**Staphylococcus aureus** Infections: New Challenges from an Old Pathogen

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**Introduction**

Despite major advances in the medical arena, *Staphylococcus aureus* remains an important agent of infectious diseases in the human host. Its significance lies in its widespread existence and the broad spectrum of infections it can produce, ranging from inconsequential superficial skin infections to deep-seated life-threatening systemic infections. Indeed, some infections caused by *S. aureus*, namely bacteremia and endocarditis, are frequently associated with serious complications and high mortality rates. The emergence of antibiotic resistance has brought renewed attention to *Staphylococcus*. Methicillin-resistant *S. aureus* (MRSA) rates both in hospitalized and ambulatory patients have been escalating, and this resistant phenotype is now considered a major public health problem. Reduced susceptibility to other antimicrobials, including glycopeptides, is being increasingly rec-
Infections in light of the organ-
S. aureus
Micrococcaceae
S. aureus
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ty was quick to develop resistance and MRSA iso-

costs in patients with prosthetic devices and
infections and $37,868 for community-acquired infections
S. aureus
hemolysis within 24 to 36 hours on horse, sheep, or hu-
mam blood agar plates43.
Microbiology
Staphylococcus aureus belongs to the Micrococcaceae
family. It is a nonmotile, non-spore forming, gram-positive
coccus that may occur singly, or in pairs, short chains, or
grape-like clusters. It is a facultative anaerobe, but grows
better under aerobic than anaerobic conditions. The or-
ganism produces catalase and coagulase and grows readi-
ly on blood and chocolate agar. Colonies measure 1 to
3 mm and typically produce a yellow to golden pigment
due to the presence of carotenoids. Most strains produce
hemolysis within 24 to 36 hours on horse, sheep, or hu-
man blood agar plates43.
Epidemiology
Worldwide epidemics of S. aureus disease have been rec-
ognized over the years4,14. Outbreaks have been reported
in a variety of settings, including hospitals15, long-term
care facilities16 and outpatient clinics17, as well as in the
community16.
Nosocomial Infections
Staphylococci have been long recognized as a problem on
hospital wards, and the policy of routine ongoing surveil-
lance for hospital-acquired staphylococcal disease is well
justified40-41. S. aureus is the leading cause of postoperative
wound infection, and the second-most frequent cause of
nosocomial pneumonia42 and bacteremia40. Together, S. au-
reus and coagulase-negative staphylococci account for 21%
of the estimated 4 million infections acquired annually in
United States hospitals44. S. aureus nosocomial infections
cost a great expenditure. Over a two-year period from
2000 to 2001, the average cost of hospitalization in 894 US
hospitals for patients with S. aureus infections was
$48,634 compared to $14,141 for patients without such in-
fecions44. In another study, the mean infection-related
costs in patients with prosthetic devices and S. aureus bac-
teremia (SAB) amounted to $67,439 for hospital-acquired
infections and $57,368 for community-acquired infections45.
In addition to the substantial economic burden, significant
morbidity and mortality are associated with staphylococcal
infections, particularly with invasive infections where mor-
tality rates range between 19% and 34%40,42.
Community-acquired infections
Staphylococcus aureus infections are commonly ac-
quired outside the hospital, particularly among colonized
individuals, and have been reported for several deca-
des46-48. However, the prevalence of infections caused by
MRSA isolates has increased significantly. A Texas-based
study in children noted a 14-fold increase in the rate of
community-acquired MRSA infections in 2002 compared
to previous years49. Similarly among adults, the incidence
of community-acquired staphylococcal infections varied
from 29% in 1997 to 74% in 200250. In addition, recent
studies have demonstrated a substantial increase in the
rate of nasal colonization with MRSA in the community,
from 0.8% in 2001 to 9.2% in 200451.
Nasal carriage
Staphylococcus aureus may be carried by normal people
at various body sites without causing disease. This condi-
tion is referred to as colonization to distinguish it from
actual infection. It should be noted, however, that colo-
ization frequently precedes infection in susceptible pa-
tients46. The anterior nares are the principal sites of colo-
nization with three distinct patterns in the population:
persistent carriers (20%), intermittent carriers (60%), or
noncarriers (20%)45. Whereas 10%-20% of healthy sub-
jects are persistently colonized with S. aureus, populations
with higher colonization rates include patients with atopic
dermatitis (up to 85%)52, as well as surgical patients53, ho-
modialysis patients54, HIV-infected patients55, and those
with intravascular devices56. Health care workers who
come in contact with patients colonized or infected with
S. aureus have higher rates of nasal carriage than provid-
ers without such contact46,57, and they may develop
clinical disease following colonization49. In turn, colonized
health care workers can serve as vehicles for the trans-
mission of S. aureus to patients. In fact, nosocomial out-
breaks are frequently attributed to colonization of the
nares and hands of health care workers58,59.
Antimicrobial Resistance Trends
The propensity of S. aureus to develop resistance to virtu-
ally all the antimicrobial agents available to date has had a
monumental impact on clinical infectious diseases. The pre-
sent day epidemiology of staphylococcal infections has been
shaped to a great extent by the rising antibiotic resistance
rates commensurate with selective antibiotic pressure.
Resistance to beta-lactams
The first report of penicillinase-producing S. aureus
was published in 1940, almost a year before penicillin
was marketed for clinical use47. Since then, beta-lacta-
mase-mediated penicillin resistance has been widely de-
scribed among S. aureus isolates, with 89%-93% resis-
tance rates currently reported in the hospital and the
community47.49. Penicillinase-stable cephalosporins and semisynthetic
penicillins were introduced in the late 1950s. Once again,
S. aureus was quick to develop resistance and MRSA iso-
lates were described shortly thereafter47. Methicillin resis-
tance has been steadily increasing. According to data from
the National Nosocomial Infections Surveillance (NNIS)
System, the prevalence of MRSA among hospitalized pa-
tients rose from 31.9% in 1996 to 60.7% in 2004 (fig. 1)47-49.
Similar trends have been observed worldwide, although ac-
tual MRSA prevalence is subject to wide geographical varia-
tion. For instance, in Europe, MRSA rates as high as
58.0% were described in 2002 and 39.5% in 2006. In Japan,
more than 60% of S. aureus bloodstream isolates in 2001
were methicillin-resistant57. On the other hand, Scandi
navian countries have shown the lowest MRSA rates58.
Several risk factors have been indepen-

