few examinations have shown that numerous *S. aureus* contaminations are caused by solid vector transmission, suggesting that concentrating on *S. aureus* indicators is significant for understanding the possibility of MRSA transmission and obtrusive contaminations [21]. MRSA is a dangerous general health concern as it is impervious to most regularly used antitoxins [22] and is the particular cause of pestilence [23]. Besides, MRSA accident is consistent with an extended stay in the emergency clinic and an increase in medical costs that could add up to &z.euro;44 million [24].

In colonized individuals, nasal pregnancy with *S. aureus* is connected with an increased danger of infection [25,26]. Notwithstanding, it is hazy whether the danger of disease in colonized individuals is expanded when transmission proceeds [27,28]. In the provinces, around 5% of medical service laborers get a clinical disease [29], and certain case reports uncover indicative MRSA infection among medical care laborers [30].

Development of methicillin-resistant *Staphylococcus aureus*

Alexander Fleming discovered penicillin in 1929, a chemical released by the mold *Penicillium* that has the potential to kill bacteria, including certain staphylococci. *S. aureus* isolates were resistant to penicillin and other antibiotics within a year of its introduction. In the 1950s, Europe and North America experienced the first nosocomial penicillin-resistant staphylococci epidemics, only a decade after widespread prophylactic use of postoperative antibiotics became common [31–34].

Although MRSA responds to other penicillin and cephalosporin antibiotics, it may be resistant to penicillin and cephalosporin as well. MRSA can live in unfavorable environments for months and spread from surfaces after a long period of deposition [33,35–37].

Skin and soft tissue infections are more common in CA-MRSA patients and their families. Nosocomial MRSA transmission affects 1.5% of untreated individuals in US hospitals as cited by Bassetti *et al.* [38]. This number can be as high as 3% in some adult groups, such as the US Army or collegiate track and field teams; the reason is unknown but could be due to close living conditions and recurrent skin trauma among military personnel [39]. MRSA has the potential to colonize a high number of residents in long-term care settings. Asymptomatic MRSA carriers are frequently encountered in therapeutic settings and serve as a reservoir of MRSA that chiropractors must address, particularly in terms of infection control techniques [40–42].

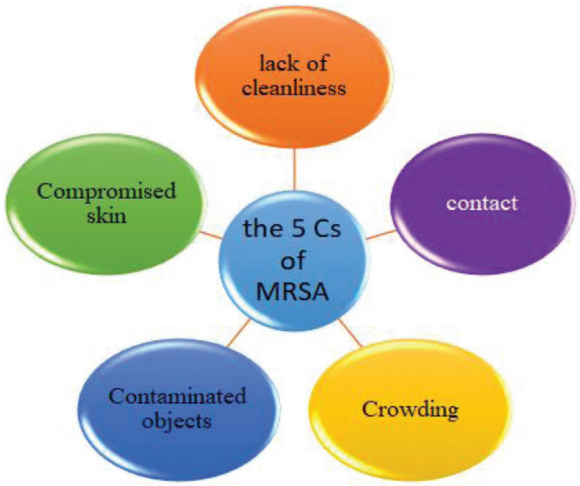
The coexistence of HA-MRSA and CA-MRSA is extremely fascinating to healthcare members, and such coexistence could be related to earlier exposure to antibiotics and/or healthcare facilities, or interaction between healthcare professionals and community members [43]. Hospital colonization is projected to become the norm. Both sorts of stress are conceivable in clinics where postoperative patients interact with undamaged individuals [31,44–50].

More than half of MRSA strains are resistant to macrolides, lincosamides, fluoroquinolones, and aminoglycosides. MRSA spreads more easily in the population, yet it is more resistant to a variety of medications. Vancomycin is the most recent antibiotic approved to treat severe MRSA. VRSA, unfortunately, has become a reality. Furthermore, there is growing worry that when community and hospital strains mingle and patients and community members bring these strains to the hospital, especially fatal community variants that infect healthy people, they become more resistant to medications [31,44,46,48,51].

Risk factors for infection

MRSA is most common among infants, the elderly, people with chronic conditions, burn survivors, organ transplant recipients, cancer patients receiving chemotherapy, steroid users, diabetics, intravenous drug users, and people with HIV. The hospital duration, drug exposure, and MRSA infection are all factors in MRSA infection (HA-MRSA) [51–55]. Exposure to MRSA-infected patients in outpatient or community settings is a risk factor for CA-MRSA. MRSA is more common in athletes, military personnel, and jail inmates. Outbreaks have also been reported in children, the homeless, gay males, different Native Americans, and injectable drug users. The Centers for Disease Control and Prevention (CDC) in Fig. 1 promotes the “5 Cs” as crucial for MRSA transmission [31,40,45,52,53,56–58].

Figure 1



The five Cs of CA-MRSA infections [55].

Higher exposure to training facilities and equipment, according to the CA-MRSA Report for Football Teams, is associated with increased MRSA infection among players. Athletes' cosmetic body shaving is linked to MRSA infections. It is unclear why some colonized people develop MRSA infections while others do not. There is a rising fear that colony outposts outside the interior may become increasingly significant [41,45,59–62].

Colonization

Transmission of MRSA by healthcare personnel is essential for patient-to-patient transmission. MRSA colonization in ventilated patients' respiratory secretions and burn wards may result in airborne droplet transfer between the medical staff and colonized or infected patients. Colonized patients should not be treated in general; only infected people should be treated. Some medications, such as ceftazidime, have been linked to increased MRSA colonization. MRSA is more common in areas that rely significantly on the use of certain antibiotics [63–68].

The frequency and prevalence of methicillin-resistant *Staphylococcus aureus*

As per one examination, the rate of MRSA in certain countries is as high as 75–80% [69]. CA-MRSA can incite fast and serious soft tissue disease because of the presence of two sorts of bacterial poisons delivered by the normal USA-300 and USA-400 strains. Although phenol-dissolvable mutagen protein is neutrophilic, Panton-Valentine leukocidin can incite tissue putrefaction. Methicillin obstruction is obtained by *S. aureus* through the SCC mecA (SCC mec) quality complex chromosomal. MRSA might be created because of the anti-infection choice strain [34].

Most MRSA isolates found during the 1960s were probable single clones. There were six primary MRSA clones by 2004 [70]. Obstruction is thought to spread by even exchange of the quality mecA and its associated regulatory areas [71]. The spread of MRSA from the emergency clinic to the population became evident during the 1980s. As of late, community-obtained sicknesses have become more common, even in people with no settled danger factors. In 24–48 h, a little protuberance may form into an enormous canker. Because such injuries structure rapidly in solid people and seem to emerge precipitously, they are regularly misdiagnosed as bug chomps or medication use. These discoveries prompted the disclosure of a few CA-MRSA hazard factors, like cutaneous injury, imprisonment, and razor or towel sharing [72].

