What Bugs Us? Methicillin-resistant *Staphylococcus aureus*

Measures currently taken to prevent the spread of MRSA and other antibiotic-resistant bacteria may be labor-intensive, however, these efforts are essential in preventing the spread of these bacteria.

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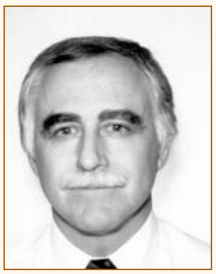

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Methicillin-resistant Staphylococcus aureus

Antibiotic resistant bacteria are bacteria that have developed properties to allow them to survive or grow in the presence of certain antimicrobial agents, which gives the bacteria a survival advantage. In practice, this usually equates to selection of therapy with a broader spectrum of activity than what would have otherwise been used to manage an infection caused by an antimicrobial susceptible strain of the same microorganism.

There are many examples of microorganisms that have exhibited increasing rates of resistance to commonly used antimicrobials. These include methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *enterococci* (VRE), multiply antibiotic resistant Shigella species, extended spectrum beta-lactam (ESBL) resistant enteric gram-negative bacilli (Klebsiella-Enterobacter species) and penicillin-resistant *Streptococcus* pneumoniae (PRSP). Some of these organisms, such as MRSA, VRE, and ESBL, are common among patients in health-care facilities, whereas PRSP and multiply resistant Shigella species are more common in the community setting. In health-care facilities, MRSA and VRE represent serious concerns, as these micro-organisms are resistant to antibiotics that had previously been effective against them. There have been reports from the U.S., Asia, and Europe of strains of *S. aureus* with intermediate susceptibility to glycopeptides (GISA), such as vancomycin.[1,2] To date, none have been identified in Canada, however, their presence is worrisome as vancomycin is the agent most frequently selected when intravenous therapy is needed for patients with MRSA infections.

Summary

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- *Staphylococcus aureus* is a gram-positive bacterium found on the skin of most people. Approximately 20% to 30% of the population are S. aureus carriers, who may harbor this microorganism in their noses, oropharynx and other mucus membrane surfaces.
- Individuals in hospitals and long-term care facilities are at the greatest risk of acquiring MRSA. The risk factors for acquiring MRSA in health-care facilities include: patients with serious medical or surgical conditions, therapy with broad-spectrum antimicrobial agents, frequent and prolonged antimicrobial therapy, treatment in an intensive care or burn unit and contact with another patient with MRSA infection or colonization.
- MRSA is not usually a clinical concern in individuals colonized with the bacteria, however, if MRSA causes an invasive infection, the initial empiric therapy that is selected may not be sufficient to treat the infection, as MRSA is resistant to all beta-lactam agents (i.e., penicillin, cloxacillin, cephalosporins, carbapenems).
- If eradication/decolonization therapy for MRSA carriage is deemed necessary, the regimen most often used is applying mupirocin (2%) to nares and wounds twice or three times a day for one to two weeks, plus once-daily chlorhexidine or triclosan for topical use.

What Are The Implications of Antibiotic-Resistant Bacteria?

There are many implications associated with infection or colonization of antimicrobial-resistant micro-organisms.[3-5] In addition to significant increases in costs and greater toxicity of newer antibiotics, antibiotic-resistant bacteria are continuously eroding the therapeutic armamentarium, leaving fewer or no alternative agents available. Health-care workers also experience an increased workload associated with the management of patients infected or colonized with antimicrobial resistant bacteria, as they try to ensure that these microorganisms are not transmitted to others.[6-8] It has been noted recently that as nursing staffing decreases in critical care areas, there is an increased potential for the transmission of antimicrobial resistant bacteria.[9,10]

What Is MRSA?

