

**Guidelines for the Prevention and Management of  
Community-associated Methicillin-Resistant  
*Staphylococcus aureus* (CA-MRSA): A Perspective for Canadian Health Care  
Practitioners**

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## EXECUTIVE SUMMARY

Methicillin resistance among community isolates of *Staphylococcus aureus* has reached a staggering 75% in some communities in the United States(1). These organisms, resistant to the entire class of  $\beta$ -lactam antibiotics, have evaded an important component of the physician's armamentarium and may require clinicians to change their management of presumed staphylococcal infections. The recent emergence of community-associated methicillin resistant *S. aureus* (CA-MRSA) strains as dominant clones signals their adaptation to survive and spread outside the hospital setting. Descriptions of severe disease and characterization of their virulence factors warn of their potential to inflict significant morbidity and mortality. Thus, we are faced with an emerging and formidable foe: a pathogen combining virulence, resistance and an ability to disseminate at large(2). At present, the prevalence of CA-MRSA in Canada is unknown but thought to be low based on the collective clinical experience of infectious disease experts across the country. If Canada is to delay or prevent the emergence of CA-MRSA in its communities, vigilance and determined control efforts will be needed.

The purpose of this document is to convey basic information regarding the epidemiology and microbiology of CA-MRSA, as well as recommendations related to the clinical management, prevention and control of CA-MRSA infections. It complements existing publications on hospital-associated methicillin resistant *S. aureus* (HA-MRSA) and CA-MRSA, including a recent statement from the U.S. Centers for Disease Prevention and Control(3).

Sources of information and recommendations derive from a comprehensive literature review, a Working Group Meeting of Canadian and US experts, and extensive discussion within an expert panel writing group. When available, published and unpublished Canadian data are presented. The highlights of the current document include clinician-oriented treatment guidelines addressing the various presentations of presumed and confirmed CA-MRSA infection and their management. Guidelines for infection prevention and control in a variety of settings are included: home, daycare centers and schools, sports settings, pet owners, prisons and homeless shelters, and neonatal care facilities. The document does not address health care settings other than nurseries, and existing guidelines for infection control in hospitals and clinics should be followed for these settings. Directions for future research are also suggested. The content of this document will be modified and updated as microbiologists and public health specialists alert us to the evolving regional prevalence of CA-MRSA and as new studies are published.

Frontline physicians need to be aware of the increasing prevalence and potential severity of CA-MRSA infection. They are advised to obtain specimens for culture from all serious skin and soft tissue infections, including abscesses and other infected sites. The management of presumed *S. aureus* infection should include the use of surgical drainage when appropriate and their empiric antibiotic therapy should be adjusted when regional rates of clinical infections due to CA-MRSA increase. Judicious use of antibiotics is emphasized as a prevention strategy. Families, school and daycare center personnel, and sports teams should be actively encouraged to practice meticulous hand-washing, the most important measure to control or attenuate the community transmission of CA-MRSA.

## 1.0 PREAMBLE

A dramatic increase in the rate of methicillin resistance among community isolates of *Staphylococcus aureus* has recently been observed in the United States(4). Community-associated methicillin resistant *S. aureus* (CA-MRSA) has emerged as the dominant pathogen in some communities in the United States, with prevalence as high as 75% of all *S. aureus* isolates(1). These community strains are genetically and clinically distinct from strains of hospital-associated methicillin resistant *S. aureus* (HA-MRSA), which has been a familiar problem in health care institutions for several decades. Currently, the prevalence of CA-MRSA in Canada is unknown, but thought to be low based on the collective clinical experience of infectious disease experts. However, as the prevalence of CA-MRSA increases, clinicians may need to change their approach to the management of presumed *S. aureus* infections. Furthermore, if Canada is to limit the emergence of CA-MRSA in its communities, vigilance and determined control efforts will be needed.

To date there are no Canadian consensus guidelines for the management and prevention of CA-MRSA infections in children and adults. Recent reports of serious invasive disease and mortality due to CA-MRSA in Canada emphasize the need for such guidelines(5-7). Focus has centered for years on the challenge of controlling the spread of MRSA in hospitals and chronic-care institutions. The present document addresses MRSA in the community and complements previously published guidelines (Appendix I). The reader is specifically referred to other excellent existing documents on CA-MRSA, including a statement from the Centers for Disease Control and Prevention and Control(3), from the British Columbia CDC(8), and from the Canadian Paediatric Society(9). The present CA-MRSA document is unique with respect to the following: (1) a national focus; (2) rigorous methodology, which included a Working Group Meeting of national experts and an Expert Panel review process; (3) practical, clinician-oriented treatment guidelines addressing multiple possible presentations of CA-MRSA; and (4) a multidisciplinary focus on prevention of transmission.

The goal of this document is to provide information about the epidemiology and microbiology of CA-MRSA in Canada and recommendations on its treatment, prevention and control. The document is directed towards health care workers including public health practitioners, laboratory personnel, clinicians, nurses, infection control practitioners, veterinary medicine personnel and other health care practitioners participating in outbreak management and direct patient care. While the guidelines provide suggestions for specific patient management, they are not meant to replace clinical judgment for care of the individual patient.

The scope of this document includes:

- a) Definitions and a general description of the epidemiology highlighting the Canadian experience, where available.
- b) Microbiology of MRSA emphasizing differences between traditional hospital-associated strains and the emerging community associated strains.
- c) Clinical management guidelines.
- d) Screening and decolonization recommendations.
- e) Recommendations for the prevention and management of outbreaks and infections occurring in the community.

f) Directions for future research, based on ideas generated at the Working Group Meeting.

## 2.0 METHODOLOGY

The information and recommendations presented in this document result from a comprehensive literature review, a Working Group Meeting of Canadian and US experts, and the discussion of an expert panel writing committee.

A review of the English language medical literature from 1980 to March 2006 was conducted. Data sources included MEDLINE, EMBASE and the Cochrane Clinical Trials Register. Published abstracts of papers presented at local and international infectious disease or microbiology conferences were cited when they were the only available information from ongoing trials or emerging reports.

An inter-disciplinary Working Group Meeting held on October 27 and 28, 2005 in Toronto, Ontario assembled seventy Canadian experts in paediatric and adult infectious disease, infection control, microbiology and public health, as well as US experts in CA-MRSA from Texas and from the Centers for Disease Prevention and Control. The meeting was supported by the Public Health Agency of Canada (PHAC), the Canadian Committee on Antibiotic Resistance (CCAR), and the Ontario Ministry of Health and Long-Term Care (MOHLTC). A rich dialogue emerged around issues in CA-MRSA treatment, prevention and control, including important questions for future research.

Recommendations were developed based on the literature review, Working Group Meeting and Expert Panel opinion. Recommendations were graded on the basis of strength and quality of the supporting evidence (Table 1). The consensus statements were proposed, debated, revised and agreed upon by members of the Expert Panel using conference calls and face-to-face meetings. The document was rigorously reviewed and debated by the expert panel committee using electronic mail in an iterative process with multiple revision steps. Suggestions were then evaluated by the panel and incorporated into the final document.

This document was approved for publication by the Guidelines Committee of the Association of Medical Microbiology and Infectious Disease of Canada (AMMI). These guidelines will be reviewed annually by the CA-MRSA expert panel. They will be considered current unless they are revised or withdrawn from distribution.

**Table 1: Strength of Recommendations and Quality of Evidence(10)**

<b>Strength</b>	<b>Definition</b>
A	Strong recommendation. Should always be offered. Experts agree.
B	Moderate recommendation. Should usually be offered. Most experts agree.
C	Optional recommendation. May be offered. Expert opinion varies.

Grade	
I	Evidence from at least one properly randomized, controlled trial.
II	Evidence from at least one well-designed clinical trial without randomization from cohort or case-controlled analytical studies, or from dramatic results of uncontrolled experiments.
III	Evidence from opinions of respected authorities that is based on clinical experience, descriptive studies, or reports of expert committees.

### 3.0 DEFINITIONS

#### 3.1 General definitions

**MRSA:** Methicillin-resistant *Staphylococcus aureus* (MRSA) demonstrate resistance to the semi-synthetic penicillins (methicillin, oxacillin, cloxacillin). They are also resistant to cephalosporins, monobactams and carbapenems. Resistance to other antibiotic classes may occur among these organisms but is strain dependent.

**HA-MRSA:** MRSA strains that circulate and are transmitted to individuals within health care facilities.

**CA-MRSA:** MRSA isolates obtained from individuals in the community who have not had recent exposure to the health care system, or from patients in healthcare facilities in whom the infection was present or incubating at the time of admission.