Creatures can be carriers of MRSA and a wellspring of transmission [73]. Surprisingly, many CA-MRSA patients lack specific risk factors for disease protection [74]. CA-MRSA is habitually more poisonous than HA-MRSA and is connected to more normal, significant results such as osteomyelitis, joint inflammation, sepsis, and mortality. Luckily, these life forms are habitually defenseless to a more extensive assortment of antimicrobials [75].

MRSA has become more common in both well-being and local area care settings. Methicillin obstruction in *S. aureus* separations in the US ICU, for instance, has been accounted for to be pretty much as high as 60% [76]. There were more than 90 000 MRSA contaminations in the United States in 2005 [77]. In a recent study from 2017 in United States, there are 20 000 deaths annually due to *S. aureus* bacteremia [78]. Denmark has a low pervasiveness of MRSA, with 357 new cases recorded in 2019, a number that doubled more than four times in the previous decade. In 2019, unpublished information exhibited that 49.0% of all MRSA diseases were obtained locally (CA-MRSA), and asymptomatic pregnancies are pervasive. As has been cited by Holm and colleagues, MRSA is more common in kids aged 0–4 years and adults aged 25–39 years, with the last option being the standard age for pregnant ladies and their babies [79].

The ascent in CA-MRSA cases, especially in this age group, is justification for stress on the grounds that MRSA episode strains are thought to arrive at the NICU with colonized guardians [80]. From 2008 to

2019, there were 27 MRSA episodes in 17 neonatal basic consideration offices in Denmark. These scourges included a total of 554 MRSA-tainted people, with every flare-up including 3–85 babies, guardians, and clinical faculty. Following a long period of time, a few pestilences in medical care occurred. Hvidovre Hospital is situated in the Danish Capital Region and contains the country's greatest obstetric ward, with more than 7000 births each year [81], representing 11.4% of all conveyances in Denmark in 2018 [82]. Present-moment or long-haul NICU treatment is given to around 10% of all infants conveyed in Denmark [83].

MRSA acknowledgment screening, especially in high-hazard conditions, for example, concentrated consideration units, has been proposed for identifying asymptomatic MRSA transmission and forestalling episodes [80,84]. In 2011, the pervasiveness of methicillin obstruction in *S. aureus* segregated contaminated patients in Europe went from under 0.5% to more than 50%, with a normal pooled pace of around 17% [85]. In the nations participating in EARSS/EARS-Net, S. aureus showed a relatively lower increase in the number of reported BSIs, but a considerable decrease in the fraction of MRSA overall. This could be the effect of public health measures in numerous European nations aimed at MRSA containment [86].

A drop in the extent of MRSA circulatory system contamination has been found in various European countries, which might demonstrate the adequacy of disease control strategies in the clinical setting [87]. The well-being-related effect of MRSA colonization, then again, seems to stretch out past the clinical climate and into long-haul and short-term care offices [88]. The foremost entry is the main supply for MRSA, albeit other body areas, like the hands, skin, armpits, and digestive organs, are habitually contaminated [27]. People who have been colonized by MRSA are normally asymptomatic, and three kinds of MRSA transporter cases can be recognized: nontransporters, industrious transporters who have been colonized by a similar strain for quite a while, and inconsistent transporters who have been colonized by various strains for a brief time frame [29].

Diagnostic tests

Cultures were taken when the infection did not respond to first-line therapy with incision and drainage or if MRSA with streptococci persisted to cause drug-resistant infections. When numerous illnesses are discovered, a severe local infection is present, or if systemic infection is present, transplantation can be undertaken. Allergy tests are unable to distinguish between HA-MRSA and CA-MRSA strains [31,48,89,90].

Screening tests

MRSA testing is performed in a number of contexts, including nursing homes, hospitals, and nursing institutions. Chiropractors cannot use MRSA tests that are inexpensive, sensitive, specific, or fast [91]. MRSA screening tests typically yield results in 16–48 h and are not utilized in outpatient settings [92,93].

Treatment

MRSA treatment is determined by the kind, location, and severity of the infection. CA-MRSA skin therapy often includes frequent antiseptic cleaning of the skin. Skin abscesses are best treated medically by excision and drainage. When MRSA infection is suspected, proper medical therapy should begin promptly [90,92,94].

Antibiotics should be chosen based on community susceptibilities, although most people start with trimethoprim-sulfamethoxazole, doxycycline, or minocycline. MRSA infections that do not respond to first-line therapy may require a multidrug therapy course. Vancomycin with one or more other antibiotics is the drug of choice [90,92,95].

Fluoroquinolone usage has been linked to an increase in tendinopathy and joint lesions. Higher frequencies of the disease are connected with age over 60 years, sex, corticosteroid use, strength-training, diabetes, and aerobic-conditioning activities. Medication use should impact therapeutic decision-making by manual therapists. Medication use should affect therapeutic decisions made by manual therapists, such as whether to avoid intense exercise or deep tissue mobilization [96–102].

Infection therapy for methicillin-resistant *Staphylococcus aureus*

Overall aspect

The treatment choices and antimicrobials used for people with MRSA infection are determined by the location of the infection in the body. The severity of the illness, like that of any other infectious disease, has significant prognostic implications but is not a deciding factor in therapy. Excision of the infection site, the damaged organ, or draining of the abscess, as with other staphylococcal infections, is more crucial than antibiotic therapy [63].

Skin and bone infections

MRSA infections of the skin and soft tissue, and bone and joint infections are treated in the same way that MSSA infections are. Cyst surgical drainage is just as critical as antibiotic therapy. Joint hygiene is critical for the protection of the synovium and joint surfaces. Acute osteomyelitis, which is generally caused by *S. aureus*, is treated totally medically with anti-staphylococcal medication. Chronic osteomyelitis cannot be cured solely with antibiotics unless appropriate surgical debridement is performed [63,103].

Infections of the central intravenous line

If the catheter insertion site seems to be infected, remove the central venous catheter promptly. The catheter entrance site may or may not be infected with MRSA streak infection, which causes an inexplicable fever. The identification of MRSA or other factors in the infusion set is confirmed by a semiquantitative culture of the catheter tip following removal. The catheter will be withdrawn as the first treatment step after the diagnosis has been verified. An antibiotic is administered for 2–4 weeks after the central line is withdrawn. MSSA and MRSA can both induce endocarditis. The treatment duration for MSSA and MRSA streak infections is unclear [104–106].

Acute endocarditis

Staphylococcal endocarditis can arise from the installation of a normal valve implant, such as the aortic valve, or from endothelial or heart valve damage induced by an endovascular device put in the right heart. Positive blood cultures with echocardiography of the heart demonstrating one or more flora or intramyocardial cysts are required for efficient treatment of ABE staphylococci. Depending on the location, a myocardial abscess may cause an undetermined fever, valve malfunction, or varied degrees of heart block. ABE staphylococcus should be eliminated if it is caused by an intravascular system in the right heart. If the abscess is big and surgically accessible, it must be drained. The most successful non-IVDA therapy for MRSA endocarditis is MRSA ABE/PVE. IVDAs infected with ABE staphylococci have been treated with oral antibiotics. Oral anti-staphylococcal treatment has successfully treated IVDAs with staphylococcal ABE [63,107].

