Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Prevention and control

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INTRODUCTION — Prevention and control of methicillin-resistant *Staphylococcus aureus* (MRSA) infection is among the most important challenges of infection prevention. About 100,000 invasive MRSA infections occur annually, and the associated number of death is estimated to be 19,000 [1]. Factors in transmission include colonization, impaired host defenses, and contact with skin or contaminated fomites [2,3]. Further study of *S. aureus* pathogenesis is important for prevention optimization.

The success of MRSA control has varied substantially with different strategies [4,5]. Some European countries have managed to contain MRSA at a low prevalence using active surveillance cultures and contact precautions, with or without decolonization (examples include the Netherlands, Finland, and France) [6-10]. Other countries have struggled to control MRSA epidemics but have progressed over the last decade (examples include Germany and Canada) [11-14]. The countries with greatest MRSA prevalence include the United States and Japan [15-17]. In the last few years, the incidence of MRSA infections in the United States has plateaued and is decreasing [8,9]. (See "Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Epidemiology".)

Many important clinical studies addressing control of MRSA have been in intensive care units, including studies on contact precautions, decolonization, and the role of active surveillance. The clinical approach to prevention of MRSA infection among patients in intensive care units, including universal decolonization with chlorhexidine bathing, is discussed separately. (See "Infections and antimicrobial resistance in the intensive care unit: Epidemiology and prevention".)

Issues related to prevention and control of MRSA outside intensive care units will be reviewed here. Issues related to the treatment and epidemiology (including transmission) of these infections are discussed in detail separately. (See "Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Epidemiology" and "Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Treatment of bacteremia and osteomyelitis" and "Methicillin-resistant Staphylococcus aureus (MRSA): Microbiology".)

IN HEALTHCARE SETTINGS

Basic infection prevention principles — Principles of infection prevention for reducing spread of methicillin-resistant *S. aureus* (MRSA) include attention to careful hand hygiene and adherence to contact precautions for care of patients with known MRSA infection.

Hand hygiene consists of cleaning hands with soap and water or an alcohol-based hand gel before and after clinical encounters with patients who have MRSA infection [18]. Hand hygiene is an important factor in controlling the transmission of healthcare-associated infection [19,20]. This was illustrated in a study in which implementation of a hand-hygiene campaign led to an increase in the rate of hand hygiene compliance (48 to 66 percent) with a concomitant decrease in the rate of MRSA transmission (2.16 to 0.93 episodes per 10,000 patient-days) and the overall rate of healthcare-associated infections (16.9 to 9.9 percent) [20].

Principles regarding hand hygiene are discussed further separately. (See "General principles of infection control", section on 'Hand hygiene'.)

Contact precautions include use of gowns and gloves during clinical encounters with patients who have MRSA infection; multiple studies have demonstrated the efficacy of contact precautions for reducing spread of MRSA [21,22]. Masks may offer some benefit for reducing colonization among healthcare workers caring for patients with active pulmonary infection due to MRSA [21,23]. Patients colonized or infected with MRSA may be cohorted with other such patients. Ideally, patients with MRSA isolates that are potentially eradicable via decolonization (ie, known to be susceptible to mupirocin, rifampin, minocycline, and trimethoprim-sulfamethoxazole) should not be cohorted with patients whose MRSA isolates are resistant to these drugs.

MRSA colonization status should be noted in the hospital record so that appropriate precautions can be arranged promptly if colonized patients require repeat admission [24]. This is important because MRSA colonization can persist for months; in one study including 78 previously colonized patients readmitted to the same facility ≥3 months later, colonization persisted in 40 percent of cases [25].

The optimal approach for documenting MRSA clearance and subsequent discontinuation of precautions is uncertain. One randomized trial comparing active screening with passive screening among more than 600 patients with prior documented MRSA colonization noted that active screening led to more frequent discontinuation of contact precautions when they were no longer needed (relative risk 2.5; 95% CI 1.5-4.7), resulting in reduction in inappropriate isolation and cost of isolation [26].

The United States Centers for Disease Control and Prevention has indicated that, in general, it is reasonable to discontinue contact precautions when three or more surveillance cultures are negative over the course of a week or two in the absence of antimicrobial therapy (for several weeks), a draining wound, respiratory secretions, or evidence implicating the patient in ongoing transmission [27].