#### 3.2 Operational definition of CA-MRSA

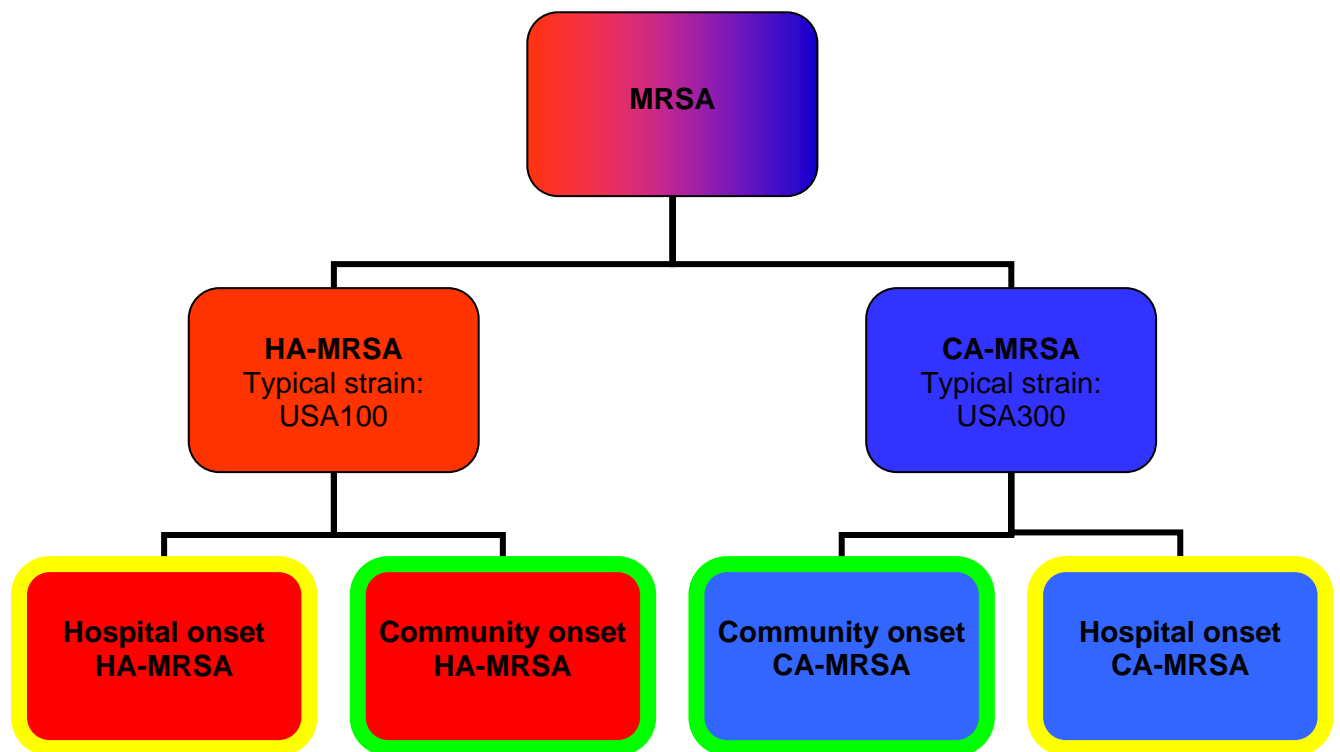
The case definition for CA-MRSA endorsed by the Expert Panel, consistent with that used by the U.S. Center for Disease Control and Prevention (CDC), is an MRSA infection in a person who has none of the following risk factors for HA-MRSA: isolation of MRSA more than 48 hours after hospital admission; history of hospitalization, surgery, dialysis or residence in a long-term care facility within one year of the MRSA culture date; the presence of an indwelling catheter or a percutaneous device at the time of culture; or previous isolation of MRSA(11).

#### 3.3 Definition limitations

Using a standard definition is important for consistently estimating of the burden of CA-MRSA infection(12); however, operational definitions of CA-MRSA have varied among studies. MRSA detected within 24, 48 or 72 hours of admission has been variably considered to be of community origin(13). Isolates from patients with healthcare contact such as recent hospitalization, hemodialysis, or indwelling catheters have been excluded in some studies, but not in others(13).

The source of MRSA is not always possible to identify with certainty, making the classification of “community-associated” and “hospital-associated” strains based on epidemiologic criteria somewhat imprecise. As genetic and molecular distinctions between community and hospital-associated strains have been described, molecular markers can now be used to define isolates as

CA-MRSA or HA-MRSA. MRSA disease with onset in the community may be attributable to bacterial strains acquired by discharged inpatients or health care personnel and subsequently transmitted to close contacts in the community(14, 15). In a meta-analysis, approximately half of community-based subjects colonized with MRSA had a health-care associated risk factor, suggesting a hospital origin of the isolates(13). Conversely, the ability to track strains using molecular epidemiological markers has enabled investigators to describe the spread of community associated MRSA strains within the hospital(16-18). As hospital strains have moved into the community and community strains have spread within hospitals, it has become increasingly difficult to distinguish CA-MRSA and HA-MRSA by epidemiologic criteria(19). Figure 1 illustrates a classification scheme for MRSA based on molecular and epidemiologic characteristics, and the challenge of accurately discriminating between “community” and “hospital” isolates.



**Fig. 1: Classification of MRSA**

Molecular techniques allow MRSA strains to be identified as CA-MRSA (e.g., the epidemic USA300 strain - strain nomenclature described in section 5.3), or HA-MRSA (e.g., the USA100 strain - strain nomenclature described in section 5.3). Epidemiologic information can be used to further determine whether the infection arose in the community or hospital. Although typically HA-MRSA strains are isolated within health care facilities (i.e., hospital onset HA-MRSA), “spill-over” of these strains into the community (i.e., community onset HA-MRSA) has been observed(13). Conversely, CA-MRSA strains were first described in the population at large (i.e.,

community onset CA-MRSA) but have since been observed in health care settings (i.e., hospital onset CA-MRSA)(16-18).

## **4.0 EPIDEMIOLOGY**

### **4.1 The rise of CA-MRSA**

MRSA was first described in 1961(20), shortly after the introduction of semi-synthetic penicillins (methicillin, oxacillin and cloxacillin). MRSA has long been recognized as a nosocomial pathogen: in the U.S., up to 40% of hospital *S. aureus* strains are methicillin resistant, and in Canada, nosocomial MRSA rates are increasing, from 0.95% in 1995 to 10.4% in 2003(21). A new phenomenon has been observed over the past decade: MRSA strains have emerged, increased in prevalence, and become the dominant strains in some US communities. These clones are genetically distinct from HA-MRSA, are well adapted to spread within the community, and have the potential to cause severe disease. The rise of MRSA first in hospitals and now in the community has been likened to the historically similar trend of resistance of *S. aureus* to penicillin, which emerged first in hospitals in the 1940s and later in the community throughout the 1960s(22).

Cases of severe MRSA infection in patients without contact with health care institutions were reported in a remote aboriginal population in Australia in 1993(23). The pathogen gained North American attention when the CDC reported four paediatric deaths from CA-MRSA in 1999(24). Since then, methicillin resistance among isolates of *S. aureus* outside of health care institutions has reached epidemic proportions in some US communities(25-28). Over a ten year period, the Driscoll Children's Hospital in Texas documented an increase in the rate of methicillin resistance among community isolates from 2.9% in 1990 to 40.3% in 2001(4). The Texas Children's Hospital in Houston now reports that over 75% of community isolates are methicillin resistant, so MRSA, rather than methicillin-sensitive *S. aureus* (MSSA), is now the dominant community pathogen(1). Increasingly, CA-MRSA is being detected around the globe(29), with multiple reports from Europe(30-32), Southeast Asia(33-36), and Australia(37, 38).

To date, a spectrum of clinical manifestations of CA-MRSA infection have been described. The most common manifestation of CA-MRSA infection is skin and soft tissue infection (SSTI)(39). However, there are accumulating reports of severe disease, including sepsis(40), necrotizing fasciitis(41), purpura fulminans(42), toxic shock syndrome(43, 44), necrotizing pneumonia(45, 46) and empyema(47, 48) caused by CA-MRSA. These severe presentations may occur in otherwise healthy children and young adults.

### **4.2 CA-MRSA in Canada**

The first reported cases of CA-MRSA in Canada occurred in an aboriginal community in Alberta between 1986 and 1989(49). A cluster of 15 cases of CA-MRSA infections, predominantly soft tissue in origin, with organisms which remained relatively susceptible to non- $\beta$ -lactam antibiotics, was reported from a small rural town in southern Manitoba in 1997 and 1998(50). This strain is rapidly emerging in several neighbouring communities in northern Manitoba and Saskatchewan(51). In 1998, the first case of CA-MRSA disease and transmission in a child care center was reported from Toronto(52). In Ontario in 2004, 11% of 10,301 MRSA isolates were

thought to be community-acquired(53). However, it is possible that the overall prevalence of this emerging pathogen has been underestimated.

This pathogen’s potential to cause severe disease has been demonstrated in several Canadian reports. Severe soft tissue infections due to CA-MRSA have been reported in Western Canada, including an outbreak in the Calgary Health Region in 2004 involving illicit drug users and homeless persons(54). The first case of fatal necrotizing pneumonia in a young, otherwise healthy adult was reported recently from the Calgary Health Region(6) and the first fatal paediatric case was described in Ontario(5). Several additional cases of severe necrotizing pneumonia without clinical or laboratory evidence of antecedent viral respiratory tract infection have been reported in southern Alberta(7).