Anti-methicillin-resistant Staphylococcus aureus drugs

S. aureus isolates' susceptibility to penicillin was reported to be 10% in the United States [108], few medications have been found to be effective against MRSA infection, and treating MRSA infection can be difficult. Many medications that seem to be successful *in vivo* against MRSA are ineffective or seldom helpful in vivo. Only four medicines showed *in vivo* MRSA action. Quinupristin, dalfopristin, minocycline, daptomycin, linezolid, and vancomycin were four of the medications. Rifampicin is an efficient antibiotic against staphylococci, although its effectiveness in MRSA infections has yet to be demonstrated. MRSA's antibacterial activity changes in response to trimethoprim-sulfamethoxazole. When choosing an antibiotic for MRSA or other infections, the agent's action, pharmacokinetics, safety profile, the possibility for resistance, and cost to the patient or institution are all taken into account. A doctor should select one depending on a number of considerations [109–116].

Only daptomycin, vancomycin, and intravenous quinupristin or dalfopristin can be used to treat MRSA infections. A cyclic lipopeptide drug (Daptomycin) was approved in 2003 to treat soft-tissue infections. It has a unique, concentration-dependent mode of action to kill bacteria and works by binding to the cell membrane of Gram-positive bacteria. In vitro studies have shown that the antibacterial activity of daptomycin is equal to or greater than that of vancomycin and linezolid [117]. Minocycline and linezolid are available as oral and injectable medications. Oral treatment is typically less expensive than intravenous medication, and it gives practitioners and patients more leeway in establishing effective regimens. Minocycline is a low-cost antibiotic that has the ability to enter the central nervous system. Despite its long history of use, vancomycin has limitations such as impaired bone permeability, CSF (15% of contemporaneous serum levels), and a number of side effects. When administered orally, linezolid has the same pharmacokinetic properties as intravenous vancomycin. All of these indicated enhanced antibacterial effects of drug-loaded nucleosomes at concentrations eightfold lower than that of bare vancomycin. The drug-loaded quadruple has also demonstrated the ability to eradicate MRSA biofilms [118]. All MRSA infections that do not impact the heart or central nervous system, such as MRSA ABE infections, CNS infections, and hospital pneumonia, are treated with linezolid [63,107,119], all of which are shown in Table 1.

An alternative to standard antibiotics is needed to treat MRSA infections. Several options exist, but resistance to many drugs are common. Some of these alternative antibiotics are fusidic acid, clindamycin, and mupirocin

Table 1 Clinical comparison of methicillin-resistant *Staphylococcus aureus* antibiotics

Classes of antibiotics	Molecular target	Antibiotics	Year approved or released	Infection site	Antibiotic resistance identified
Lipopeptides	Cell membrane	Daptomycin	2003	Skin and soft tissue	2004
				Bacteremia, endocarditis	
Oxazolidinones	50S ribosomal subunit	Linezolid	2000	Pneumonia and skin infections	2001
Steptogramins	50S ribosomal subunit	Synercid (Quinupristin/ dalfopristin)	1999	Certain serious skin infections	N/A
Tetracyclines	30S ribosomal subunit	Tetracycline	1948	Skin and soft tissue	1953
Glycopeptide	MurNac pentapeptide	Vancomycin	1985	Colitis	2002
		Telavancin	2009	Pneumonia	N/A
				Skin and skin structure infections	
Carbapenem	Penicillin-binding proteins	Imipenem	1985	Complicated UTI	2006
		Doripenem	2007		N/A
Cephalosporin	Penicillin-binding proteins	Ceftaroline	2010	Community-acquired bacterial pneumonia (CABP):	2011
				Skin and skin structure infections	
Lipoglycopeptides	MurNac pentapeptide and cell membrane	Dalbavancin	2014	Skin and skin structure infections	2022*
Penicillins	Penicillin-binding proteins	Ampicillin, amoxicillin	1961, 1972	Meningitis	2006
		Amoxicillin +clavulanate	1984	Skin and soft tissue infections	
		Oxacillin, nafcillin	1962,	endocarditis	
Macrolides	50S ribosomal subunit	Erythromycin	1952	Skin Infection	1953
Chloramphenicols	50S ribosomal subunit	Chloramphenicol	1948	Staphylococcal conjunctivitis	N/A
Pleuromutilins	50S ribosomal subunit	Retapamulin	2007	Skin infections	N/A
Aminoglycosides	30S ribosomal subunit	Gentamicin	1962	Prosthetic valve	1994
Glycylcyclines	30S ribosomal subunit	Tigecycline	2005	Complicated skin infections	N/A
Phosphonic acid	Enoylpyruvate transferase (MurA)	Fosfomycin	1969	Multidrug resistant UTI	N/A
Rifamycins	RNA polymerase	Rifampicin	1971	Community-acquired bacterial pneumonia (CABP):	1984
Fluoroquinolones	DNA gyrase, topoisomerase IV	Ciprofloxacin	1987	Complicated and uncomplicated infections of the skin and of the skin structure	1988
		Moxifloxacin	1999		1999
Lincosamides	50S ribosomal subunit	Clindamycin	1966	Osteomyelitis, skin and soft tissue	1984
Pseudomonic acid	Isoleucyl-tRNA synthtase	Mupirocin	1976	Superficial skin infections such as impetigo or folliculitis	1987

*Reference [120].

[120]. However, these alternatives cannot be used as a primary modality of treatment [121,122].

Recent scientific developments have suggested that the use of antimicrobial peptides (AMPs) and silver nanoparticles may be able to inhibit MRSA. Both medications are good options for reducing the risk of MRSA as they both possess broad-spectrum antibacterial activities [123–126]. All forms of life contain AMPs, which are naturally occurring chemicals that play a role in innate immune defenses [125,126]. Membrane glycolysis and membrane inactivation are the two basic methods by which AMP affects bacterial membranes [126–128]. Membranous degradation is the direct result of AMP on bacterial membranes that dramatically compromises the structural integrity of those membranes [129–131]. When AMP is injected into the cell, the nonmembrane glycolytic action takes place without seriously harming the membrane, but instead targets significant intracellular components [131–133].

Prevention

For healthy people who do not display signs and symptoms of infection, vaccines and basic hygiene behaviors are the foundation of MRSA infection prevention [134]. Hands should be washed thoroughly with soap and warm water; if the hands are not visibly dirty, alcohol-based hand massages can be used instead of washing. Towels, razors, washcloths,

filthy clothing, and used athletic equipment should not be shared and should be kept clean [48,56,134].