Staphylococcus aureus is a gram-positive bacterium found on the skin of most people. Approximately 20% to 30% of the population are *S. aureus* carriers, who may harbor this micro-organism in their noses, oropharynx and other mucus membrane surfaces. It is rarely a significant concern. *S. aureus* traditionally causes skin and soft-tissue infections and may result in endocarditis in injection drug users or bacteremias in those with in-dwelling vascular access catheters. *S. aureus* was susceptible to penicillin during the 1940s and 1950s. Shortly after the introduction of penicillin, however, penicillin-resistant strains of *S. aureus* were reported.[11] *S. aureus* initially developed beta lactamases capable of degrading penicillin, therefore, rendering penicillin ineffective. Methicillin, a member of the penicillin family that is very similar to cloxacillin, provided the next line of defense against penicillin resistant *S. aureus*. The presence of naturally occurring strains of MRSA was recognized soon after the introduction of methicillin in the early 1960s. These strains of *S. aureus* were able to modify the penicillin-binding proteins within the cell membrane to resist the actions of methicillin, therefore, leading to the evolution of MRSA. MRSA was first identified in Canada in the early 1980s, but remained infrequent, and *staphylococcal* infections could still be treated with agents, such as cloxacillin and cefazolin. Over the past 15 years, the prevalence of MRSA has increased in Canada, with MRSA identification rates of 0.95 MRSA/100 *S. aureus* isolates in 1995 to 5.97 in 1999,[12] and more recently, 8.3/100 in 2000, (Canadian Nosocomial Infections Program/Canadian Hospital Epidemiology Committee). MRSA strains are generally no more harmful than the methicillin-susceptible strains of *S. aureus*, however, infections with these micro-organisms are more difficult to treat because cloxacillin is no longer effective. Once MRSA is introduced into a health-care facility, it may be difficult to eradicate even with aggressive infection prevention and control measures.[13] Although MRSA has traditionally affected patients in health-care facilities, there are an increasing number of reports documenting MRSA acquisition in the community.[14-16]

Who Is At Risk of Acquiring MRSA?

Individuals in hospitals and long-term care facilities are at the greatest risk of acquiring MRSA. The risk factors for acquiring MRSA in health-care facilities include: patients with serious medical or surgical conditions, therapy with broad-spectrum antimicrobial agents, frequent and prolonged antimicrobial therapy, treatment in an

People suspected of having MRSA infection or being colonized with MRSA usually have been in contact with other patients who reside in long-term care facilities where MRSA is endemic.

intensive care or burn unit and contact with another patient with MRSA infection or colonization.[17,18] The general public are usually not at risk of acquiring MRSA.[18] If a healthy person acquires these bacteria, they may be carried asymptomatically, however, the actual prevalence of asymptomatic carriage in healthy persons in a community is not known.

The major concern with MRSA is that it may spread rapidly within a health-care facility by health-care workers with unwashed hands.[9,10] Transmission of MRSA will lead to the colonization of many patients and staff, therefore, serving as a potential reservoir for outbreaks and invasive infections. Preventing transmission requires aggressive infection prevention and control measures.[17-20]

Transmission of MRSA

MRSA is transmitted from person to person by direct contact with someone who has the infection or is colonized with MRSA.[7] MRSA is less frequently transmitted by contact with contaminated surfaces. It is speculated that MRSA is spread by cross-contamination from the hands of caregivers, who transiently carry the organism, to patients who subsequently become colonized.[9,11,18]

Colonization *Versus* Infection

A person is considered to be colonized with MRSA if the bacterium is recovered from cultures, but signs and symptoms of infection are not present. The anterior nares, throat, axilla, and perineal area are the sites from which MRSA can be most frequently recovered in those who are colonized. If the bacterium is recovered from a site where signs of infection are present, the patient is diagnosed as having MRSA infection. Such results may be obtained from a patient's blood culture or from an ulceration in the skin with purulence at its base or with surrounding cellulitis. Colonization is almost always precedes the development of infection.[5]

What Is The Concern About MRSA?

MRSA is not usually a clinical concern in individuals colonized with the bacteria, however, if

MRSA causes an invasive infection, the initial empiric therapy that is selected may not be sufficient to treat the infection, as MRSA is resistant to all beta-lactam agents (*i.e.,* penicillin, cloxacillin, cephalosporins, carbapenems). Although some MRSA isolates may be susceptible to trimethoprim/sulfamethoxazole, clindamycin, aminoglycocides,and vancomycin, this is frequently not known when empiric antimicrobial therapy is initiated. Vancomycin is, therefore, frequently selected as empiric therapy when MRSA is suspected. Unfortunately, this selection raises concerns regarding the appropriate use of antimicrobial agents. Infections or colonization with MRSA add additional costs associated with a patient's care. These costs include additional medications, extra materials, such as gowns, gloves, masks and designated patient-care equipment and the potential additional expense for patient accommodation.[7]

Most, if not all, Canadian health-care facilities, regard MRSA as a significant nosocomial pathogen and have specific policies and procedures to manage patients colonized or infected with MRSA.

Who Should Be Suspected Of Having MRSA?

People suspected of having MRSA infection or being colonized with MRSA usually have been in contact with other patients who reside in long-term care facilities where MRSA is endemic. Other at-risk patients have undergone invasive procedures in U.S. health-care facilities.