### 4.3 Origin of CA-MRSA and its ability to disseminate

As CA-MRSA has emerged very recently, several questions regarding its origin and ability to spread in the community have been the focus of intensive investigation. Where did CA-MRSA come from? Among other hypotheses, horizontal gene transfer of the resistance determinants from coagulase-negative staphylococci to community adapted strains of MSSA has been postulated(55). Did antibiotic pressure contribute to the emergence of this pathogen? *S. aureus* and coagulase negative staphylococci may co-exist on the skin of patients treated with  $\beta$ -lactam antibiotics, providing an environment conducive to the selection of CA-MRSA strains after horizontal transfer of resistance genes(56). What properties of CA-MRSA have allowed it to propagate in the community and indeed arise as the dominant clone in some settings? CA-MRSA strains are genetically distinct and do not simply represent the “spill-over” of hospital strains into the community(56, 57). CA-MRSA grows more rapidly *in vitro* than HA-MRSA(58), likely because HA-MRSA strains carry many antibiotic resistance genes and have a high “fitness cost” of resistance(59). The genome of the epidemic CA-MRSA USA300 strain (strain nomenclature described in section 5.3) has recently been sequenced in its entirety and reveals a novel mobile genetic element, the arginine catabolic mobile element (ACME), also present in the ubiquitous skin commensal *Staphylococcus epidermidis*, that may enhance fitness and pathogenicity(60). Thus, CA-MRSA may be better suited to competition with other bacteria in the environment whereas HA-MRSA dominates in hospital settings under intense antibiotic pressure. Interested readers are referred to several comprehensive reviews of these topics for more detailed explanations(55, 56, 61).

### 4.4 Populations at risk

Community transmission of MRSA has been documented in several identifiable populations. These groups, listed in Table 2, are considered at high risk of CA-MRSA.

**Table 2: Risk factors for CA-MRSA Infections**

Risk Categories	Factors	Annotated References
<b>High risk population</b>	Young age	<ul style="list-style-type: none"> <li>• Age distribution in CA-MRSA younger than HA-MRSA(39)</li> <li>• High rate of CA-MRSA in children under 2 years(62)</li> <li>• CA-MRSA more common in Canadian children</li> </ul>

		compared to adults(63)
	Minority Populations: Native or Aboriginal African-American	<ul style="list-style-type: none"> <li>• Aboriginal communities in mid-western U.S. (24, 64, 65)</li> <li>• Alaskan natives(66)</li> <li>• More common in African Americans(62, 67, 68)</li> <li>• Aboriginal communities in Canada(49, 50, 63, 69, 70)</li> </ul>
	Athlete: mainly contact sports	<ul style="list-style-type: none"> <li>• Outbreaks on football teams(71-75)</li> <li>• Outbreak in wrestling team(76)</li> <li>• Other competitive sports(72, 77)</li> </ul>
	Intravenous drug users (IVDU)	<ul style="list-style-type: none"> <li>• San Francisco IVDU(78)</li> <li>• Western Canadian report of USA300 strain outbreak(79)</li> </ul>
	Men who have sex with men (MSM)	<ul style="list-style-type: none"> <li>• CA-MRSA described in HIV-positive population of MSM(80, 81)</li> </ul>
	Military personnel	<ul style="list-style-type: none"> <li>• 3% of US Army soldiers colonized(82)</li> </ul>
	Inmates of correctional facilities	<ul style="list-style-type: none"> <li>• Reports of outbreaks in U.S. prisons(83-87)</li> <li>• Two outbreaks (total 10 inmates) in Hamilton, Ontario(88)</li> </ul>
<b>Previous positive MRSA cultures</b>	MRSA Carriage	<ul style="list-style-type: none"> <li>• Colonized soldiers more likely to get CA-MRSA disease(82)</li> </ul>
	Past MRSA infection	<ul style="list-style-type: none"> <li>• Prior abscess risk factor for CA-MRSA(89)</li> </ul>
<b>Medical History</b>	Chronic skin disorder	<ul style="list-style-type: none"> <li>• Dermatologic condition most common underlying medical disorder for CA-MRSA infection(39)</li> <li>• Classroom contact of index CA-MRSA case had chronic dermatitis(52)</li> </ul>
	Recurrent or recent antibiotic use	<ul style="list-style-type: none"> <li>• Antibiotic use associated with CA-MRSA infection in rural Alaska(66)</li> </ul>
<b>Environmental</b>	Low Socioeconomic status	<ul style="list-style-type: none"> <li>• Medically underserved populations at higher risk of CA-MRSA(89, 90)</li> </ul>
	Overcrowding	<ul style="list-style-type: none"> <li>• Close contact implicated in jail outbreak(85), NICU transmission(91)</li> </ul>
	Contact with colonized pet	<ul style="list-style-type: none"> <li>• Family dog source of recurrent infection(92)</li> </ul>
	Veterinary worker	<ul style="list-style-type: none"> <li>• Veterinarians working with horses(93-95)</li> <li>• Small animal veterinarians(96, 97)</li> <li>• Pig farmers(98)</li> </ul>

#### 4.5 Transmission

The spread of CA-MRSA, like *S. aureus* in general, occurs through direct contact between an infected person and an uninfected person, or by indirect contact through touching contaminated objects or surfaces that are part of the infected person's environment. Zoonotic transmission (from animals to humans) has also been documented(92, 94, 96, 97, 99-104).

## 5.0 MICROBIOLOGY

### 5.1 *S. aureus* and MRSA

*Staphylococcus aureus* is a gram-positive coccus that tends to form clusters. Resistance to methicillin and the entire class of  $\beta$ -lactam antibiotics in *S. aureus* is determined by an altered penicillin binding protein, PBP-2a. This enzyme is encoded by the gene *mecA*, which is located within a larger mobile genetic element called the staphylococcal chromosomal cassette *mec* (SCC*mec*). Currently, there are five types of SCC*mec* distinguished by their genetic sequence, labeled SCC*mec* I to V. CA-MRSA strains usually contain SCC*mec* types IV or V, whereas HA-MRSA strains usually contain SCC*mec* types I, II or III(105).

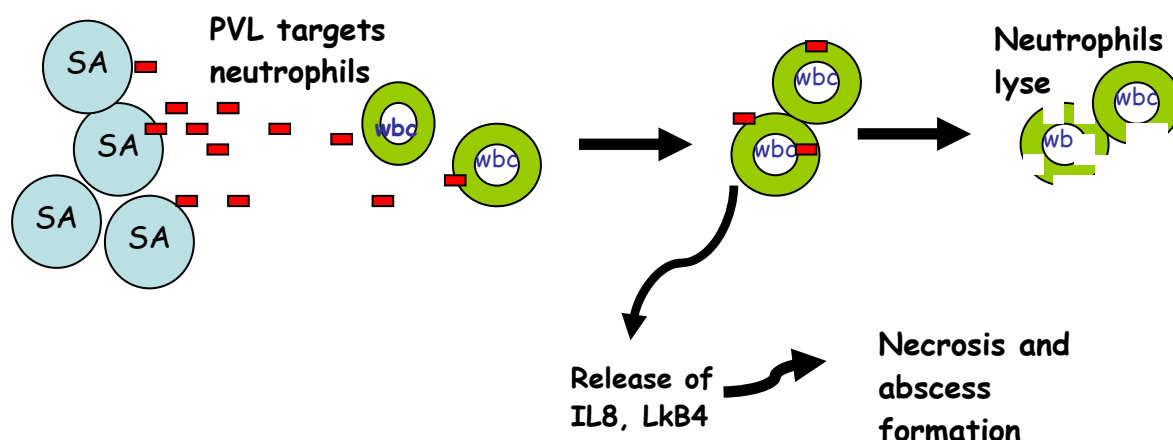
### 5.2 Virulence factors

Factors produced by *S. aureus* that may play a role in virulence are shown in Table 3.

**Table 3: Virulence factors of *S. aureus***

Category	Toxin
Cytolytic toxins	Panton-valentine leukocidin (PVL) S & F
	Fibronectin-binding proteins (Fnb) A and B
	Leukocidin R
Superantigenic toxins	Enterotoxins (A-J)
	Epidermolytic toxins
	Toxic shock syndrome toxin-1
Enhanced growth and survival	Arginine catabolic mobile element (ACME)

The role of each of these factors in clinical disease is not clear, although considerable attention has been focused on the Panton-Valentine leukocidin(105). The Panton-Valentine leukocidin (PVL), an extracellular product of *S. aureus*, is encoded by the genes *lukS-PV* and *lukF-PV*(105). This factor, by its cytolytic pore-forming activity, damages the cell membranes of neutrophils, monocytes and macrophages (see Figure 2). Infection caused by PVL-positive strains tends to occur in children and young adults and is associated with higher mortality(106, 107). In patients with staphylococcal osteomyelitis, the presence of PVL positive isolates is associated with higher likelihood of complications(108, 109).



**Figure 2: Mechanism of action of the Pantone-Valentine leukocidin (PVL)**

PVL is a putative virulence factor associated with severe clinical disease. The toxin is released from *S. aureus* (SA) and targets the cell membrane of leukocytes (wbc). This causes the release of cytokines such as interleukin-8 (IL8) and leukotriene B4 (Lkb4) which produce necrosis and abscess formation. The toxin also causes lysis of neutrophils, such that infection with PVL positive strains may be associated with neutropenia.

### 5.3 Nomenclature of strains

Independent studies of the molecular epidemiology of MRSA have resulted in a confusing nomenclature of circulating strains(61). In Canada, based on *Sma*I macrorestriction patterns from pulsed-field gel electrophoresis (PFGE), ten major clusters have been labeled CMRSA-1 to CMRSA-10(110). In the U.S., also using PFGE profiles, eleven major epidemic strains of MRSA labeled USA100-1100 have been described to date(111). The USA300 (equivalent to CMRSA-10) strain is the dominant circulating clone of CA-MRSA in North America(18, 40, 41, 74, 112, 113). Another molecular method, multilocus sequence typing (MLST), has been used internationally to unambiguously categorize MRSA strains by using the sequence of internal fragments of seven chromosomal housekeeping genes(61). Table 4 shows the common circulating strains and the relationship between the different systems of nomenclature. Also provided are the associated SCCmec types and the presence or absence of PVL genes in the various strains.