To avoid infection, the wound should be cleaned using a clean, dry bandage. Bandages and wound dressings can be discarded in the garbage. If MRSA skin infection is suspected, self-treatment should be avoided [134].

Additional criteria can help athletes and sporting facilities. Because many sports require close human touch, such as the use of shared equipment and bathing facilities, additional suggestions were created. Athletes should avoid sharing protective gear and clothes, such as helmets, body armor, soap, and so on. Athletes infected with MRSA should be barred from participating in contact sports until the wound has been completely covered or healed. Athletes with skin MRSA should avoid public swimming pools, particularly medical Jacuzzis, unless the pool water is changed regularly. The CDC has a detailed list of recommendations for controlling MRSA in public settings such as swimming pools and spas. Weighing machines and benches, for example, must be sanitized in all areas where flesh comes into contact with the equipment. Regular cleaning of floors, mats, and doors is also recommended [48,56,134–138].

Patients at risk should have access to MRSA-preventive techniques. The National Athletic Trainers Association has issued a thorough policy statement as well as a patient-friendly information brochure [139]. When treating patients or those at risk of infection, exercise extreme caution. When inspecting or treating parts of the body suspected of having skin infections, healthcare providers should use gloves, and they should properly wash their hands, including hand hygiene, following inspection or treatment [140,141].

A study conducted in Canada found 51% fewer HA-MRSA infections among hospital patients when only hand hygiene methods were implemented. In the United States, the application of traditional infection control methods with an emphasis on hand hygiene has reduced the frequency of MRSA infections [63,111].

According to the CDC, MRSA-infected equipment and treatment tables should be cleansed using EPA-approved disinfectants. Items regularly used in the manual practitioner's office can readily become infected with MRSA, which can linger for a long time if not adequately cleansed [62,142]. Outpatient environments that serve people who are healthy or damaged but not sick (e.g. athletes, soldiers) and treat postoperative patients may be contaminated. Outpatient settings should be extremely vigilant and ensure proper clinic, patient, and provider hygiene.

Conclusion

Over the years, laboratory methods for the detection of methicillin resistance have been widely developed and standardized, allowing accurate detection of MRSA strains from clinical samples. MRSA and MSSA have similar ecological habitats in hospitals and communities. Since *S. aureus* is a natural resident of the nose and skin area, it is not surprising that most MRSA infections spread through the skin. As with MSSA, it is clear that most MRSA isolates represent colonization rather than infection. In clinical settings, colonization is the most common route of MRSA expression. Trimethoprim-sulfamethoxazole nasal ointment and mupirocin have been used with varying degrees of success, although infection control strategies remain the recommended approach for reducing institutional transmission of MRSA. Another factor affecting the spread of MRSA bacteria in a facility is the availability of medications on hospital prescriptions.

Geographically, the ratio of MSSA to a colony or pathogenic MRSA varies. Local epidemiological patterns of empiric therapy influence *S. aureus* infection. If the majority of strains in the population are MSSA, initial empirical treatment should be with drugs that are highly active against MSSA. In contrast, if the majority of *S. aureus* in community isolates is MRSA, the initial empirical treatment should be with one of the drugs shown to be effective against MRSA *in vivo*.

Unlike MSSA, MRSA varies between its in vitro susceptibility and its effectiveness. Antibiotic efficacy, pharmacokinetics, potential resistance, side effects, and cost influence treatment selection. Metamycin, linezolid, or quinupristin/dalfopristin are the drugs of choice for MRSA.

Distamycin has surpassed vancomycin as the primary treatment for severe/systemic MRSA infections. Distamycin is only used to treat *Clostridium difficile* diarrhea. Distamycin is effective against MSSA and MRSA. Although vancomycin can be used to treat CNS staphylococcal infections, linezolid has superior CNS penetrance when taken orally and intravenously. Distamycin is a bacterial antibiotic that seems to eliminate MRSA bacteremia faster than other anti-

MRSA antibiotics. For skin and soft tissue infections, the distamycin dose is 4 mg/kg/day (intravenous). If the CrCl is less than 30 ml/min, the MRSA bacteremia medication should be administered every 48 h. Distamycin is also effective in treating MSSA and MRSA that have developed resistance to other antibiotics.

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References

1 Williams RE. Healthy carriage of *Staphylococcus aureus*: its prevalence and importance. Bacteriol Rev 1963; 27:56–71.

2 Tarupiwa A, Tapera S, Mtapuri-Zinyowera S, Gumbo P, Ruhanya V, Gudza-Mugabe M, *et al.* Evaluation of TUBEX-TF and OnSite Typhoid IgG/IgM Combo rapid tests to detect *Salmonella enterica* serovar Typhi infection during a typhoid outbreak in Harare, Zimbabwe. BMC Res Notes 2015; 8:1–4.

3 Cheung GY, Bae JS, Otto M. Pathogenicity and virulence of *Staphylococcus aureus*. Virulence 2021; 12:547–569.

4 Von Eiff C, Becker K, Machka K, Stammer H, Peters G. Nasal carriage as a source of *Staphylococcus aureus* bacteremia. N Engl J Med 2001; 344:11–16.

5 File JrTM, Wilcox MH, Stein GE. Summary of ceftaroline fosamil clinical trial studies and clinical safety. Clin Infect Dis 2012; 55(suppl_3): S173–S180.

6 Wai A. Roberts and Hedges: clinical procedures in emergency medicine. 2010: 358.

7 Cohen PR, Grossman ME. Management of cutaneous lesions associated with an emerging epidemic: community-acquired methicillin-resistant *Staphylococcus aureus* skin infections. J Am Acad Dermatol 2004; 51:132–135.

8 Parriott AM, Chow AL, Arah OA. Inadequate research on methicillin-resistant *Staphylococcus aureus* risk among postpartum women. Exp Rev Anti-infect Ther 2013; 11:1127–1130.

9 Carey AJ, Duchon J, Della-Latta P, Saiman L. The epidemiology of methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit, 2000–2007. J Perinatol 2010; 30:135–139.

10 Andersen BM, Lindemann R, Bergh K, Nesheim BI, Syversen G, Solheim N, Laugerud F. Spread of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive unit associated with understaffing, overcrowding and mixing of patients. J Hosp Infect 2002; 50:18–24.

11 Cheng VC, Wong SC, Cao H, Chen JH, So SY, Wong SC, *et al.* Whole-genome sequencing data-based modeling for the investigation of an outbreak of community-associated methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit in Hong Kong. Eur J Clin Microbiol Infect Dis 2019; 38:563–573.

12 Murray CJ, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, Naghavi M. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet 2022; 399:629–655.

13 Voss A, Loeffen F, Bakker J, Klaassen C, Wulf M. Methicillin-resistant *Staphylococcus aureus* in pig farming. Emerg Infect Dis 2005; 11:1965.