What Should Be Done If MRSA Is Suspected?

When a person infected or colonized with MRSA is identified, the major concerns relate to the potential for spread throughout the facility. Isolation procedures with barrier precautions are, therefore, frequently undertaken for such hospitalized patients. There is a lower risk of transmission of MRSA in primary (ambulatory) and home health-care settings (*i.e.,* home nursing services for dressing changes, medication administration), therefore, specific isolation procedures are not routinely recommended and specific environmental decontamination practices are not required.[21] It would be prudent, however, to review the recommendations with local health authorities if questions arise regarding the management of patients infected or colonized with MRSA.

Why Are Screening Cultures Performed?

Most health-care facilities have specific guidelines for screening people entering the institution to determine if they are colonized with MRSA. Cultures may be obtained at the time of admission if the patient is being transferred from, or has recently been in, a health-care facility where there is a high prevalence of MRSA. It is important to identify these patients as soon as possible to minimize the potential spread of MRSA within the specific health-care facility.[19,20,22,23] Based upon the policies of the specific health-care facility, the screening cultures usually obtained include specimens from both nares, a urine sample, rectal or colostomy/ileostomy stoma sites, and clinically indicated specimens (*i.e.,* sputum or endotracheal secretions, throat swab, all open wounds or draining sites, the exit sites of invasive catheters if drainage is apparent). Some facilities also obtain groin and axillary screening swabs. These specimens are not indicated in ambulatory and home health settings.

What Are The Necessary Infection Prevention And Control Measures?

It is important to be familiar with your facility's specific infection prevention and control guidelines, since there are variations in the degree to which barrier precautions are applied. For antibiotic-resistant bacteria, such as MRSA, contact precautions are sufficient.[21] Contact transmission includes direct and indirect contact, therefore, in situations where MRSA is suspected or known to be present, staff should use gloves and gowns and the patients should be isolated or physically segregated.[21] Specific ventilation requirements are not necessary.[21] Masks may be used as an additional barrier to protect health-care workers from mucous membrane exposures to MRSA, although, there is little evidence to support or refute the usefulness of masks in this setting. It is predominately a personal choice of the facility.

Management Of MRSA Infection

Managing infections caused by MRSA is difficult because it is often not known initially what micro-organism(s) is/are actually causing the infection. Empiric therapy is, therefore, required. An appropriate route of administration should be selected according to the criteria normally used for determining whether oral or parenteral therapy is necessary. If a serious infection is suspected, empiric therapy with parenteral vancomycin may be warranted. Less severe infection, depending on the site, may be managed with an oral antibiotic. Beta lactams, such as cloxacillin and the cephalosporins, are not effective against MRSA. Clindamycin, trimethoprim/sulfamethoxazole or fusidic acid with or without rifampin may be used empirically, depending on local susceptibility profiles. Two new additions to the therapeutic armamentarium include linezolid and quinipristin-dalfopristin, but these agents are often restricted in their use given their expense and toxicities. It is important to use existing agents, such as trimethoprim/sulfamethoxazole, clindamycin or vancomycin as first-line agents, reserving the newer antimicrobial agents for when the first-line agents are no longer effective. Once the micro-organisms' antibiotic susceptibility profile is determined, therapy should be modified accordingly. The duration of therapy should be guided by clinical judgment, as with other infections.

Decolonization Therapy

Decolonization refers to the attempt to eradicate the MRSA carrier state of a specific patient. In certain circumstances, MRSA colonizes post-operative wounds, leg ulcers and diabetic foot ulcers.[4,24] In most of these colonized wounds, once the lesion heals completely, further interventions are not necessary. Considerable controversy exists surrounding the need for, and efficacy of, decolonization therapy. Prospective randomized controlled clinical trials evaluating the role of MRSA decolonization therapy are lacking. Much of the support for decolonization is based on case studies, observational cohort studies and expert opinion.