Principles regarding contact precautions are discussed further separately. (See "General principles of infection control", section on 'Contact precautions'.)

Role of active surveillance

Definitions — Active surveillance consists of performing screening cultures (of the nares, oropharynx, and/or perineum) to identify asymptomatic patients who are colonized with antibiotic-resistant bacteria, with the goal of intervening to minimize the likelihood of spread to other patients (via implementation of contact precautions) [21,28]. A large proportion of patients with MRSA colonization develop MRSA infection, and transmission occurs among both colonized and infected patients [24,29,30].

The anterior nares are a frequent site of MRSA carriage (positive in 73 to 93 percent of carriers); however, nasal colonization has not been universally found among MRSA-positive patients with implanted devices, and the rectum may be an important reservoir among those with community-acquired MRSA [31-33]. Throat cultures have been shown to detect MRSA with sensitivity equal to or greater than that of nasal cultures and may be used in addition or as an alternative to nasal cultures. Areas of skin breakdown (if present) should also be sampled.

Different microbiological methods exist for surveillance testing; these include standard microbiology methods, selective media, and polymerase-chain reaction–based tests. Rapid whole-genome sequencing is an alternative method that may be useful for outbreak investigation but is not yet widely available [34]. (See "Rapid detection of methicillin-resistant Staphylococcus aureus".)

Healthcare settings not using active surveillance are able to identify patients with MRSA infection only via clinical cultures obtained from symptomatic patients (ie, passive surveillance). Clinical cultures alone may underestimate the prevalence of MRSA by as much as 85 percent [33,35].

Clinical approach — The optimal role for active surveillance is not known, and there is insufficient evidence for a single routine approach [4]. Active surveillance cultures appear to be most useful in the setting of hospital outbreaks and among patients at high risk for MRSA carriage [36]. Such patients include [28,36-50]:

- Patients with history of MRSA colonization (such patients should be isolated initially pending surveillance testing results)
- Patients in intensive care units (ICUs)
- Patients who are immunocompromised
- Residents of long-term care facilities
- Patients on hemodialysis
- Patients hospitalized in the previous 12 months
- Patients who have received antibiotic therapy in the last three months
- Patients with skin or soft tissue infection at admission

Advocates of active surveillance have pointed to its success among several European countries where MRSA has been contained at a low prevalence (examples include the Netherlands, Finland, and France) [6,7,51-53]. These strategies

involved a multifaceted approach including surveillance, contact isolation, healthcare worker screening with decolonization, and closing units for comprehensive screening and cleaning when warranted [54-56]. Given this combination of interventions, it is not certain which intervention or combination of interventions is required for MRSA control. Therefore, extrapolating these experiences to other healthcare settings with variable MRSA prevalence and other factors may be difficult.

Institutions performing surveillance cultures should establish clear policies regarding how the results will be used to make decisions about contact precautions, cohorting, and decolonization. Educational programming about adherence is imperative for patients, visitors, healthcare workers, environmental cleaners, and other hospital personnel.

Patient bathing — Patient bathing with chlorhexidine has been shown to be useful for reducing MRSA colonization and infection [41,57]. This issue has been studied best in intensive care unit settings and is discussed in detail separately. (See "Infections and antimicrobial resistance in the intensive care unit: Epidemiology and prevention", section on 'Decolonization/patient bathing' and "General principles of infection control", section on 'Patient bathing'.)

Decolonization — Issues related to MRSA colonization are discussed further separately. (See "Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Epidemiology", section on 'MRSA colonization'.)

Efficacy — The role of decolonization in the control of MRSA spread is uncertain. MRSA nasal colonization appears to precede infection, although asymptomatic nasal carriage is not always identifiable in the setting of MRSA infections [58].

Decolonization does not appear to be consistently effective for eliminating MRSA carriage [39,59-61]. One systematic review and meta-analysis in nonsurgical settings noted mupirocin reduced the risk for *S. aureus* infection in dialysis and nondialysis settings by 59 and 40 percent, respectively [62]. The meta-analysis noted the significant heterogeneity in study designs and study populations. Decolonization has been studied in the context of large studies including other infection prevention measures, so it can be difficult to discern the effect of this particular intervention [39,59]. Furthermore, emergence of resistance to agents used for decolonization limits the utility of this strategy.