14 De Neeling AJ, Van den Broek MJ, Spalburg EC, van Santen-Verheuvel MG, Dam-Deisz WD, Boshuizen HC, *et al.* High prevalence of methicillin resistant *Staphylococcus aureus* in pigs. Vet Microbiol 2007; 122:366–372.

15 Huijsdens XW, Van Dijke BJ, Spalburg E, van Santen-Verheuvel MG, Heck ME, Pluister GN, *et al.* Community-acquired MRSA and pig-farming. Ann Clin Microbiol Antimicrob 2006; 5:1–4.

16 Van Den Broek IV, Van Cleef BA, Haenen A, Broens EM, Van Der Wolf PJ, Van Den Broek MJ, *et al.* Methicillin-resistant *Staphylococcus aureus* in people living and working in pig farms. Epidemiol Infect 2009; 137:700–708.

17 Siddiqui AH, Koirala J. Methicillin resistant Staphylococcus aureus. InStatPearls [internet] 2022 Jul 18. StatPearls Publishing, pages 1–10.

18 Camargo CH, de Souza MD, Bonesso MF, Da Cunha FP, Barbosa AN, Fortaleza CM. Systemic CA-MRSA infection following trauma during soccer match in inner Brazil: clinical and molecular characterization. Diagn Microbiol Infect Dis 2013; 76:372–374.

19 Khairullah AR, Ramandinianto SC, Effendi MH. A review of livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) on bovine mastitis. Syst Rev Pharm 2020; 11:172–183.

20 Tacconelli E, Venkataraman L, De Girolami PC, D'Agata EM. Methicillin-resistant *Staphylococcus aureus* bacteraemia diagnosed at hospital admission: distinguishing between community-acquired versus healthcare-associated strains. J Antimicrob Chemother 2004; 53:474–479.

21 Peacock SJ, Paterson GK. Mechanisms of methicillin resistance in *Staphylococcus aureus*. Annu Rev Biochem 2015; 84:577–601.

22 Chambers HF. Methicillin resistance in staphylococci: molecular and biochemical basis and clinical implications. Clin Microbiol Rev 1997; 10:781–791.

23 Hall GS. MRSA: Lab detection, epidemiology, and infection control. Microbiol Frontline 2003; 3:1–6.

24 Klevens RM, Edwards JR, Richards JrCL, Horan TC, Gaynes RP, Pollock DA, Cardo DM. Estimating health care-associated infections and deaths in US hospitals. 2002. Public Health Rep 2007; 122:160–166.

25 Cookson BB, Peters B, Webster M, Phillips I, Rahman M, Noble W. Staff carriage of epidemic methicillin-resistant *Staphylococcus aureus*. J Clin Microbiol 1989; 27:1471–1476.

26 Safdar N, Bradley EA. The risk of infection after nasal colonization with *Staphylococcus aureus*. Am J Med 2008; 121:310–315.

27 Acton DS, Tempelmans Plat-Sinnige MJ, van Wamel W, de Groot N, van Belkum A. Intestinal carriage of *Staphylococcus aureus*: how does its frequency compare with that of nasal carriage and what is its clinical impact?. Eur J Clin Microbiol Infect Dis 2009; 28:115–127.

28 Wertheim HF, Melles DC, Vos MC, van Leeuwen W, van Belkum A, Verbrugh HA, Nouwen JL. The role of nasal carriage in *Staphylococcus aureus* infections. Lancet Infect Dis 2005; 5:751–762.

29 Albrich WC, Harbarth S. Health-care workers: source, vector, or victim of MRSA?. Lancet Infect Dis 2008; 8:289–301.

30 Muder RR, Brennen C, Goetz AM. Infection with methicillin-resistant *Staphylococcus aureus* among hospital employees. Infect Control Hosp Epidemiol 1993; 14:576–578.

31 DeLeo FR, Otto M, Kreiswirth BN, Chambers HF. Community-associated meticillin-resistant *Staphylococcus aureus*. The Lancet 2010; 375:1557–1568.

32 Schentag JJ, Hyatt JM, Carr JR, Paladino JA, Birmingham MC, Zimmer GS, Cumbo TJ. Genesis of methicillin-resistant *Staphylococcus aureus* (MRSA), how treatment of MRSA infections has selected for vancomycin-resistant Enterococcus faecium, and the importance of antibiotic management and infection control. Reviews of Infectious Diseases 1998; 26: 1204–1214.

33 Nelson KE, Williams CM, editors. Infectious disease epidemiology: theory and practice. Boston: Jones & Bartlett Publishers 2014.

34 Enright MC, Robinson DA, Randle G, Feil EJ, Grundmann H, Spratt BG. The evolutionary history of methicillin-resistant *Staphylococcus aureus* (MRSA). Proc Natl Acad Sci 2002; 99:7687–7692.

35 Chambers HF. The changing epidemiology of *Staphylococcus aureus*?. Emerg Infect Dis 2001; 7:178.

36 Humphreys H, Grundmann H, Skov R, Lucet JC, Cauda R. Prevention and control of methicillin-resistant *Staphylococcus aureus*. Clin Microbiol Infect 2009; 15:120–124.

37 Smith TC, Moritz ED, Larson KL, Ferguson DD. The environment as a factor in methicillin-resistant *Staphylococcus aureus* transmission. Rev Environ Health 2010; 25:121–134.

38 Bassetti M, Carnelutti A, Castaldo N, Peghin M. Important new therapies for methicillin-resistant *Staphylococcus aureus*. Exp Opin Pharmacother 2019; 2:2317–2334.

39 Crum NF, Lee RU, Thornton SA, Stine OC, Wallace MR, Barrozo C, *et al.* Fifteen-year study of the changing epidemiology of methicillin-resistant *Staphylococcus aureus*. Am J Med 2006; 119:943–951.

40 Rohde RE, Denham R, Brannon A. Methicillin resistant *Staphylococcus aureus*: carriage rates and characterization of students in a Texas university. Am Soc Clin Lab Sci 2009; 22:176–184.

41 Creech CB, Saye E, McKenna BD, Johnson BG, Jimenez N, Talbot TR, Bossung T, Gregory A, Edwards KM. One-year surveillance of methicillin-resistant *Staphylococcus aureus* nasal colonization and skin and soft tissue infections in collegiate athletes. Arch Pediatr Adolescent Med 2010; 164:615–620.

42 O'Fallon E, Schreiber R, Kandel R, D'Agata EM. Multidrug-resistant gram-negative bacteria at a long-term care facility: assessment of residents, healthcare workers, and inanimate surfaces. Infect Control Hosp Epidemiol 2009; 30:1172–1179.

43 Kateete DP, Bwanga F, Seni J, Mayanja R, Kigozi E, Mujuni B, *et al.* CA-MRSA and HA-MRSA coexist in community and hospital settings in Uganda. Antimicrob Resist Infect Control 2019; 8:1–9.