**Table 4: Nomenclature of *S. aureus* strains**

US PFGE	CMRSA	MLST	SCCmec type	PVL
USA100	2	5	II	Neg
USA200	3, 6	36	II	Neg
USA300	10	8	IVa	Pos
USA400	7	1	IVa	Pos
USA500	5, 9	8	IV	Neg
USA600	1	45	II	Neg
USA700	?	72	IVa	Neg
USA800	2	5	IV	Neg
USA1000	?	59	IV	Pos

USA1100	?	30	IV	Pos
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#### 5.4 Resistance to non- $\beta$ -lactam antibiotics

##### 5.4.1 Clindamycin

While clindamycin resistance is common in HA-MRSA (observed in 79% of isolates)(39), CA-MRSA has low baseline resistance to clindamycin in some communities. Clindamycin resistance rates among CA-MRSA vary across the US, from 2% (Texas in 2001) to 17% (Minnesota in 2000)(62, 114). In Canada, 49% of paediatric and 85% of adult MRSA isolates were resistant to clindamycin between 1995-2002(63), but this reflects a preponderance of hospital strains within the Canadian Nosocomial Infection Surveillance Program (CNISP).

Laboratory testing for clindamycin resistance should include the double disk diffusion test (D test) for inducible clindamycin resistance(115). A clindamycin disk is placed at a fixed distance from an erythromycin disk, and a D-shaped zone of inhibition around the clindamycin disk indicates that resistance has been induced by the diffusion of erythromycin (i.e.,  $MLS_B$  phenotype)(116). Clinical failures have been documented in CA-MRSA infection when clindamycin was used to treat strains with inducible clindamycin resistance (positive D-test)(116, 117). Therefore, laboratories should routinely test for inducible clindamycin resistance and clindamycin should be avoided when inducible resistance is detected.

##### 5.4.2 Erythromycin

Both HA-MRSA or CA-MRSA are frequently resistant to erythromycin. For example, resistance was detected in vitro in 91% and 56% of HA-MRSA and CA-MRSA isolates respectively in Minnesota in 2000(62). A large laboratory-based survey indicated that 93% of Canadian MRSA isolates demonstrated resistance to erythromycin(118).

##### 5.4.3 Quinolones

Emergence of resistance during therapy leading to treatment failure may occur when quinolones are used for the treatment of *S. aureus* infections including CA-MRSA(119).

#### 5.5 Differences between CA-MRSA and HA-MRSA

In summary, CA-MRSA strains are genetically and phenotypically distinct from HA-MRSA strains, as highlighted in Table 5.

**Table 5: Contrasting CA-MRSA and HA-MRSA**

	CA-MRSA	HA-MRSA
<b>Typical demographic characteristics</b>	Younger Minority population	Older Nursing home resident
<b>Common SCCmec type</b>	IV	II
<b>PVL virulence factor</b>	common	unusual
<b>Predominant strains</b>	USA300 (CMRSA-10) USA400 (CMRSA-7)	USA100 (CMRSA-1) USA200 (CMRSA-3,6)
<b>Multidrug resistance</b>	rare	common

(other than $\beta$ -lactam)		
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## 6.0 MANAGEMENT

### 6.1 Diagnostic evaluation

At initial clinical presentation, CA-MRSA may not be easily distinguishable from HA-MRSA, MSSA, or streptococci as the agent of infection. Epidemiologic risk factors (Table 2) should heighten suspicion of CA-MRSA. Furthermore, microbiologic diagnosis can be helpful in guiding management and may prove helpful in monitoring local rates of CA-MRSA as this pathogen emerges in the community. The following principles of management are intended to assist the clinician faced with a possible or proven case of CA-MRSA infection, and address clinical presentations that are potentially consistent with *S. aureus* infection.

#### 6.1.1 When to suspect CA-MRSA

##### **Recommendations**

- In areas where more than 10-15% of community isolates of *S. aureus* are methicillin resistant, CA-MRSA should be suspected in any patient who presents with a skin or soft tissue infection (SSTI). **(BIII)**
- Suspect CA-MRSA in severe infections compatible with *S. aureus*, e.g., sepsis(40), necrotizing fasciitis(41), necrotizing pneumonia(45, 46) and empyema(47, 48). **(AIII)**
- Suspect when risk factors for CA-MRSA are present (listed in Table 2). **(AIII)**
- Suspect CA-MRSA when there is a poor response to  $\beta$ -lactam therapy in individuals with presumed staphylococcal infection. **(AIII)**

#### 6.1.2 When to obtain cultures

##### **Recommendations**

- Cultures should be obtained from skin and soft tissue infections, as well as other sites where *S. aureus* infection is suspected, which have not responded to initial therapy. **(AIII)**
- Culture recurrent furuncles or abscesses ( $\geq 2$  in 6 months). **(AIII)**
- Obtain cultures in any severe presentation of disease (should include blood cultures). **(AIII)**
- Obtain cultures when an outbreak is suspected in consultation with Public Health. **(AIII)**
- Consider an attempt to obtain material for culture from areas of cellulitis by aspiration of the area with or without preceding saline injection, particularly for patients who are going to be admitted for inpatient therapy or whose cellulitis progresses on treatment. **(BIII)**
- Specimens for culture of skin and soft tissue infections should **NOT** be routinely obtained for all individuals presenting with minor skin infection and without previous CA-MRSA. **(AIII)**

### 6.2 Treatment

Studies have demonstrated that antibiotics may not be necessary in patients with minor skin and soft tissue infections due to CA-MRSA(120). When systemic antimicrobial therapy is indicated for an infection consistent with *S. aureus*, clinicians should bear in mind the possibility of methicillin resistance. The prevalence of CA-MRSA in the community is an important factor in guiding empiric antibiotic choice, but is unknown in most areas in Canada. The rate of methicillin-resistance among community strains of *S. aureus* is assumed to be low at the present time because of the relatively few cases of antibiotic failures reported to date, but may rise in the near future as has occurred in many U.S. cities. The threshold of resistance that should prompt a change in empiric therapy is felt to be approximately 10-15%(114). However, even in communities where the rate is lower than 10-15%, clinicians may wish to include antimicrobial coverage for CA-MRSA in cases where the infection is severe or life-threatening. In the absence of data to suggest a high prevalence of methicillin resistance in Canada, no change in empiric therapy of presumed *S. aureus* infections is advocated at the present time. As resistance rates are better defined, recommendations for empiric therapy may change.

Table 6 summarizes the treatment principles and antimicrobial options for various presentations of CA-MRSA infection. Further details of the antimicrobial agents useful in the treatment of CA-MRSA are presented in Table 7. The following recommendations are categorized according to empiric therapy for suspected CA-MRSA infection versus therapy for confirmed infection, and according to severity and location of infection.

### ***6.2.1 Minor skin and soft tissue infections (folliculitis, furuncles and small abscesses without cellulitis)***

#### ***Recommendations***

- One or more of the following measures may be employed:
  - Local therapy using hot soaks and elevation. **(AIII)**
  - Incision and drainage without antimicrobial therapy(120). **(AII)**
  - Topical mupirocin or bacitracin. **(AIII)**
  - Topical antiseptics may be considered. **(BIII)**
- For young infants and for the immunocompromised host, antimicrobial therapy is recommended in addition to local measures, incision and drainage. **(BIII)**
- In follow-up, routine screening for colonization of the nares or other body sites is **NOT** recommended. **(AIII)**

### ***6.2.2 Empiric therapy of non-life-threatening infections other than minor skin infections, potentially due to CA-MRSA***

#### ***Recommendations***

- Antibiotic choice should be based on the severity of illness at presentation, clinical judgment, and regional susceptibilities of strains. **(AIII)**
- At present, cloxacillin or cefazolin remain appropriate empiric antibiotic choices for moderate infections (serious enough to require systemic antibiotics, but not considered life-threatening) consistent with *S. aureus*. **(AIII)**

### ***6.2.3 Empiric therapy of life-threatening infections potentially due to CA-MRSA***

### ***Recommendations***

- Include MRSA coverage, regardless of prevalence rates of CA-MRSA in the community. **(AIII)**
- Include an effective anti-MSSA agent until susceptibility results become available (cloxacillin is superior to vancomycin against MSSA)(121, 122). **(BIII)**

#### ***6.2.4 Confirmed non-life-threatening CA-MRSA infections other than minor skin infections***

### ***Recommendations***

- Guided by susceptibility pattern. Clindamycin should only be considered an appropriate choice if susceptibility is confirmed using the D-test. **(AIII)**
- For adults and children over 8 years, first line oral agents include clindamycin, trimethoprim/sulfamethoxazole, or doxycycline. Fusidic acid in combination with another agent may also be considered. **(AIII)**
- For children less than 8 years of age, first line oral agents include clindamycin and trimethoprim/sulfamethoxazole. Doxycycline is contraindicated in children < 8 years, as are all tetracyclines, and there are limited data regarding the use of fusidic acid in children. **(AIII)**
- Do not use doxycycline in pregnancy. **(AIII)**
- Patients should be followed and the antimicrobial therapy reconsidered if there is evidence of treatment failure. **(CIII)**
- In follow-up, routine screening for colonization of the nares or other body sites is **NOT** recommended. **(AIII)**