The best success rates are in colonized health-care workers or ambulatory patients without a high burden of illness. The least success occurs among bedridden patients, those with invasive devices, high burdens of illness and those who have MRSA recovered from multiple sites, who have received previous fluoroquinolones and whose MRSA isolates are resistant to mupirocin.[13,17,25-27] Once again, specific recommendations may be available from local health authorities with regard to the use

and duration of decolonization therapy. It is not clear whether any of the new wound treatment agents, such as cadexomer iodine or silver impregnated dressings are of benefit in eradicating MRSA carriage, as data from prospective, randomized, controlled clinical trials is lacking. If eradication/decolonization therapy for MRSA carriage is deemed necessary, the regimen most often used is applying mupirocin (2%) to nares and wounds twice or three times a day for one to two weeks, plus once-daily chlorhexidine or triclosan for topical use. This may be used in combination with oral systemic therapy, such as trimethoprim/sulfamethoxazole (one double strength tablet orally twice a day and rifampin 600 mg orally once a day for 14 days).[28] The rationale for the use of rifampin is its synergistic anti-*staphylococcal* activity. If the patient is allergic or intolerant to trimethoprim/sulfamethoxazole, or if the micro-organism is resistant to it, clindamycin, fusidic acid or doxycycline are alternatives to consider. If therapy and/or decolonization is attempted, it may be prudent to seek the assistance of those knowledgable in the management of MRSA infections or colonization.

MRSA Management In Health-Care Facilities

Prior to implementing any isolation or therapeutic interventions, it is prudent to follow the written policies of the infection prevention and control staff at your health-care facility.[21,22] The most common protocol in facilities actively trying to control and prevent the spread of MRSA is as follows:

- Isolation in a single room of the patient infected/colonized with MRSA.
- Gowns and gloves for the staff and visitors who enter the room. Masks are used by some centres as an additional barrier precaution.
- After leaving the room, dispose of the gowns and gloves in the designated receptacle and wash your hands.
- Designated patient equipment for patients with MRSA is preferred. If it is necessary to use the same equipment for another patient, it must be reprocessed, or, if appropriate, disinfected with a facility-approved antimicrobial agent.
- Special precautions for handling the dishes of isolated patients are not necessary. Disposable dishes and cutlery are not necessary.
- Linen and waste is handled in the same fashion as for other patients.
- Diagnostic procedures should be performed at the bedside whenever possible.
- If the patient must be transported to another department for investigations, therapeutic procedures or an operation, the referring ward must notify the receiving department that that patient is on isolation for MRSA. In some circumstances, this may be excessive and not realistic, due to the acuity of patient illness.
- Special transportation procedures for patients infected/colonized with MRSA may be necessary. The patient may be required to wear a mask and any open wounds should be covered. Transportation equipment must be cleaned immediately after use and before being used by another patient.
- When isolation is discontinued, or if the patient is discharged or transferred, the housekeeping department must be notified to do a thorough terminal cleaning of the isolation room before it is used for another patient.

Measures To Take In An Ambulatory Setting

The precautions used in acute-care settings are more intensive than those necessary in an ambulatory-care setting. The intensive precautions previ-

ously outlined are often discontinued once the individual is discharged from the acute-care facility. General measures to take in an ambulatory and home-health setting are as follows:

- *Handwashing:* Handwashing with soap or an alcohol-based hand sanitizer, before and after every patient contact is necessary. Hands should be washed once gloves are removed.
- *Personal Protective Attire:* Disposable gowns/aprons, masks and protective eyewear are not normally required and should be used only when the potential for soiling or splashing exists (*i.e.,* open draining wounds where drainage cannot be easily contained). Disposable gloves should be used when handling potentially infectious material, such as feces, wound secretions, non-intact skin and mucous membranes.
- *Equipment:* Reusable equipment should be cleaned, using established office protocol. Stethoscopes should be wiped with 70% alcohol (*i.e.,* commercial alcohol swabs). Any visibly contaminated office or environmental surfaces can be cleaned with regular household cleansers.
- *Household Equipment:* Specific measures are not necessary in the home, as there is a low risk of transmitting MRSA to healthy family members.[18] If additional cleaning is necessary, household cleaning solutions will suffice.
- *Linen:* Linen and clothing do not require special handling.
- *Dishes and Garbage:* Dishes should be washed in the usual fashion and garbage disposed of in an appropriate manner.

Summary

The management of patients infected or colonized with antibiotic-resistant bacteria varies from ambulatory to institutional settings. In the latter, there is a significant concern about spread of these antibiotic-resistant microorganisms between patients or residents, which may lead to significant infections. More rigorous measures must, therefore, be undertaken. In an ambulatory-care setting, this is less likely to occur, and there is no need for rigorous measures. The indication for decolonization therapies is not firmly established and the protocol should be handled on a case-by-case basis, as guided by local policies and procedures. Consulting with an infectious disease specialist should be considered.

Measures currently taken to prevent the spread of MRSA and other antibiotic-resistant bacteria may be labor-intensive, however, these efforts can prevent the spread of these bacteria. Health-care facilities can, in turn, halt the increase of MRSA from reaching the levels seen in other countries.[12]

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