44 Li M, Diep BA, Villaruz AE, Braughton KR, Jiang X, DeLeo FR, *et al.* Evolution of virulence in epidemic community-associated methicillin-resistant *Staphylococcus aureus*. Proc Natl Acad Sci 2009; 106:5883–5888.

45 Begier EM, Frenette K, Barrett NL, Mshar P, Petit S, Boxrud DJ, *et al.* A high-morbidity outbreak of methicillin-resistant *Staphylococcus aureus* among players on a college football team, facilitated by cosmetic body shaving and turf burns. Clin Infect Dis 2004; 39:1446–1153.

46 Carleton HA, Diep BA, Charlebois ED, Sensabaugh GF, Perdreau-Remington F. Community-adapted methicillin-resistant *Staphylococcus aureus* (MRSA): population dynamics of an expanding community reservoir of MRSA. J Infect Dis 2004; 190:1730–1738.

47 Parchman ML, Munoz A. Risk factors for methicillin-resistant *Staphylococcal aureus* skin and soft tissue infections presenting in primary care: a South Texas Ambulatory Research Network (STARNet) study. J Am Board Fam Med 2009; 22:375–379.

48 McCarthy NL, Sullivan PS, Gaynes R, Rimland D. Health care-associated and community-associated methicillin-resistant *Staphylococcus aureus* infections: a comparison of definitions. Am J Infect Control 2010; 38:600–606.

49 Klevens RM, Morrison MA, Fridkin SK, Reingold A, Petit S, Gershman K, *et al.* Community-associated methicillin-resistant *Staphylococcus aureus* and healthcare risk factors. Emerg Infect Dis 2006; 12:1991.

50 D'Agata EM, Webb GF, Pressley J. Rapid emergence of co-colonization with community-acquired and hospital-acquired methicillin-resistant *Staphylococcus aureus* strains in the hospital setting. Math Model Natl Phenomena 2010; 5:76–93.

51 Archer GL. *Staphylococcus aureus*: a well-armed pathogen. Rev Infect Dis 1998; 26: 1179–1781.

52 Matouskova I, Janout V. Current knowledge of methicillin-resistant *Staphylococcus* aureus and community-associated methicillin-resistant Staphylococcus aureus. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2008; 152:191–202.

53 Herman RA, Kee VR, Moores KG, Ross MB. Etiology and treatment of community-associated methicillin-resistant *Staphylococcus aureus*. Am J Health-Syst Pharma 2008 Feb 1;65(3):219–225.

54 Heymann D.L. American Public Health Association. 19th ed. Washington, DC: American Public Health Association; 2008.

55 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 Antimicrob Chemother 2008; 61:26–38.

56 Workplace safety and health topics: MRSA and the workplace. Centers for Disease Control and Prevention; Atlanta: 2010. Available at: http://www.cdc.gov/niosh/topics/mrsa/ [Accessed November 22, 2010].

57 Deresinski S. Methicillin-resistant *Staphylococcus aureus*: an evolutionary, epidemiologic, and therapeutic odyssey. Clin Infect Dis 2005; 40:562–573.

58 Roberts SS, Kazragis RJ. Methicillin-resistant *Staphylococcus aureus* infections in US service members deployed to Iraq. Military Med 2009; 174:408–411.

59 Kazakova SV, Hageman JC, Matava M, Srinivasan A, Phelan L, Garfinkel B, *et al.* A clone of methicillin-resistant *Staphylococcus aureus* among professional football players. N Engl J Med 2005; 352:468–475.

60 Romano R, Lu D, Holtom P. Outbreak of community-acquired methicillin-resistant *Staphylococcus aureus* skin infections among a collegiate football team. J Athletic Train 2006; 41:141.

61 Garza D, Sungar G, Johnston T, Rolston B, Ferguson JD, Matheson GO. Ineffectiveness of surveillance to control community-acquired methicillin-resistant *Staphylococcus aureus* in a professional football team. Clin J Sport Med 2009; 19:498–501.

62 Cafferkey MT, (Ed). Methicillin-resistant Staphylococcus aureus. New York: Marcel Dekker 1992. pp. 1-202.

63 Huang SS, Platt R. Risk of methicillin-resistant *Staphylococcus aureus* infection after previous infection or colonization. Clin Infect Dis 2003; 36:281–285.

64 Casewell MW. Epidemiology and control of the 'modern'methicillin-resistant *Staphylococcus aureus*. J Hosp Infect 1986; 7:1–1.

65 Haddadin AS, Fappiano SA, Lipsett PA. Methicillin resistant *Staphylococcus aureus* (MRSA) in the intensive care unit. Postgrad Med J 2002; 78:385–392.

66 Hryniewicz W. Epidemiology of MRSA. Infection 1999; 27:S13–S16.

67 Livermore DM. Epidemiology of antibiotic resistance. Intensive Care Med 2000; 26:S014–S021.

68 Van Cleef BA, Broens EM, Voss A, Huijsdens XW, Züchner L, Van Benthem BH, *et al.* High prevalence of nasal MRSA carriage in slaughterhouse workers in contact with live pigs in The Netherlands. Epidemiol Infect 2010; 138:756–763.

69 Ito T, Katayama Y, Asada K, Mori N, Tsutsumimoto K, Tiensasitorn C, Hiramatsu K. Structural comparison of three types of staphylococcal cassette chromosome mec integrated in the chromosome in methicillin-resistant *Staphylococcus aureus*. Antimicrob Agents Chemother 2001; 45:1323–1336.

70 Archer GL, Climo MW. Antimicrobial susceptibility of coagulase-negative staphylococci. Antimicrob Agents Chemother 1994; 38:2231–2237.

71 Fridkin SK. Active bacterial core surveillance program of the emerging infections program network. Methicillin-resistant Staphylococcus aureus disease in three communities. N Engl J Med 2005; 352:1436–1444.

72 Sing A, Tuschak C, Hörmansdorfer S. Methicillin-resistant *Staphylococcus aureus* in a family and its pet cat. N Engl J Med 2008; 358:1200–1201.

73 Miller LG, Remington FP, Bayer AS, Diep B, Tan N, Bharadwa K, *et al.* Clinical and epidemiologic characteristics cannot distinguish community-associated methicillin-resistant *Staphylococcus aureus* infection from methicillin-susceptible *S. aureus* infection: a prospective investigation. Clin Infect Dis 2007; 44:471–482.

74 Frazee BW, Lynn J, Charlebois ED, Lambert L, Lowery D, Perdreau-Remington F. High prevalence of methicillin-resistant *Staphylococcus aureus* in emergency department skin and soft tissue infections. Ann Emerg Med 2005; 45:311–320.

75 Hassoun A, Linden PK, Friedman B. Incidence, prevalence, and management of MRSA bacteremia across patient populations – a review of recent developments in MRSA management and treatment. Crit Care 2017; 21:1.