#### ***6.2.5 Confirmed CA-MRSA life-threatening infections***

### ***Recommendations***

- Treatment options include parenteral vancomycin, clindamycin (provided susceptibility confirmed with D-test) and trimethoprim-sulphamethoxazole. **(AIII)**
- Some experts recommend against the use of bacteriostatic agents, such as clindamycin, alone for the treatment of life-threatening infections. **(CIII)** Fusidic acid and rifampin should not be used alone, because of rapid emergence of resistance. **(AIII)**
- Newer drug therapies such as linezolid, tigecycline or quinupristin/dalfopristin should be guided by an infectious disease specialist. In particular, drugs like quinupristin/dalfopristin and daptomycin should be used with caution in paediatric populations where there are limited data for their use. **(CIII)**
- Linezolid is preferred over vancomycin for the treatment of MRSA pneumonia because of superiority in clinical trials for adults with HA-MRSA pneumonia(125), possibly explained by better penetration into the lung parenchyma(126). **(BII)**
- In follow-up, routine screening for colonization of the nares or other body sites is **NOT** recommended. **(AIII)**

#### ***6.2.6 Adjunctive therapy***

***Recommendations***

- Combination of first line drugs with rifampin or gentamicin to enhance killing in serious invasive disease should be decided on a case-by-case basis in discussion with an infectious disease specialist(127). **(BIII)**
- Other adjunctive therapy such as intravenous immunoglobulin (IVIG) may play a role in neutralizing toxin-mediated effects and may be considered for selected patients with severe disease as guided by an infectious disease or critical care specialist(128). **(CII)**

**Table 6: Guidelines for Management of Infections due to CA-MRSA**

Clinical Disease	Key features	Management principles	Antimicrobial Choices <sup>§</sup>
<b>Skin and Soft Tissue Infection (SSTI)</b>			
Mild	Localized disease Infected scratches Insect bites Furuncles Small abscesses Absence of systemic illness	Culture selectively* No antibiotic therapy recommended <i>EXCEPT for young or immunocompromised host</i> Cover draining lesions Emphasize personal hygiene Close follow-up Return if worsening	Generally not indicated Topical antiseptic or antibacterial (e.g., bacitracin) therapy may be considered. <i>Systemic antimicrobial therapy may be considered in the young infant or immunocompromised host</i>
Moderate	Cellulitis Moderate abscesses Minimal or no associated systemic features	Culture (blood - if febrile, site - if purulent) Drainage of abscess or needle aspiration Oral therapy in older child and adult <i>Consider parenteral therapy for young or immunocompromised host.</i> Appropriate infection control measures Imaging for extent & complications (case by case) Close follow-up Return if worsening	<u>Empiric:</u> Include Clindamycin 150-450 mg q6h po <b>Ped dose: 30 mg/kg/day ÷ q6-8h po</b> <i>OR</i> {TMP-SMX 1 DS tab q12h po <b>Ped dose: 8-12 mg/kg/day (of TMP) ÷ q12h po/IV</b> <i>PLUS</i> coverage for group A streptococcus} <i>OR</i> Doxycycline <sup>†</sup> 100 mg q12h po <i>If parenteral therapy necessary, see choices for severe SSTI</i>  <u>Proven MRSA:</u> As above, based on sensitivity testing. <i>If parenteral therapy necessary, see choices for severe SSTI</i>
Severe	Extensive cellulites Large or multiple abscesses Associated systemic features	Culture (blood - if febrile, site - if purulent) Drainage of abscess Hospitalize Parenteral therapy Appropriate infection control measures Infectious Disease consultation Imaging for extent & complications	<u>Empiric:</u> Include Vancomycin 1 g q12h IV <b>Ped dose: 40-60 mg/kg/day ÷ q6h IV</b> <i>Some experts recommend adding cloxacillin or a 1<sup>st</sup> generation cephalosporin while awaiting culture and sensitivity results (superior for MSSA).</i> <i>Clindamycin may be added in case of toxin-mediated syndrome.</i>  <u>Proven MRSA:</u> Include Vancomycin 1 g q12h IV <b>Ped dose: 40-60 mg/kg/day ÷ q6h IV</b> <i>ALTERNATIVES:</i> Clindamycin 600-900 mg q8h IV/IM (if sensitive) <b>Ped dose: 30-40 mg/kg/day ÷ q6-8h IV</b> <i>OR</i> TMP/SMX <sup>§</sup> 8-10 mg/kg/day (of TMP) ÷ q12h IV (if sensitive) <b>Ped dose: 8-12 mg/kg/day (of TMP) ÷ q6h IV</b> <i>Clindamycin is bacteriostatic and should not be used alone if a bactericidal drug is required.</i>
<b>Musculoskeletal Infection (MSI)</b>			
Osteomyelitis	Preceding trauma Tendency for multifocality Disease in adjacent muscle not uncommon Progression to chronic osteomyelitis possible May be complicated by DVT	Cultures (blood, bone, and tissue) Involve surgical team (early debridement and drainage) Infectious Disease consultation Parenteral therapy Consider combination therapy for severe cases or if slow to respond Infection control measures	<u>Empiric:</u> Include Vancomycin 1 g q12h IV <b>Ped dose: 40-60 mg/kg/day ÷ q6h IV</b> <i>OR</i> Clindamycin 600-900 mg q8h IV/IM/po <b>Ped dose: 30-40 mg/kg/day ÷ q6-8h IV or po</b> <i>OR</i> TMP/SMX 8-10 mg/kg/day (of TMP) ÷ q12h IV <b>Ped dose: 8-12 mg/kg/day (of TMP) ÷ q6h IV</b>

		Look for other infected sites (imaging)	<u>Proven MRSA:</u> As above, based on sensitivity testing. <i>Addition of rifampin may be considered for osteomyelitis.</i>
Pyomyositis	May be extensive Tendency for multifocal involvement	Cultures (blood, tissue) Surgical drainage Infectious Disease consultation Parenteral therapy Infection control measures Imaging	
Necrotizing fasciitis	Clinically indistinguishable from GAS Toxic High complication rate	Cultures (blood, tissue) Surgical debridement Infectious Disease consultation Parenteral therapy Infection control measures Imaging	<u>Empiric:</u> Include Vancomycin 1 g q12h IV <b>Ped dose: 40-60 mg/kg/day ÷ q6h IV</b> <i>Some experts recommend adding cloxacillin or a 1<sup>st</sup> generation cephalosporin while awaiting culture and sensitivity results (superior for MSSA).</i> <i>Clindamycin may be added in case of toxin-mediated syndrome.</i> <i>Adjuncts such as IVIG should be considered on a case-by-case basis in conjunction with ID specialist.</i>  <u>Proven MRSA:</u> Include As above, based on sensitivity testing.
<b>Respiratory Tract Infection (RTI)</b>			
Necrotizing pneumonia	Influenza-like prodrome, hemoptysis, fever, shock, leucopenia, pneumatoceles, abscesses, consolidation Respiratory failure High mortality	Cultures (blood, pleural fluid, sputum) Infectious Disease consultation ICU care Infection control measures Combination parenteral therapy Chest drainage if empyema	<u>Empiric:</u> Include Vancomycin 1 g q12h IV <b>Ped dose: 40-60 mg/kg/day ÷ q6h IV</b>  <u>Proven MRSA:</u> As above, based on sensitivity testing. <i>Consider linezolid (superior for HA-MRSA pneumonia(125, 126)), as guided by ID opinion.</i>
<b>Other</b>			
Sepsis syndrome	Shock Multi-organ failure May have purpura fulminans Associated SSTI, MSI, RTI May be complicated by Waterhouse-Friedrichsen syndrome High mortality	Blood cultures Culture any pus or fluid collection Look for primary or secondary focus Infectious Disease consultation ICU care Imaging: look for occult abscesses, bone infection or endocarditis Involve surgery and other specialists as needed Infection control measures Parenteral, multi-drug therapy Prolonged therapy for endovascular infections	<u>Empiric:</u> Include Vancomycin 1 g q12h IV <b>Ped dose: 40-60 mg/kg/day ÷ q6h IV</b> <i>Some experts recommend adding cloxacillin or a 1<sup>st</sup> generation cephalosporin while awaiting culture and sensitivity results (superior for MSSA).</i> <i>Clindamycin may be added in case of toxin-mediated syndrome.</i> <i>Adjuncts such as IVIG should be considered on a case-by-case basis in conjunction with ID specialist.</i>  <u>Proven MRSA:</u> Include Vancomycin 1 g q12h IV <b>Ped dose: 40-60 mg/kg/day ÷ q6h IV</b> <u>ALTERNATIVES:</u> Clindamycin 600-900 mg q8h IV/IM (if sensitive) <b>Ped dose: 30-40 mg/kg/day ÷ q6-8h IV</b>

			<p>OR TMP/SMX 8-10 mg/kg/day (of TMP) ÷ q12h IV (if sensitive)</p> <p><b>Ped dose: 8-12 mg/kg/day (of TMP) ÷ q6h IV</b></p> <p><i>Clindamycin is bacteriostatic and should not be used alone if a bactericidal drug is required.</i></p>
Septic thrombophlebitis, DVT	Complicates MSI	As for sepsis syndrome, plus: Doppler ultrasound, often found on MRI Anticoagulation, under direction of Hematology (129)	As above. <i>For endovascular infections, combination antimicrobial therapy is recommended (i.e., vancomycin plus either gentamicin or rifampin). Prolonged therapy is required for endovascular infection and expert advice from an ID specialist should be considered.</i>
Endocarditis	Suspect if persistent bacteremia Pre-existing valvular heart disease may not be present	As for sepsis syndrome, plus: Echocardiogram Cardiology consultation Infectious Disease consultation Parenteral therapy Monitor for complications: embolic phenomena and hemodynamic instability	

§Choice of antimicrobial therapy depends on local susceptibility patterns.

