

# Characterization and proposed nomenclature of epidemic strains of MRSA in Canada

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The incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) has been increasing in many Canadian hospitals over the past few years. Some strains may be considered 'epidemic', in that they are clinically or epidemiologically significant, and have been identified in patients from multiple hospitals and geographic regions across the country. This paper describes phenotypic and genotypic characteristics of four epidemic MRSA strains in Canada and proposes standardized nomenclature.

**Key Words:** *Methicillin-resistant Staphylococcus aureus*

## Caractérisation et suggestion de nomenclature des souches épidémiques de MRSA au Canada

**Résumé :** L'incidence des infections causées par des souches de *Staphylococcus aureus* méthicillino-résistantes (ou MRSA, pour *methicillin-resistant Staphylococcus aureus*) est à la hausse dans de nombreux hôpitaux canadiens depuis quelques années. Certaines souches seraient même considérées « épidémiques », en ce sens qu'elles sont importantes sur les plans clinique ou épidémiologique et qu'elles ont été signalées chez des patients de plusieurs hôpitaux de différentes régions du pays. Cet article porte sur les caractéristiques de quatre souches épidémiques de MRSA sur le plan du phénotype et du génotype signalées au Canada et propose une nomenclature standardisée.

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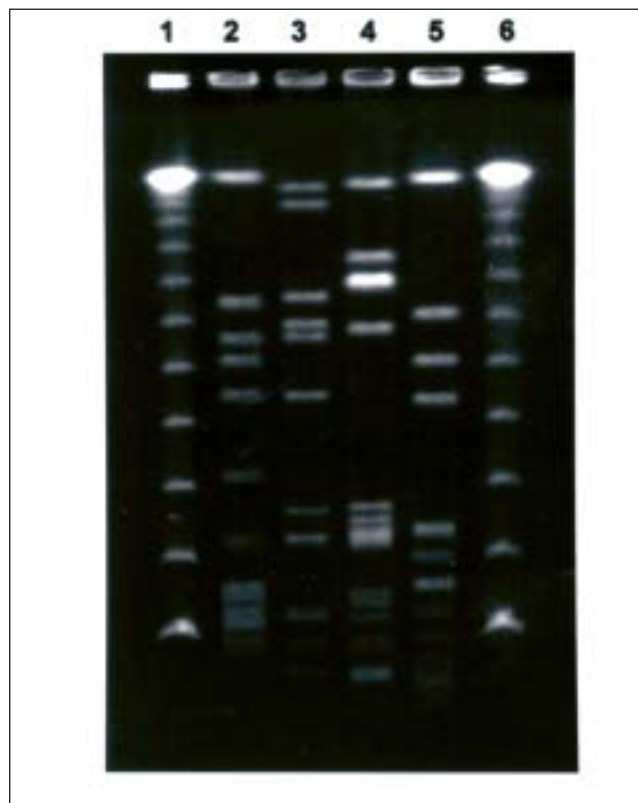
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The Canadian Hospital Epidemiology Committee (CHEC) in collaboration with the Canadian Nosocomial Infection Surveillance Program (CNISP) has been tracking methicillin-resistant *Staphylococcus aureus* (MRSA) in sentinel Canadian hospitals since January 1995. This surveillance program has documented a significant increase in the number of patients colonized and/or infected with MRSA in each of the past four years (1,2). Some MRSA strains appear to be able to spread more rapidly or easily within hospitals, nursing homes and other health care facilities, causing outbreaks or epidemics. Molecular typing of isolates may assist hospital epidemiologists, infection control practitioners and public health personnel in tracking the epidemiology and transmission of MRSA. Accurate identification and characterization of epidemic strains are essential to be able to apply appropriate infection control and prevention measures most effectively.

In an attempt to standardize the terminology used to describe epidemic strains of MRSA prevalent in Canadian hospitals, CNISP has characterized MRSA isolates from across the country by standard phenotypic typing methods, antibiogram determination, bacteriophage typing and various molecular typing procedures such as pulsed field gel electrophoresis (PFGE). Guidelines used for designating strains as 'epidemic' MRSA include the following: the strain is recognized to be clinically or epidemiologically significant (eg, associated with outbreaks of infection in health care facilities) or to possess important or unique microbiological characteristics (eg, distinct colonial morphology or phenotypic properties); the strain has been identified in patients from five or more hospital sites, or from three or more geographic regions within the country; and the strain has been characterized by standardized typing methods.