Kandasamy KA and Fisher D V. Staphylococcus aureus Infections: New Challenges from an Old Pathogen
Enfer Infecc Microbiol Clin 2006;24(3):182-93
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S. aureus is an important cause of both healthcare-associated and community-acquired infections. Recent reports document that the epidemiology of community-acquired MRSA (CA-MRSA) infections caused by Staphylococcus aureus has been described. CA-MRSA isolates with intermediate and high-level resistance to glycopeptides have been reported. Different mechanisms account for the two types of resistance. Vancomycin-intermediate S. aureus (VIRA) harbors mutations that result in thickening of the peptidoglycan layer. Such resistance might be overcome with high doses of vancomycin. Conversely, vancomycin-resistant S. aureus (VRSA) have acquired the VanA resistance gene from enterococcal species and therefore do not exhibit a dose-dependent resistance to vancomycin. Although vancomycin resistance rates are still low, the emergence of such strains might be inevitable, especially with the continued pressure posed by intense glycopeptide use.

**Diagnosis**

Sites of staphylococcal infection are usually teeming with organisms. S. aureus grows on ordinary laboratory media and can be readily recognized on Gram stains from most clinical specimens. Definitive identification then relies on the tube or slide coagulase test, although all tests lack specificity. Studies suggest that cell ELISA has been shown to be the most sensitive assay for recognizing MRSA isolates, and are especially valuable in detecting nasal colonization and bloodstream infections. Similar assays can now detect the pvl gene in clinical S. aureus isolates. During outbreaks, phage typing of staphylococci is useful for recognizing the epidemic strain. Molecular typing methods have provided reliable results. These include restriction endonuclease analysis of plasmid DNA, pulsed-field gel electrophoresis of DNA, and polymerase chain reaction amplification of selected DNA sequences.

The serological diagnosis of S. aureus bacteremia has been evaluated. Antibodies to a variety of staphylococcal antigens have been tested including peptidoglycan, teichoic acid, S. aureus osteo, and alpha-toxin, lipase, and capsular polysaccharide. Whole cell ELISA has been shown to be the most sensitive assay although all tests lack specificity. Studies suggest that the presence of antibodies to S. aureus teichoic acid might indicate a chronic deep seated infection, including endocarditis, chronic osteomyelitis, and septic arthritis, whereas patients with uncomplicated bacteremia, acute os-
Clinical Syndromes

Virtually any organ system is prone to infection with S. aureus. This review does not present an exhaustive discussion of all the clinical manifestations of staphylococcal infections as these are reviewed elsewhere. We rather focus on systemic infections that have been associated with significant morbidity and mortality and that represent diagnostic and therapeutic challenges for clinical infectious disease specialists.