\*Patients with risk factors, as a part of an outbreak investigation, patients with slowly responding or recurrent lesions.

†Not recommended for paediatric patients under 8 years of age or in pregnancy. **(AIII)**

Further information on antibiotic dosages and adverse effects can be found in Table 7.

**Table 7: Recommended antibiotics and doses**

DRUG	Dose (adult)	Dose (paediatric)*	Adverse reaction	Notes
<b>Oral options for mild to moderate SSTI with no systemic features</b>				
Clindamycin	150-450 mg q6h po.	30 mg/kg/day ÷ q6-8h po	Pseudomembranous colitis	Resistance may occur Check susceptibility with D-test
TMP-SMX	1 DS tab (160 mg TMP/ 800 mg SMX) q12h po	8-12 mg/kg/day (of TMP) ÷ q12h po	Allergy (skin rash) Bone marrow suppression	Not recommended for Group A streptococcus
Doxycycline	100 mg q12h po	2-4 mg/kg/day ÷ q12h to maximum 100 mg q12h po <i>Not for children &lt; 8yrs</i>	Photosensitivity Erosive esophagitis Teeth staining	Not for children < 8yrs Not for use in pregnancy
Linezolid	400 mg q12h po	20 mg/kg/day ÷ q12h po(130)	Dose dependent bone marrow suppression Peripheral neuropathy Optic neuritis (rare)	Selected cases only Expensive ID consultation recommended
<b>Parenteral therapy for systemic and severe infections</b>				
Vancomycin	1 g q12h IV	40-60 mg/kg/day ÷ q6h to a maximum 4 g/day IV	Renal toxicity	Lower efficacy in pneumonia Monitor levels
Clindamycin	600-900 mg q8h IV/IM	30-40 mg/kg/day ÷ q6-8h IV	Pseudomembranous colitis	Resistance may occur Check susceptibility with D-test Bacteriostatic
TMP-SMX	8-10 mg/kg/day ÷ q12h IV	8-12 mg/kg/day (of TMP) ÷ q12h IV	Allergy (skin rash) Bone marrow suppression	Not recommended for Group A streptococcus
Linezolid	600 mg q12h IV/po	children <12 years: 30 mg/kg/day ÷ q8h IV(130) children >12 years: 20 mg/kg/day ÷ q12h IV	Dose dependent bone marrow suppression Peripheral neuropathy Optic neuritis (rare)	Selected cases only Expensive ID consultation recommended Bacteriostatic
<b>Adjunctive therapy</b>				
Rifampin	600 mg po qd	10-20 mg/kg/day ÷ q12-24h po/IV	Hepatotoxicity Rash Discoloured urine Stains soft contact lenses	Consider in high bacterial burden Never use alone Potential for drug interactions
Fusidic acid	500 mg tid po/IV	No data in children	Skin rash Jaundice	No CSF penetration Not excreted in urine Never use alone(131) Bacteriostatic

\*Doses in the neonate may be different.

## 7.0 SCREENING AND DECOLONIZATION

### 7.1 Screening for CA-MRSA

*S. aureus* may asymptotically colonize body surfaces, particularly the nares. Rates of colonization in a recent US population-based survey were 31.6% for *S. aureus* and 0.84% for

MRSA(132). These asymptomatic carriers may act as a reservoir for infection; therefore, identifying *S. aureus* carriers and eradicating the carriage state might theoretically prevent recurrent *S. aureus* infections or person-to-person spread. However, at present, there is insufficient evidence to support the use of eradication regimens; thus, there is no clear role for screening(133).

### **Recommendations**

- In the non-outbreak setting, routinely screening individuals infected with CA-MRSA or their contacts for colonization of nares or other sites is **NOT** recommended. **(AIII)**
- In selected circumstances, following consultation with public health or an infectious disease consultant, nasal and/or additional site screening may be considered. These selected circumstances include:
  - Individuals with recurrent *S. aureus* skin infection ( $\geq 2$  per 6 months), where eradication therapy is being considered. **(BIII)**
  - In a family setting, where recurrent skin infections continue despite repeated review and re-enforcement of hygiene measures, and there is not known to be a high prevalence of CA-MRSA in the community. **(BIII)**
  - To investigate an outbreak in a closed population with continuing new infections despite repeated reinforcement of hygiene practices. **(BIII)** When a colonization survey is performed as part of an outbreak investigation, assessing carriage sites other than the nares may be considered, in consultation with public health officials and/or other experts(52). **(BIII)**

### **7.2 Decolonization**

Decolonization refers to the process of eradicating or reducing carriage of a particular organism from the skin, nose and/or other mucosal surface. In the case of staphylococcal carriage, decolonization has been attempted using topical or systemic (usually oral) therapy. The available systemic options include rifampin plus another anti-staphylococcal antibiotic such as TMP-SMX, clindamycin, fusidic acid, doxycycline or minocycline. Eradication from skin can be attempted using topical agents such as chlorhexidine or triclosan, whereas nasal decolonization usually requires intranasal mupirocin. Eradication from sites other than the nose usually requires systemic and topical therapy in addition to intranasal therapy. However, decolonization regimens have met with limited success. A systematic review of the literature published in 2003 concluded that there is insufficient evidence to support the use of topical or systemic antimicrobial therapy for eradicating nasal or extra-nasal MRSA(133). Experience in hospitals indicates that re-colonization is frequent(134, 135). In the community setting, decolonization has been attempted with mixed success: decolonization was successful in eradicating CA-MRSA carriage in a daycare facility(52); however, recurrent infection occurred despite decolonization attempts in two CA-MRSA outbreaks involving football teams(74, 75).

One disadvantage of attempted decolonization is the development of resistance to the agents used. Mupirocin resistance has been documented in several studies, usually associated with prolonged use or repeated courses of mupirocin(136-139). In Canada, Mulvey et al have reported mupirocin resistance rates of up to 50% in community isolates on the Prairies(110). Limiting its use to a maximum course of five to ten days, and ensuring a minimum time period

of one month between recurrent use are strategies that have been found to be effective in preventing the emergence of mupirocin resistance(138, 139).

#### ***Recommendations***

- Decolonization is **NOT** recommended for usual management of individual CA-MRSA infections, endemic infection or outbreaks(133, 136, 140-143). **(AI)**
- Decolonization should be considered only in exceptional circumstances, which may include:
  - Recurrent CA-MRSA skin infections ( $\geq 2$  in 6 months) with no evidence of repeated re-exposures when hygiene measures have been reinforced and after discussion with an infectious disease expert. **(BIII)**
  - As a public health strategy for ongoing transmission despite repeated review and reinforcement of appropriate hygiene interventions in outbreaks in selected closed settings. **(BIII)**

### ***7.3 Guidelines for the use of decolonization regimens***

In the exceptional situations where decolonization regimens are used, several options are available: intranasal mupirocin ointment, topical antiseptics applied to the skin, and systemic antibiotics active against the colonizing strain, particularly those that achieve high levels in body secretions, such as rifampin and clindamycin. Some experts favour a combined approach (including intranasal mupirocin, topical antiseptics and two systemic agents) for maximum possible effect in the rare circumstances when decolonization is indicated. Other experts offer only intranasal mupirocin to patients with isolated nasal carriage of *S. aureus*(144).

#### ***Recommendations***

- Decolonization regimens should be administered only to individual patients or well-defined closed cohorts, and only over a limited time interval to minimize the potential for resistance to develop. **(BIII)**
- Selection of a decolonization regimen should take into consideration the sensitivities of the organism isolated as well as the sites colonized, and infectious disease consultation should be sought. **(BIII)**
- The recommended regimen for nasal decolonization, for mupirocin-susceptible isolates, is mupirocin ointment twice daily for 5 to 10 days to the nares(138, 139, 145). **(BII)**
- When mupirocin is used to eradicate carriage, isolate susceptibility to mupirocin should be tested. **(BIII)**
- No recommendations can be made at this time for use of other topical intranasal agents for decolonization. **(CIII)**
- There is insufficient evidence to make a recommendation for or against the use of topical antiseptics for cleaning or cutaneous decolonization. **(CIII)**
- A combined strategy of intranasal mupirocin, topical antiseptics and systemic antibiotics (active against the colonizing strain and achieving high levels in body secretions, e.g., rifampin or clindamycin) may be considered(145). **(BIII)**

## **8.0 POPULATION SURVEILLANCE**

### **8.1 Population surveillance program for CA-MRSA**

The Working Group Meeting identified several possible purposes of a population surveillance program: (1) to document the emergence of resistance to methicillin among community isolates of *S. aureus* in order to inform empiric therapy; (2) to describe the occurrence and impact of severe *S. aureus* disease in a community, irrespective of resistance pattern; and (3) to facilitate timely identification of potential outbreaks.