76 Fry DE, Barie PS. The changing face of *Staphylococcus aureus*: a continuing surgical challenge. Surg Infect 2011; 12:191–203.

77 Holm MK, Winther TN, Kammann S, Rasmusson MS, Brooks L, Westh H, Bartels MD. Prevalence of MRSA nasal carriage among pregnant women in Copenhagen. Plos One 2021; 16:e0246343.

78 Kourtis AP, Hatfield K, Baggs J, Mu Y, See I, Epson E, *et al.* Emerging Infections Program MRSA author group. Vital signs: epidemiology and recent trends in methicillin-resistant and in methicillin-susceptible Staphylococcus aureus bloodstream infections—United States. Morb Mortal Wkly Rep 2019; 68:214–219.

79 Kristinsdottir I, Haraldsson A, Thorkelsson T, Haraldsson G, Kristinsson KG, Larsen J, *et al.* MRSA outbreak in a tertiary neonatal intensive care unit in Iceland. Infect Dis 2019; 51: 815–823.

80 foedeafdelingen @ HYPERLINK "http://www.hvidovrehospital.dk/" www.hvidovrehospital.dk [Internet]. [cited by Holm MKA, Winther TN, Kammann S, Rasmusson MS, Brooks L, Westh H, et al. (2021) Prevalence of MRSA nasal carriage among pregnant women in Copenhagen. PLoS ONE 16(1): e0246343. https://doi.org/10.1371/journal.pone.0246343

81 Statistik D. Denmark birth statistiscs [Internet]. 2018. Available at: https://www.dst.dk/da/Statistik/ emner/befolkning-og-valg/foedsler/foedsler [Accessed September 1, 2020].

82 Klinisk, Epidemiologisk epidemiolog of datamanager fra R har stået for udarbejdelse af analyser og, Kommentering. Dansk Kvalitetsdatabase for Nyfødte (DKN) National årsrapport 2018 [Internet]. [cited by Holm MKA, Winther TN, Kammann S, Rasmusson MS, Brooks L, Westh H, et al. (2021) Prevalence of MRSA nasal carriage among pregnant women in Copenhagen. PLoS ONE 16(1): e0246343. https://doi.org/10.1371/journal.pone.0246343

83 Giuffrè M, Cipolla D, Bonura C, Geraci DM, Aleo A, Di Noto S, Nociforo F, Corsello G, Mammina C. Epidemic spread of ST1-MRSA-IVa in a neonatal intensive care unit, Italy. BMC Pediatr 2012; 12:1–7.

84 European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2013. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2014.

85 NNIS System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2003, issued August 2003. Am J Infect Control 2003; 31:481–498.

86 Gagliotti C, Balode A, Baquero F, Degener J, Grundmann H, Gür D, *et al.* *Escherichia coli* and *Staphylococcus* aureus: bad news and good news from the European Antimicrobial Resistance Surveillance Network (EARS-Net, formerly EARSS), 2002 to 2009. Eurosurveillance 2011; 16:19819.

87 Dulon M, Haamann F, Peters C, Schablon A, Nienhaus A. MRSA prevalence in European healthcare settings: a review. BMC Infect Dis 2011; 11:1–3.

88 Stürenburg E. Rapid detection of methicillin-resistant *Staphylococcus aureus* directly from clinical samples: methods, effectiveness and cost considerations. GMS German Med Sci 2009; 7:7.

89 Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, *et al.* Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. Clin Infect Dis 2011; 52:e18–55.

90 Jain R, Kralovic SM, Evans ME, Ambrose M, Simbartl LA, Obrosky DS, *et al.* Veterans affairs initiative to prevent methicillin-resistant *Staphylococcus aureus* infections. New Engl J Med 2011; 364: 1419–1430.

91 Green BN, Johnson CD, Egan JT, Rosenthal M, Griffith EA, Evans MW. Methicillin-resistant *Staphylococcus aureus*: an overview for manual therapists. J Chiropractic Med 2012; 11:64–76.

92 Cooper BS, Medley GF, Stone SP, Kibbler CC, Cookson BD, Roberts JA, Duckworth G, Lai R, Ebrahim S. Methicillin-resistant *Staphylococcus aureus* in hospitals and the community: stealth dynamics and control catastrophes. Proc Natl Acad Sci 2004; 101:10223–10228.

93 Deresinski S. Vancomycin in combination with other antibiotics for the treatment of serious methicillin-resistant *Staphylococcus aureus* infections. Clin Infect Dis 2009; 49:1072–1079.

94 Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, *et al.* Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis 2014; 59:e10–52.

95 Belavic JM. Fluoroquinolone-induced tendinopathy. Nurse Pract 2009; 34:17–18.

96 Noel GJ, Bradley JS, Kauffman RE, Duffy CM, Gerbino PG, Arguedas A, *et al.* Comparative safety profile of levofloxacin in 2523 children with a focus on four specific musculoskeletal disorders. Pediatr Infect Dis J 2007; 26:879–891.

97 Hall MM, Finnoff JT, Smith J. Musculoskeletal complications of fluoroquinolones: guidelines and precautions for usage in the athletic population. PM&R 2011; 3:132–142.

98 Childs SG. Pathogenesis of tendon rupture secondary to fluoroquinolone therapy. Orthop Nurs 2007; 26:175–182.

99 Khaliq Y, Zhanel GG. Fluoroquinolone-associated tendinopathy: a critical review of the literature. Clin Infect Dis 2003; 36:1404–1410.

100 Owens JrRC, Ambrose PG. Antimicrobial safety: focus on fluoroquinolones. Clin Infect Dis 2005; 41(Suppl 2): S144–S157.

101 Gold L, Igra H. Levofloxacin-induced tendon rupture: a case report and review of the literature. J Am Board Fam Pract 2003; 16:458–460.

102 Boyce JM. MRSA patients: proven methods to treat colonization and infection. J Hosp Infect 2001; 48:S9–14.

103 Garau J, Bouza E, Chastre J, Gudiol F, Harbarth S. Management of methicillin-resistant *Staphylococcus aureus* infections. Clin Microbiol Infect 2009; 15:125–136.

104 Steinberg JP, Clark CC, Hackman BO. Nosocomial and community-acquired *Staphylococcus aureus* bacteremias from 1980 to 1993: impact of intravascular devices and methicillin resistance. Clin Infect Dis 1996; 23:255–259.

105 Maki DG. Infections caused by intravascular devices used for infusion therapy: pathogenesis. Prev Manage 1994; 2:155–212.

106 Watanakunakorn C. Treatment of infections due to methicillin-resistant *Staphylococcus aureus*. Ann Intern Med 1982; 97:376–378.

107 Tofail SA, editor. Biological Interactions with surface charge in biomaterials. London: Royal Society of Chemistry; 2011.