Bacteremia

Staphylococcus aureus bacteremia is now classified into three categories: hospital-acquired, health-care-associated, and community-acquired SAB. Hospital-acquired and health-care associated infections exhibit similar epidemiological characteristics: both are related to comparable risk factors, such as intravascular devices and comorbid conditions. On the other hand, community-acquired SAB traditionnally afflicts intravenous drug users and otherwise healthy patients with infections at various sites. Resistance is more apparent in hospital-acquired (61%) and health-care-acquired SAB. No difference in duration of mechanical ventilation or ICU mortality

TABLE 1. Selection of studies comparing outcomes of patients with S. aureus infections with respect to methicillin resistance

<table>
<thead>
<tr>
<th>Author (reference)</th>
<th>Setting</th>
<th>Findings</th>
</tr>
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<tbody>
<tr>
<td>Austin et al 19</td>
<td>Bacteremia</td>
<td>Trend towards increased attributable mortality with MRSA</td>
</tr>
<tr>
<td>Blot et al 20</td>
<td>Bacteremia in critically ill patients</td>
<td>Higher attributable mortality with MRSA</td>
</tr>
<tr>
<td>Chang et al 21</td>
<td>Community-acquired bacteremia</td>
<td>Higher mortality, increased risk of persistent bacteremia and renal insufficiency with MRSA</td>
</tr>
<tr>
<td>Combs et al 22</td>
<td>Post-sternotomy mediastinitis</td>
<td>No difference in duration of mechanical ventilation or ICU mortality</td>
</tr>
<tr>
<td>Coughtrie et al 23</td>
<td>Bloodstream infections</td>
<td>Longer hospital stay and higher hospital charges with MRSA</td>
</tr>
<tr>
<td>Condie et al 24</td>
<td>Nosocomial infections</td>
<td>Increased hospital stay with MRSA, no effect on mortality</td>
</tr>
<tr>
<td>Engemann et al 25</td>
<td>Surgical site infections</td>
<td>Increased mortality and hospital charges with MRSA</td>
</tr>
<tr>
<td>Harbarth et al 26</td>
<td>Bacteremia</td>
<td>No effect on in-hospital mortality</td>
</tr>
<tr>
<td>Hershey et al 27</td>
<td>Nosocomial infections</td>
<td>No effect on outcome</td>
</tr>
<tr>
<td>Kopp et al 28</td>
<td>Various infections</td>
<td>Worse clinical and economic outcomes with MRSA</td>
</tr>
<tr>
<td>Lodise et al 29</td>
<td>Bacteremia</td>
<td>Increased length of stay and higher costs of hospitalisation with MRSA</td>
</tr>
<tr>
<td>Martinez-Aguilar et al 30</td>
<td>Musculoskeletal infections in children</td>
<td>Greater febrile days and hospital days with MRSA, no effect on final outcome</td>
</tr>
<tr>
<td>Marty et al 31</td>
<td>Bacteremia in cancer patients</td>
<td>No effect on outcome</td>
</tr>
<tr>
<td>Mekontso-Dessap et al 32</td>
<td>Post-sternotomy mediastinitis</td>
<td>Worse clinical outcome and higher overall mortality with MRSA</td>
</tr>
<tr>
<td>Melaner et al 33</td>
<td>Nosocomial bacteremia</td>
<td>Trend towards increased mortality with MRSA, no effect on risk of dissemination</td>
</tr>
<tr>
<td>Reed et al 34</td>
<td>Bacteremia in HD patients</td>
<td>Higher mortality, longer hospital stay, higher inpatient costs with MRSA</td>
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<tr>
<td>Romero-Vivas et al 35</td>
<td>Nosocomial bacteremia</td>
<td>Higher mortality with MRSA</td>
</tr>
<tr>
<td>Selvey et al 36</td>
<td>Nosocomial bacteremia</td>
<td>No difference in mortality</td>
</tr>
<tr>
<td>Whitby et al 37</td>
<td>Bacteremia (meta-analysis)</td>
<td>Increased mortality with MRSA</td>
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<tr>
<td>Yoon et al 38</td>
<td>Infective endocarditis</td>
<td>Higher risk of persistent bacteremia and trend towards higher mortality with MRSA</td>
</tr>
<tr>
<td>Zahar et al 39</td>
<td>Ventilator-associated pneumonia</td>
<td>No effect on ICU or hospital mortality</td>
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MRSA: methicillin-resistant S. aureus; HD: hemodialysis; ICU: intensive care unit.
associated SAB (52%) than in community-acquired SAB (14%) (P = .001). Approximately one-third of patients with SAB develop one or more complications. Acute systemic complications typically manifest within 48 hours of diagnosis; these include septic shock, acute respiratory distress syndrome, and disseminated intravascular coagulation. On the other hand, metastatic complications of SAB may only become evident several weeks later. In one large retrospective study, common sites of metastatic disease were joints (36%), kidneys (29%), central nervous system (28%), skin (18%), intervertebral disks (15%), liver/spleen (13%), bone (11%), and heart valves (8%). Importantly, more than one metastatic site of infection was present in 43% of cases. Distant foci of infection in SAB develop preferentially in populations with certain predisposing conditions: 1) Underlying cardiac disease, such as native valvular abnormalities, congenital heart disease, and prior infective endocarditis; 2) Prosthetic implants, such as prosthetic valves; intracardiac devices; and orthopedic implants; and 3) Community-acquired SAB, due in part to the typically prolonged disease course and duration of bacteremia prior to detection. For instance, Fernandez-Guerro et al reported a 10-fold increase in the number of cases of infective endocarditis occurring from 1960 to 1975. The increasing frequency of S. aureus IE can also be ascribed to better recognition of the disease through the widespread application of echocardiography in evaluating patients with SAB. In patients with SAB frequently involves normal cardiac valves and is seldom accompanied by the physical stigmata of IE, rendering the diagnosis of the disease difficult. In fact, reliance solely upon physical examination findings is likely to result in underdiagnosis of S. aureus IE in a large number of cases. Because of the difficulty in clinically identifying S. aureus IE, the use of echocardiography has been advocated to evaluate patients with SAB. Despite its limited sensitivity in detecting vegetations (64%), transthoracic echocardiography (TTE) is a widely available, non-invasive screening modality in the setting of SAB. Conversely, transesophageal echocardiography (TEE) offers significant advantages over TTE, including higher sensitivity in identifying IE (80%) and improved identification of IE complications, and an enhanced ability to exclude IE in patients with native valves (negative predictive value 100%).