#### **Recommendations**

- Surveillance for methicillin-resistance among community acquired strains of *S. aureus* should be considered. **(CIII)**
- Population-based surveillance for severe community acquired *S. aureus* infections (including severe SSTI, osteomyelitis, pyomyositis, necrotizing fasciitis, sepsis and endocarditis; see Table 6), irrespective of susceptibility, should be considered. **(CIII)**
- Intermittent or targeted surveillance of all purulent skin lesions in patients presenting to primary care may be considered to support timely identification of outbreaks and recognize emergence and spread of new strains in the community. **(CIII)**
- Populations recognized to be at increased risk (e.g., sports teams, aboriginal communities), should be included in the development of a surveillance program. **(BIII)**

### **8.2 Laboratory Support**

Monitoring CA-MRSA in the community will require collaboration between the clinician managing individual patients, the microbiology laboratory and public health departments.

#### **Recommendations**

- Clinicians and public health personnel should develop, together with microbiologic laboratories, in a given region, a method for rapid dissemination and timely feedback of susceptibility profiles for CA-MRSA in the region. **(AIII)**
- Clinical microbiology laboratories should follow current CLSI guidelines in testing erythromycin resistant strains of CA-MRSA for inducible clindamycin resistance (i.e., D-testing). **(AIII)**
- Antimicrobials which are tested and reported back to practitioners should reflect the usual standard of care for CA-MRSA (e.g., fluoroquinolone susceptibilities should not be provided). **(AIII)**

## **9.0 PREVENTION**

### **9.1 Prevention of transmission of CA-MRSA**

The goal of community control of CA-MRSA is to prevent spread of the bacteria from an infected or colonized individual to other persons in the family and the community. This requires individuals to take a proactive role to limit transmission. As a general rule, the prevention of CA-MRSA and infections with other common skin pathogens requires consistent application and reinforcement of good hygienic practices with emphasis on handwashing, not sharing potentially contaminated personal articles and covering of draining skin lesions in order to prevent direct or indirect contact with infected secretions of another person. These measures are not specific to

CA-MRSA, and apply to draining lesions, wounds or potentially infected sites caused by any micro-organism.

### ***9.1.1 Role of the individual***

#### ***Recommendations***

- Individuals should follow basic practices for good hygiene at all times and in all settings. These include, but are not limited to:
  - Regular hand hygiene to limit personal contamination and transmission. **(AIII)**
  - Regular bathing with soap and water. **(AIII)**
- If skin lesions are present:
  - Cover lesions with appropriate dressings to contain drainage or exudate, and ensure that appropriate medical care has been received. **(AIII)**
  - Do not share creams, lotions, soaps, cosmetics and other personal products that are in contact with the skin. **(AIII)**
  - Do not share unwashed towels. **(AIII)**
  - Do not share personal items that come in contact with the skin lesions such as razors, toothbrushes, towels, nail files, combs, brushes without cleaning. **(AIII)**
  - Discard contaminated waste, including used dressings, in a safe and timely manner to avoid exposure to other individuals. **(AIII)**
  - Wash hands with soap and water after touching any skin lesions and potentially infected materials such as soiled dressings. **(AIII)**

### ***9.1.2 Role of the health care practitioner***

#### ***Recommendations***

- Practitioners should use antibiotics judiciously(146). **(AIII)**
  - Treatment of viral infections with antimicrobials should be avoided.
  - Patients should be encouraged to complete all courses of antibiotics as prescribed.
- Public Health officials should be notified if spread occurs beyond a family unit to a localized community group such as a school or sports team, i.e., if an outbreak of disease is suspected. **(AIII)**
- Educate patients about appropriate hygiene practices, as outlined in section 9.1.1. **(AIII)**

### ***9.1.3 Role of health authorities***

#### ***Recommendations***

- Communication strategies that inform the general public, as well as high risk groups about CA-MRSA and practices to limit infection need to be developed, implemented and evaluated. **(AIII)**
- Strategies for ensuring early diagnosis and appropriate treatment of skin infections should target physicians and include education about risk factors, clinical features and expected treatment response time. **(AIII)**
- Regional and local programs to review antibiotic use and resistance should be developed. **(BIII)**

- Education programs should be developed to educate the public on the proper use of antibiotics in the community. **(AIII)**

## ***9.2 Prevention in Specific Settings***

### ***9.2.1 Household with CA-MRSA infection***

**In addition to the general measures outlined in section 9.1**, specific measures can be recommended within households where one or more members have infection with CA-MRSA.

#### ***Recommendations***

- The household environment should be regularly cleaned with a standard household detergent. **(AIII)**
- Clothes and linen from individuals who are MRSA positive or have other skin lesions can be included in the regular household laundry. Usual laundry washing and drying will destroy most potentially pathogenic bacteria. **(AIII)**
- Cutlery and dishes may be washed in the usual manner with other household utensils using soap and hot water, or a dishwasher. **(AIII)**
- Individuals who are MRSA positive or their family members should be advised to notify, at the time of contact with the health care system, that they are either MRSA positive or living in a household with someone who is MRSA positive. **(BIII)**

### ***9.2.2 Daycare centers and Schools***

Isolation of children with CA-MRSA in childcare settings or schools is not a practical solution and impacts negatively on the child's wellbeing. The emphasis must be placed on the consistent application of hygienic measures within the daycare or school setting to reduce the risk of transmission. **In addition to the general measures outlined in section 9.1**, specific measures are recommended to prevent transmission in schools and daycare centers.

#### ***Recommendations***

- Educate providers, teachers, children and families on general hygiene practices (e.g., hand hygiene, respiratory etiquette, staying home if ill). **(AIII)**
- Ensure availability of products to allow hand hygiene to be performed. This includes access to liquid soap in pump dispensers, running water and paper towels to dry hands. Alcohol-based waterless hand sanitizers can be used as an alternative as long as hands are not visibly soiled. **(AIII)**
- Structure activities to include opportunities for hand hygiene to be practiced (before eating, after outdoor play, after toileting). **(BIII)**
- In situations where open lesions cannot be kept covered, consider temporary exclusion from the daycare or school setting until the wound has healed or drainage can be contained. **(BIII)**
- Ensure frequently touched surfaces (e.g., counters, desks, toys) are cleaned at least daily with a disinfectant solution. **(AIII)**
- Items soiled with body fluids should be cleaned and disinfected as soon as possible and before use by another child. **(AIII)**

### 9.2.3 Sports settings

CA-MRSA transmission has been documented in several reports among athletes and contact sports participants(71-75). **In addition to the general measures outlined in section 9.1**, the following recommendations address infection prevention and control in this high risk group.

#### **Recommendations**

##### **At all times:**

- Use alcohol-based hand antiseptic rinse or gel when hand-washing facilities are not available. **(AIII)**
- Individuals participating in sports should shower with soap and water after every practice or tournament. **(AIII)**
- Do not share hygiene items such as bar soap, towels(74). **(AIII)**
- Ensure regular cleaning of communal bathing facilities and frequently touched surfaces. **(AIII)**
- Personal items such as towels and supporters should be laundered or cleaned after each use. **(AIII)**
- Clean or launder shared athletic equipment such as pads or helmets at least once a week, but ideally after each use. Establish a routine cleaning schedule for non-personal devices such as sensor wires used in fencing. **(AIII)**

##### **Individuals with skin lesions:**

- Provide both verbal and written instructions describing management of skin lesions infected with CA-MRSA or other potential pathogens to coaches and/or participants. **(BIII)**
- Individuals who have open lesions which cannot be kept covered should not participate in contact sports until the wound has healed or drainage can be contained. **(AIII)**
- Individuals who have open skin lesions should be excluded from common whirlpools or saunas. **(AIII)**
- Persons with skin lesions should not share athletic equipment that is in contact with the skin. **(AIII)**

### 9.2.4 Pets and other animals

Recurrent MRSA infections in household contacts of colonized companion animals (pets) have been described(92, 97, 103, 104). Given the evidence of transmission of MRSA between humans and animals, there is concern that pets may serve as a reservoir for MRSA in the community(97). **In addition to the general measures outlined in section 9.1**, the following are recommended for owners of pets infected or colonized with MRSA.

#### **Recommendations**

- Pet ownership and contact information may identify risk and should be queried as part of the standard history for any patient. Known MRSA status of pet or owner when available should be documented. **(AIII)**
- Pet screening should only be considered when recurrent infections are occurring within an isolated group exposed to the pet, and despite repeated reinforcement of hygiene practices. Consultation with a veterinarian as well as a public health or infectious disease expert is recommended. **(BIII)**

- Treatment of colonized pets is not indicated as there is little evidence that antimicrobial-based eradication therapy is effective in colonized pets and colonization tends to be short-term. **(BIII)**
- In exceptional circumstances, when a colonized pet is implicated as a source of infection and the infection is serious and recurrent, temporary removal of the pet from the household may be considered. While there is the potential for pets to be involved in dissemination of MRSA in the community, the beneficial effects of pet contact should be considered in any discussion about removal of the pet from the household. **(BIII)**
- There should be increased awareness in the veterinary community about MRSA infection and colonization in pets, interspecies transmission of MRSA, appropriate testing, management of infected and colonized pets, and relevant infection control measures. **(BIII)**

### 9.2.5 Correctional Facilities or Shelters

Outbreaks of CA-MRSA have been documented in incarcerated populations in the U.S. and in Canada(83-85, 87, 147). **In addition to the general measures outlined in section 9.1**, the following recommendations address this high risk group.

#### **Recommendations**

- Educate correctional facility staff and inmates on transmission, prevention, treatment and containment of MRSA infections. **(BIII)**
- Restrict inmates who have uncovered draining skin lesions and inmates with skin lesions and poor hygiene, to prevent exposure of other inmates. **(BIII)**
- Consider housing assignments based on the potential harm to individuals who could acquire infection. **(BIII)**

### 9.2.6 Newborn care facilities

Routine practices can be expected to limit the transmission of CA-MRSA within newborn care facilities and must be followed at all times(148).