The durability of MRSA decolonization is limited [21]. Recolonization rates at 12 months following treatment range from 50 to 75 percent among healthcare workers and patients undergoing peritoneal dialysis, respectively [63]. Short-term recolonization rates are similar: 56 percent at 4 months in patients undergoing hemodialysis and 71 percent at 2.5 months in patients with HIV infection [64,65].

Nonetheless, some clinicians favor attempting MRSA decolonization, but there are many uncertainties about the optimal approach. Should decolonization be pursued only in the setting of MRSA outbreaks or as a component of routine management of MRSA infection? Should it be used for prevention of MRSA infection among hospitalized patients, in the community, or both? Might widespread decolonization lead to evolution and spread of increasingly resistant antibiotic-resistant strains?

Most of the available data have been collected in the ICU setting; less is known about the optimal role of decolonization in other circumstances. Studies have evaluated the role of decolonization among patients and healthcare workers [66,67], although the limited durability of MRSA decolonization complicates determination of its optimal role among these groups.

Clinical approach — In general, there is insufficient evidence to support routine MRSA decolonization. However, decolonization may be appropriate in the setting of MRSA outbreaks, particularly if there is epidemiologic evidence pointing to transmission by one or more healthcare workers in a healthcare setting or among individuals in a specific population. In addition, decolonization may be reasonable for patients with multiple documented recurrences of MRSA infection or if ongoing transmission is occurring among household members or other close contacts despite optimizing hygiene measures [4,18,68].

The optimal regimen and duration of therapy for eradicating MRSA colonization is uncertain. If decolonization is pursued, we favor a 5- to 10-day course of therapy with the following topical agents [18,69-74]:

- Chlorhexidine gluconate daily washes (2 or 4 percent solution)
- Mupirocin ointment (2 percent) applied to nares with a cotton-tipped applicator two to three times daily

Routine surveillance cultures following decolonization are not necessary in the absence of active infection [18].

The efficacy of successful decolonization following a failed initial attempt is relatively low. If repeat infection occurs, repeat decolonization may be attempted; the topical agents may be readministered as outlined above, together with oral

antibiotic therapy.

No clinical trials have evaluated the role of oral antimicrobial agents for management of recurrent MRSA infections, and the optimal regimen and duration are unknown. Oral antimicrobials should be considered only in patients who continue to have recurrent MRSA infection in spite of other measures [18]. In such cases, rifampin (600 mg orally once daily) may be administered, in combination with either doxycycline (100 mg orally twice daily) or trimethoprim-sulfamethoxazole for (one double-strength tab orally twice daily) for a 5- to 10-day course.

Prolonged use of topical or systemic agents is not appropriate as it has been associated with evolution and spread of antibiotic-resistant strains, loss of valuable therapeutic agents for subsequent treatment of infection, and adverse drug effects [69,75].

Mupirocin and chlorhexidine resistance have been described [76]. Mupirocin resistance has been reported (24 percent of MRSA isolates in one study) [69,77-80]. The gene for high-level mupirocin resistance, *mupA*, has been found on a plasmid in USA300 MRSA clones, suggesting that the future utility of this drug may be limited since this clone has been implicated in many community-associated MRSA infections [81,82]. Thus far, no breakpoints have been established for mupirocin susceptibility testing, and commercial tests are limited.

Issues related to *S. aureus* decolonization in surgical patients are discussed separately. (See "Adjunctive measures for prevention of surgical site infection in adults", section on 'S. aureus decolonization'.)

Environmental cleaning — Meticulous cleaning of patient care surfaces is essential for control of MRSA environmental contamination [4,21,83,84]. MRSA is sensitive to routinely used hospital disinfectants but can survive on surfaces for hours, days, or months. Its viability depends on a variety of factors including temperature, humidity, the number of organisms present, and the type of surface.

Medical equipment should be dedicated to a single patient when possible to avoid transfer of pathogens via fomites. Equipment that must be shared should be cleaned and disinfected before use for another patient [21].