Whether TTE or TEE should be employed in the initial screening of the patient presenting with SAB remains a controversial issue. TEE is currently highly favored at our institution for the evaluation of most patients with SAB. The authors believe that TEE is likely to be cost-effective to guide duration of therapy in patients with intravascular catheter-associated SAB or for patients at higher risk for IE or associated complications. Despite early diagnosis and appropriate therapy, IE following SAB is often associated with devastating and life-threatening sequelae. The overall mortality of S. aureus IE ranges from 19% to 56%, with worse outcomes with more comorbid conditions such as hemodialysis and infection with the human immunodeficiency virus. The absence of the aforementioned risk factors, however, does not exclude the presence of metastatic disease.

Endocarditis Infective endocarditis (IE) complicates the course of SAB in ~12% of cases. S. aureus was the most common cause of native valve endocarditis. Recent years have witnessed a rise in the rates of IE due to S. aureus. S. aureus is now the leading cause of IE in many parts of the world. This trend is mostly attributed to the increasing prevalence of healthcare-associated S. aureus IE that has accompanied the growing use of interventional procedures, intravascular catheters, and implantable devices. For instance, Fernandez-Guerro et al reported a 10-fold increase in the number of cases of hospital-acquired IE (most of which were due to S. aureus) from 1976 to 1992 compared to the number of cases occurring from 1960 to 1975. The increasing frequency of S. aureus IE can also be ascribed to better recognition of the disease through the widespread application of echocardiography in evaluating patients with SAB. Endocarditis in patients with SAB frequently involves normal cardiac valves and is seldom accompanied by the physical stigmata of IE, rendering the diagnosis of the disease difficult. In fact, reliance solely upon physical examination findings is likely to result in underdiagnosis of S. aureus IE in a large number of cases. Because of the difficulty in clinically identifying S. aureus IE, the use of echocardiography has been advocated to evaluate patients with SAB. Despite its limited sensitivity in detecting vegetations (64%), transthoracic echocardiography (TTE) is a widely available, non-invasive screening modality in the setting of SAB. Conversely, transesophageal echocardiography (TEE) offers significant advantages over TTE, including higher sensitivity in identifying IE (80%) and improved identification of IE complications, and an enhanced ability to exclude IE in patients with native valves (negative predictive value 100%).
emboli secondary either to right-sided endocarditis or to soft tissue or joint infection. In this type of S. aureus pneumonia, pleuritic chest pain is a hallmark feature whereas cough and sputum production are less likely\cite{181,182}.