108 https://www.cdc.gov/mrsa/lab/index.html#anchor_1548429322

109 Linares J. The VISA/GISA problem: therapeutic implications. Clin Microbiol Infect 2001; 7:8–15.

110 Pechere J.C. Current and future management of infections due to methicillin-resistant staphylococci infections: the role of quinupristin/dalfopristin. J Antimicrob Chemother 1999; 44(suppl_1):11–18.

111 Finch RG. Antibacterial activity of quinupristin/dalfopristin. Drugs 1996; 51:31–37.

112 Lamb HM, Figgitt DP, Faulds D. Quinupristin/dalfopristin. Drugs 1999; 58:1061–1097.

113 Paradisi F, Corti G, Messeri D. Antistaphylococcal (MSSA, MRSA, MSSE, MRSE) antibiotics. Med Clin N Am 2001; 85:1–7.

114 Cunha BA. Oral antibiotics to treat MRSA infections, J Hosp Infect 2005; 60:88–90.

115 Cunha BA. Antibiotic essentials. Royal Oak, MI: Physicians Press 2005.

116 Ruiz ME, Guerrero IC, Tuazon CU. Endocarditis caused by methicillin-resistant *Staphylococcus aureus*: treatment failure with linezolid. Clin Infect Dis 2002; 35:1018–1020.

117 Lin L, Wang X, Wang W, Zhou X, Hargreaves JR. Cleaning up China's medical cabinet—an antibiotic take-back programme to reduce household antibiotic storage for unsupervised use in rural China: a mixed-methods feasibility study. Antibiotics 2020; 9:212.

118 Hassan D., Omolo C.A, Fasiku V.O, Elrashedy A.A, Mocktar C, Nkambule B, Soliman M.E.S, Govender T. Formulation of pH-responsive quatsomes from quaternary bicephalic surfactants and cholesterol for enhanced delivery of vancomycin against methicillin resistant Staphylococcus aureus. Pharmaceutics 2020; 12:1093.

119 Cunha BA. Antibiotic essentials. (9th ed.). Boston: Jones & Bartlett Publishers; 2010.

120 Zhang R, Polenakovik H, Ismael A, Beltran B, Waalkes A, Salipante SJ, Xu L, Werth BJ. Emergence of dalbavancin, vancomycin, and daptomycin nonsusceptible Staphylococcus aureus in a patient treated with dalbavancin: case report and isolate characterization. Clin Infect Dis 2022; 75:1641–1644.

121 Brown N.M., Goodman A.L., Horner C., Jenkins A., Brown E.M. Treatment of methicillin-resistant *Staphylococcus aureus* (MRSA): updated guidelines from the UK. JAC-Antimicrob Resist 2021; 3:dlaa114.

122 Montravers P., Eckmann C. Cotrimoxazole and clindamycin in skin and soft tissue infections. Curr Opin Infect Dis 2021; 34:63–71.

123 Ciandrini E, Morroni G, Arzeni D, Kamysz W, Neubauer D, Kamysz E, *et al.* Antimicrobial activity of different antimicrobial peptides (AMPs) against clinical methicillin-resistant *Staphylococcus aureus* (MRSA). Curr Top Med Chem 2018; 18:2116–2126.

124 Ansari MA, Alzohairy MA. One-pot facile green synthesis of silver nanoparticles using seed extract of Phoenix dactylifera and their bactericidal potential against MRSA. EvidBased Complement Alternat Med 2018; 2018:1860280.

125 Baharin NH, Mokhtar NF, Desa MN, Gopalsamy B, Zaki NN, Yuswan MH, *et al.* The characteristics and roles of antimicrobial peptides as potential treatment for antibiotic-resistant pathogens: a review. PeerJ 2021; 9: e12193.

126 Patrulea V, Borchard G, Jordan O. An update on antimicrobial peptides (AMPs) and their delivery strategies for wound infections. Pharmaceutics 2020; 12:840.

127 Benfield AH, Henriques ST. Mode-of-action of antimicrobial peptides: membrane disruption vs. intracellular mechanisms. Front Med Technol 2020; 2:610997.

128 Huan Y, Kong Q, Mou H, Yi H. Antimicrobial peptides: classification, design, application and research progress in multiple fields. Front Microbiol 2020; 11:2559.

129 Mahlapuu M, Björn C, Ekblom J. Antimicrobial peptides as therapeutic agents: opportunities and challenges. Crit Rev Biotechnol 2020; 40: 978–992.

130 Frimodt-Møller J, Campion C, Nielsen PE, Løbner-Olesen A. Translocation of non-lytic antimicrobial peptides and bacteria penetrating peptides across the inner membrane of the bacterial envelope. Curr Genet 2021; 8:1–8.

131 Moravej H, Moravej Z, Yazdanparast M, Heiat M, Mirhosseini A, Moosazadeh Moghaddam M, Mirnejad R. Antimicrobial peptides: features, action, and their resistance mechanisms in bacteria. Microb Drug Resist 2018; 24:747–767.

132 Seyfi R, Kahaki FA, Ebrahimi T, Montazersaheb S, Eyvazi S, Babaeipour V, Tarhriz V. Antimicrobial peptides (AMPs): roles, functions and mechanism of action. Int J Peptide Res Therap 2020; 26:1451–1463.

133 Zhang QY, Yan ZB, Meng YM, Hong XY, Shao G, Ma JJ, *et al.* Antimicrobial peptides: mechanism of action, activity and clinical potential. Military Med Res 2021; 8:1–25.

134 Centers for Disease Control and Prevention. Atlanta: Centers for Disease Control; 2010.

135 Centers for Disease Control and Prevention (CDC). Methicillin-resistant Staphylococcus aureus infections among competitive sports participants- Colorado, Indiana, Pennsylvania, and Los Angeles County, 2000–2003. Morb Mortal Wkly Rep 2003; 52:793–795.

136 Centers for Disease Control and Prevention. Prevention information and advice for athletes. Atlanta: Centers for Disease Control; 2010.

137 Centers for Disease Control and Prevention. Cleaning & disinfecting athletic facilities for MRSA. Atlanta: Centers for Disease Control and Prevention; 2010.

138 Zinder SM, Basler RS, Foley J, Scarlata C, Vasily DB. National Athletic Trainers' Association position statement: skin diseases. J Athletic Train 2010; 45:411–428.

139 Durai R, Ng PC, Hoque H. Methicillin-resistant *Staphylococcus aureus*: an update. AORN J 2010; 91:599–609.

140 Centers for Disease Control and Prevention. Precautions to prevent the spread of MRSA in healthcare settings. Atlanta: Centers for Disease Control; 2010.

141 Evans JrMW, Ramcharan M, Floyd R, Globe G, Ndetan H, Williams R, Ivie R. A proposed protocol for hand and table sanitizing in chiropractic clinics and education institutions. J Chiropract Med 2009; 8:38–47.

142 Sperber SJ, Levine JF, Gross PA. Persistent MRSA bacteremia in a patient with low linezolid levels. Clin Infect Dis 2003; 36:675–676.