Environmental services personnel should be included as an integral part of the infection prevention team. Checklists for cleaning frequently touched patient care surfaces (such as bed controls, light switches, doorknobs, etc) can be useful for reinforcing consistency [36]. Ultraviolet markers may be useful for monitoring thoroughness of room cleaning [85-87].

Issues related to environmental cleaning are discussed further separately.

Antibiotic stewardship — Inappropriate or excessive antibiotic use can lead to selection of resistant organisms [88,89]. The risk of MRSA colonization has been correlated with the frequency and duration of prior antimicrobial therapy [90,91]. Several studies have documented a higher risk of MRSA colonization following therapy with fluoroquinolones in particular [92-94].

Reductions in the use of certain antibiotics can reduce the incidence of MRSA infection [95-97]. However, altering an antibiotic formulary can in turn lead to emergence of other resistant pathogens [88,96].

IN THE COMMUNITY — Tools for preventing methicillin-resistant *S. aureus* (MRSA) spread in the community include hand hygiene and minimizing risk factors for transmission (table 1) [50,98]. Hand hygiene is as important in the community as in the hospital. Hands should be cleaned thoroughly with soap and water or an alcohol-based hand sanitizer, immediately after touching the skin or any item that has come in direct contact with a draining wound.

Wounds that are draining should be kept covered with clean, dry bandages. Patients with open wounds should not participate in activities involving skin-to-skin contact with others until wounds are fully healed. Individuals should avoid sharing personal items that may become contaminated with wound drainage, such as towels, clothing, bedding, bar soap, razors, or athletic equipment that touches the skin. Clothing that comes into contact with wound drainage should be laundered and dried thoroughly. Environmental surfaces with which multiple individuals have bare skin contact should be cleaned with an over-the-counter cleaner with activity against *S. aureus*. Cross-transmission of MRSA between humans and their pets has been described [3,99,100].

Decolonization may be appropriate if there is epidemiologic evidence pointing to transmission within a household [101]. However, decolonization efforts in large community settings are of unclear benefit. In one cluster-randomized controlled trial including over 30,000 military recruits, education about preventing infections along with an extra weekly shower (with

or without a weekly 4 percent chlorhexidine body wash) did not result in fewer MRSA infections [102]. (See 'Decolonization' above.)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: Methicillin-resistant Staphylococcus aureus (MRSA) (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Basic infection prevention principles include attention to careful hand hygiene and adherence to contact precautions for care of patients with known MRSA infection. (See 'Basic infection prevention principles' above.)
- Active surveillance cultures identify asymptomatic individuals with MRSA colonization to be placed on contact precautions with the goal of minimizing MRSA spread to other patients. This practice is appropriate in the setting of an outbreak; its role for routine screening is a question of ongoing debate. (See 'Role of active surveillance' above.)
- We suggest that decolonization not be performed in the routine management of MRSA infections (**Grade 2B**). Decolonization does not appear to be consistently effective for eliminating MRSA carriage, and emergence of resistance to agents used for decolonization will limit the utility of such protocols. (See 'Decolonization' above.)
- We suggest performing decolonization in the setting of a MRSA outbreak, particularly if there is epidemiologic evidence pointing to transmission by one or more healthcare workers or among individuals in a specific population (**Grade 2C**). Regimens are outlined above. (See 'Decolonization' above.)
- Additional important components for MRSA prevention and control include environmental cleaning and prudent antibiotic use. (See 'Environmental cleaning' above and 'Antibiotic stewardship' above.)
- Tools for preventing MRSA spread in the community include hand hygiene and minimizing risk factors for transmission (table 1). Decolonization may be appropriate if there is epidemiologic evidence pointing to transmission within a household. (See 'In the community' above.)

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GRAPHICS

Risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) colonization

Recent hospitalization
Residence in a long-term care facility
Recent antibiotic therapy
HIV infection
Men who have sex with men
Injection drug use
Hemodialysis
Incarceration
Military service
Sharing needles, razors, or other sharp objects
Sharing sports equipment
Diabetes
Prolonged hospital stay
Swine farming

Graphic 53504 Version 8.0

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