**Novel therapies for MRSA**

The use of beta-lactams in the treatment of S. aureus infections has been greatly handicapped by the increasing prevalence of MRSA strains. Although vancomycin, the traditional alternative antimicrobial agent, still maintains in vitro activity against the majority of MRSA isolates, clinical cure rates in serious infections are disheartening. Treatment failure rates exceeding 40% have been recently quoted for SAB\cite{183,184} and S. aureus pneumonia\cite{185} treated with vancomycin. This has kindled great interest in developing new treatment options for MRSA.

**Quinupristin/dalfopristin**

Quinupristin and dalfopristin belong to the streptogramin class of antibiotics. When combined, these two agents are bactericidal and act in synergy on the 50S ribosomal subunit to inhibit protein synthesis. Quinupristin/dalfopristin is active in vitro against both MSSA and MRSA\cite{186}. The drug is approved by the Food and Drug Administration (FDA) only for the treatment of complicated skin and skin structure infections (cSSSI) due to MSSA\cite{187}. However, data from a small controlled trial have suggested that quinupristin/dalfopristin is equivalent to vancomycin in the treatment of catheter-related bacteremia caused by S. aureus or coagulase-positive staphylococci\cite{188}.

Another study compared in a randomized design quinupristin/dalfopristin to vancomycin in the treatment of nosocomial pneumonia. Although both drugs were comparable in clinical efficacy (56% vs. 58%, respectively), the number of episodes of pneumonia caused by S. aureus was relatively small in both arms\cite{189}. Quinupristin/dalfopristin has also showed promising results in experimental rat and rabbit models of ventilator-associated pneumonia\cite{190}. A major advantage offered by this new drug is its oral bioavailability of approximately 100%\cite{191}. Despite lacking a formal indication, quinupristin/dalfopristin is being used considerably in the treatment of SAB\cite{192,193} and S. aureus endocarditis\cite{194,195}. Currently, phase III trials are being conducted to evaluate the efficacy of daptomycin in staphylococcal bloodstream infections. Daptomycin is being used considerably in the setting of SAB and S. aureus endocarditis\cite{195,196}. Linezolid is an oxazolidinone antimicrobial agent that inhibits protein synthesis. It exerts its action by inserting itself into the bacterial cell membrane. Subsequent events that lead to bacterial cell killing are not fully understood but are thought to involve dissipation of membrane potential. Daptomycin is FDA-approved for the treatment of cSSSI due to S. aureus including MRSA. In two distinct Phase III trials in patients with cSSSI, daptomycin resulted in similar success rates as its comparators–semisynthetic penicillin or vancomycin (71.5% and 71.1%, respectively)\cite{197}. Despite lacking a formal indication, daptomycin is being used considerably in the setting of SAB and S. aureus endocarditis\cite{198,199}. Consequently, the authors do not recommend the use of linezolid in the setting of MRSA endocarditis regardless of the antimicrobial susceptibility of the isolate.

**Tigecycline**

Tigecycline is a newly introduced glycylcycline derivative with structural homology to tetracyclines. This drug offers broad-spectrum antimicrobial coverage including MRSA through binding to the 30S ribosomal subunit. Tigecycline has received FDA approval for the treatment of complicated intraabdominal infections\cite{200}. In addition, animal models have shown promising results with tigecycline compared to vancomycin in MRSA endocarditis\cite{201}.

**Dalbavancin**

Dalbavancin is a semisynthetic glycopeptide characterized by a long half-life (9–12 days) that allows once-weekly administration. It exerts its potent activity against MRSA via inhibition of cell wall synthesis. Dalbavancin has shown positive results in Phase III studies in cSSSI\cite{202} and in a Phase II study in catheter-related bloodstream infections\cite{203}. It is currently awaiting FDA approval for these indications.