#### **Recommendations: routine care**

- Wash hands before and after contact with the newborn. **(AIII)**
- Use gloves until the newborn has been cleaned or bathed for the first time. **(AIII)**
- Clean and disinfect all used equipment before it is used with another infant (e.g., thermometers, weigh scales, glucose meters, stethoscopes, etc.). **(AIII)**
- Staff should wear a gown when holding the infant against the body. **(AIII)**

There are several reports of outbreaks of CA-MRSA strains within the nursery setting(149-153). In the outbreak setting, strategies to interrupt transmission may be directed toward infants, healthcare workers or the nursery environment, as all three elements play a role in the chain of transmission (Table 8).

**Table 8: Risk factors for neonatal infections and outbreaks**

<b>Risk Category</b>	<b>Factors</b>
<b>Staff</b>	Lack of compliance with routine practices including

	hand hygiene.
	Inadequate staff education
	Staff carriage of the outbreak strain
	Poor staff: patient ratios(91)
	Intensity of colonization, e.g., chronic skin conditions, concurrent URTI
<b>Neonate</b>	Prematurity
	Prolonged NICU stay
	Use of invasive medical devices
	Exposure intensity, e.g., to carriers with chronic skin conditions, concurrent URTI
<b>Environment</b>	Poor cleaning of equipment and environment
	Patients residing in common areas, i.e., large nurseries
	Overcrowding and inadequate spacing of patients(91); non-adherence to facility guidelines
	Common newborn bath areas
	Lack of isolation areas during an outbreak

When increased transmission of CA-MRSA is documented within the nursery, intensified infection control measures are necessary.

***Recommendations: outbreak setting***

***Measures directed at health care workers***

- Enhance hand hygiene. Consider the use of antiseptic handwashing agents, such as chlorhexidine gluconate or triclosan, before each contact with the newborn(148, 154). **(BIII)**
- Reinforce infection prevention and control practices. **(BIII)**
  - Provide staff education sessions.
  - Perform practice audits to document compliance.
- Staff screening may be considered in selected situations, e.g., if cohorting and barriers are in place and the outbreak continues, or if a staff member is epidemiologically linked to cases. **(AIII)**
  - Screen nares, examine hands for lesions, enquire about skin conditions on other areas of body (scalp, feet), enquire about upper respiratory symptoms.
  - For staff epidemiologically linked to cases, perform thorough full body skin examination and culture any lesions.
  - Staff screening should be done through the Occupational Health Department ensuring staff confidentiality. Education and counseling for staff should be provided.
  - Decolonization may be attempted for the identified staff carriers with topical and/or systemic therapy(154, 155).
  - Exclusion of carriers from the area must be carefully considered and depends on factors such as: compliance with decolonization therapy; compliance with hand hygiene and Routine Practices and Additional Precautions; severity of illness in cases; exposure intensity (e.g., chronic skin conditions, concurrent URTI or allergic rhinitis); and evidence of ongoing transmission.

- Cohort personnel who care for colonized and infected newborns. **(BIII)**
- Increase nurse to patient ratio. **(AIII)**

***Measures directed at neonates***

- There is insufficient evidence to make a recommendation for or against measures to decrease the burden of organisms through cord care, topical antiseptic baths, or intra-nasal mupirocin(154-162). **(CIII)**
- Consider screening all patients for the epidemic strain. **(AIII)**
  - Examine carefully for skin lesions and eye discharge; culture any lesions or pustules.
  - Culture nares, perineum, umbilicus, device exit sites, open skin lesions.
  - Continue weekly screening of entire cohort until outbreak over.

***At the time of discharge***

- Communicate with family physicians and paediatricians receiving newborns from the facility, bringing to their attention the risk of colonization or infection with CA-MRSA in discharged neonates. **(AIII)**
- There is insufficient evidence to make a recommendation for or against the routine screening at the time of discharge and periodically thereafter. Although colonization may not be detectable without repeated sampling, the value of screening at or after discharge is questionable if no intervention is planned for colonized infants, and this may increase parental anxiety(163). **(CIII)**
- Advise parents of discharged infants to watch carefully for skin lesions and to report immediately if these occur, at which time the lesions should be cultured. If a baby sees a physician for an infection or is to be re-admitted to hospital, parents should inform the physician of a possible MRSA exposure. **(AIII)**

***Measures directed at nursery environment***

- Institute contact precautions and cohorting for colonized and infected infants. Avoid cohorting infants with CA-MRSA together with those with HA-MRSA. **(BIII)**
- Reduce over-crowding. Strongly encourage rooming-in. Correct spacing deficiencies(91). **(AIII)**
- Consider ward closure, balancing the risks and benefits of closure versus infection risk. **(BIII)**

***Additional measures***

- Assign a dedicated additional Infection Control Professional to the nursery during the outbreak. **(BIII)**
- Perform epidemiological typing of the strains. **(BIII)**
- Consider recall of discharged infants for screening. **(BIII)**
- Notify Public Health. **(AIII)**
- Consider a case-control study. **(BIII)**

## **10.0 DIRECTIONS FOR FUTURE RESEARCH**

The Working Group Meeting identified numerous areas in need of further research, classified here by category.

### ***10.1 Epidemiology***

- Establish the current incidence and prevalence of CA-MRSA disease in Canadian communities.
- Determine modifiable risk factors for CA-MRSA infection. In particular, better define any link with antibiotic usage.
- Determine the impact of animals, especially household pets, on CA-MRSA infection.
- Determine the role that colonized persons play in the spread of CA-MRSA in the community.

### ***10.2 Biology of CA-MRSA: Organism versus Host***

- Better define the virulence factors of CA-MRSA, including the role of virulence factors such as PVL and the use of immunotherapy to neutralize these virulence factors.
- Pursue vaccine development.
- Investigate host or pathogen factors that may be implicated in the particular virulence and rapid dissemination of CA-MRSA.
- Study the effect of the pneumococcal vaccine, now in widespread use, on colonization with CA-MRSA, particularly in children.
- Study the effect of influenza and influenza vaccination on CA-MRSA colonization and disease.

### ***10.3 Clinical Outcomes and Management***

- Within the paediatric population, define the safety and efficacy of newer agents such as daptomycin.
- Investigate the use of options other than antibiotic therapy, including anti-cytokines, immunomodulators, or intravenous immunoglobulin.
- Study the effect of combination therapy, e.g., addition of fusidic acid or rifampin to standard antibiotic regimens.
- Define the role of novel testing modalities, e.g., PCR for rapid diagnosis.
- Define best practices in wound management, which may have implications for minimizing antibiotic use.

### ***10.4 Infection Prevention and Control***

- Investigate primary prevention initiatives.
- Determine the effect of infection prevention and control practices in the community on rates of CA-MRSA and clinical outcomes.
- Define appropriate infection control practices for the purulent wound, particularly the challenges of wound management outside the hospital.
- Develop strategies for managing household clusters.
- Determine the psychosocial impact on individuals ‘labeled’ as MRSA positive.
- Develop strategies for infection control in the physician’s office

### ***10.5 Knowledge Translation***

- Determine what public health communication strategies should be employed.
- Investigate factors that will result in ‘cultural’ change, e.g., improving hygienic practices at a population level.

- Discover how target groups (e.g., community, sports teams) can be involved in the development of guidelines and best practices.

## **11.0 CONCLUSION**

The epidemiology of MRSA is changing, as evidenced by the dramatic increase and stable high prevalence of CA-MRSA in several US communities. While the problem does not yet appear to be widespread in Canada, several early reports indicate that CA-MRSA is emerging as an important pathogen in Canada as well. Physicians and other health care providers should be aware of the increasing prevalence and potential severity of CA-MRSA infection because  $\beta$ -lactam antibiotics, currently used for the treatment of presumed staphylococcal infections in the community, are ineffective. The management of presumed *S. aureus* infection should include surgical drainage when appropriate, culture of significant draining lesions and abscess collections, and empiric antibiotic therapy taking into account both the severity of the infection and the regional prevalence of CA-MRSA. Families, school and daycare center personnel, and sports teams should be actively encouraged to practice meticulous hand-washing, the most important measure to control or attenuate the community transmission of CA-MRSA.

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## APPENDIX: USEFUL RESOURCES

The reader is referred to these documents for specific questions related to management in health care facilities and health care workers. Relevant documents include:

1. Public Health Agency of Canada. Prevention and Control of Occupational Infections in Health Care. *CCDR*, Vol28S1, Mar 2002.
2. Public Health Agency of Canada. Routine Practices and Additional Precautions for Preventing the Transmission of Infection in Health Care. *CCDR*, Vol25S4, Jul 1999.
3. Public Health Agency of Canada. Handwashing, Cleaning, Disinfection and Sterilization in Health Care. *CCDR*, Vol24S8, Dec 1998.
4. Public Health Agency of Canada. Foot care by health care providers; *CCDR*, Vol23S8, Dec 1997.
5. Public Health Agency of Canada. Controlling Antimicrobial Resistance an Integrated Action Plan for Canadians. *CCDR*, Vol23S7, Nov 1997.
6. Public Health Agency of Canada. Infection prevention and control practices for personal services: tattooing, ear/body piercing, and electrolysis. *CCDR*, Vol25S3, Jul 1999.
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