**Telavancin**

Telavancin is an experimental lipoglycopeptide molecule characterized by two mechanisms of action: inhibition of bacterial peptidoglycan synthesis; and alteration of bacterial cell membrane permeability and depolarization. Telavancin exhibits bacterial in vitro activity against S. aureus isolates including MSSA, MRSA and VISA isolates. In animal infection models, telavancin was efficacious in the treatment of various MRSA infections including soft tissue infections\cite{204}, pneumonia\cite{205}, and endocarditis\cite{206}. In Phase II clinical trials, telavancin was compared to stan-
dard therapy (semisynthetic penicillin or vancomycin) in patients with cSSSI [222]. Data from this study showed that telavancin was equivalent to standard therapy both in clinical cure in the all treated population (79% vs. 80%; P = 0.015). On the other hand, one study in patients with cSSSI [221] demonstrated superiority over vancomycin in the MRSA subgroup (82% vs. 69%; P < 0.001) [11]. Investigators have therefore suggested that a single course of mupirocin may be insufficient in in-hospital mortality, and duration of hospitalization when compared to vancomycin alone (P < 0.001) [225]. The results of a Phase II randomized, double-blind, multi-center clinical study of tefibazumab in patients with SAB were recently presented [223].

Prevention

Nasal decolonization

Since MRSA nasal colonization frequently precedes infection, endeavors to contain the transmission of MRSA have targeted the eradication of nasal carriage in susceptible patients. Studies evaluating this strategy have yielded conflicting results. Cardiothoracic surgery patients who received mupirocin prophylaxis had a lower surgical wound infection rate than historical controls (7.3% vs. 2.8%; P < 0.01) [225]. More recently, combining results from two randomized trials in surgical patients suggested that the administration of mupirocin in surgical patients reduced postoperative nosocomial S. aureus infections as compared to placebo (RR 0.49, 95% CI 0.29-0.83; number needed to treat 26) [226,227]. Boelaert et al found a four- to six-fold reduction in SAB rates in hemodialysis patients receiving mupirocin prophylaxis with respect to rates of nosocomial S. aureus infections, in-hospital mortality, and duration of hospitalization [228]. Investigators have therefore suggested that a single course of mupirocin may be insufficient in low-risk patients with prolonged exposure [229]. In addition to conflicting messages from clinical trials, the emergence of mupirocin-resistance has also been reported [230,231].

Vaccination

Staphylococcus aureus Polysaccharide Conjugate Vaccine (StaphVax®, Nabi Biopharmaceuticals, Rockville, MD) is an investigational polysaccharide conjugate vaccine that presents a novel approach to the prevention of S. aureus infections. It consists of type 5 and type 8 capsular polysaccharides, the strains accounting for more than 80% of infections. In one double blinded, placebo-controlled Phase III clinical efficacy trial involving 1804 hemodialysis-dependent patients, StaphVax recipients failed to meet the a priori endpoint of reduction in episodes of S. aureus bacteremia at 54 weeks. However, post hoc analysis revealed a 57% reduction in SAB episodes at 10 months compared to placebo recipients (P = 0.015) [232]. Based on these findings, a second Phase III confirmatory trial, with modified time points, was undertaken. However, this second trial also failed to meet its primary endpoint. As a result, all clinical trial development and further marketing of StaphVax have been held until assessment of the results is completed.

Infection control strategies

Several studies have established that the transmission of MRSA between patients within the hospital setting occurs to a great extent through health care workers [11,44]. Consequently, the Centers for Disease Control and Prevention (CDC) recommend the implementation of contact precautions in patients colonized or infected with MRSA [233]. Such precautions include the use of private rooms, protective attire for health care workers, and strict adherence to hand hygiene principles. There is abundant evidence to support the efficacy of these infection control programs in reducing the transmission of resistant pathogens within the hospital [234-236]. Although active surveillance for MRSA and preemptive isolation of colonized or infected patients remains an integral part of many hospital infection control programs, observance of infection control guidelines has been suboptimal [237,238]. Hand hygiene practices have been particularly inadequate [239,240]. Accordingly, continuous efforts should be made to improve compliance with isolation and hand hygiene policies to prevent the dire consequences of nosocomial MRSA transmission.

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