Based on these criteria, CHEC and CHISP propose that the four MRSA strains described below be designated epidemic strains of MRSA. Suggested nomenclature to be used when referring to these strains are Canadian MRSA strain (CMRSA)-1, CMRSA-2, CMRSA-3, etc. A representative PFGE DNA pattern, using standard typing methods (3) for each of these strains, is shown in Figure 1. A dendrogram of epidemic MRSA subtypes is shown in Figure 2. PFGE DNA profiles were digitized into the GelCompar computer software program (GelCompar, version 4.1, Kortrijk, Belgium) for analysis. DNA fragments on each gel were normalized using the molecular weight standards run on each gel to allow comparisons between different gels. A 2.0% tolerance was selected for use during comparisons of DNA profiles. Cluster analysis was performed by the unweighted pair group method using arithmetic averages (UPGMA), and DNA relatedness was calculated based on the Dice coefficient. Determination of genetic relatedness of isolates was based on criteria recommended by Bannerman et al (3) and Tenover et al (4). Isolates were considered to be genetically related if their macrorestriction DNA patterns differed by six bands or less and the Dice coefficient of correlation was 80% or greater.

Each of these epidemic strains have been associated with significant infections, including bacteremia and pneumonia. In surveillance conducted by CNISP, approximately half of all



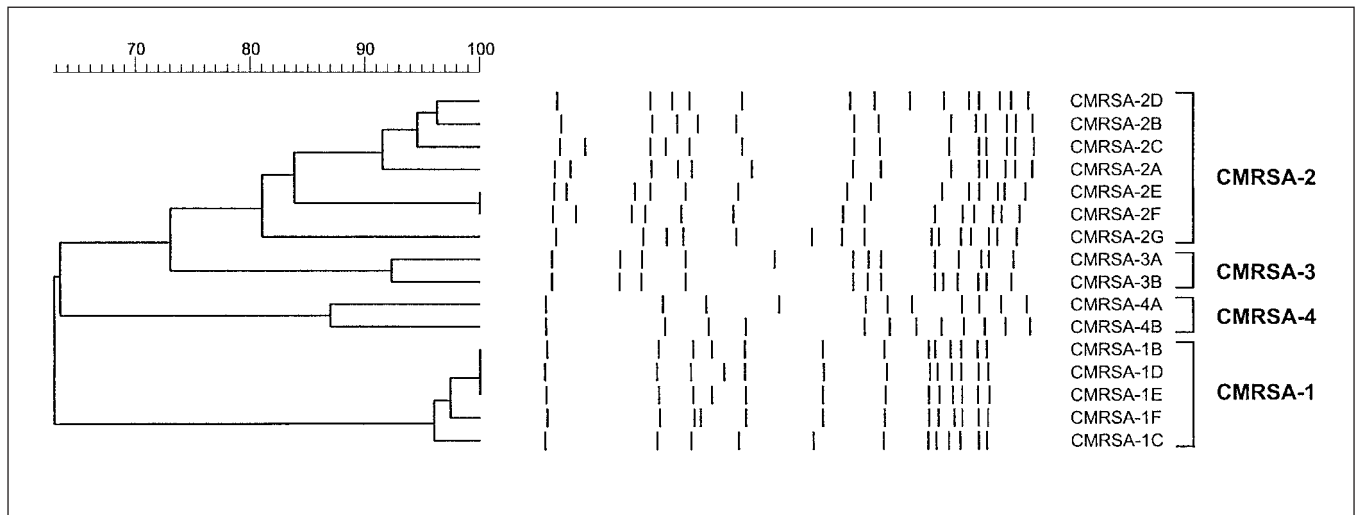
**Figure 1** Representative DNA profiles obtained by pulsed field gel electrophoresis of *Sma*I digests from Canadian epidemic strains of methicillin-resistant *Staphylococcus aureus* (MRSA). Lanes 1 and 6, lambda DNA concatamers; lane 2, Canadian MRSA strain (CMRSA)-1; lane 3, CMRSA-2; lane 4, CMRSA-3; lane 5, CMRSA-4

patients with MRSA were thought to be infected with MRSA. Clinical isolates of the four epidemic strains were reported most often from skin and soft tissue infections, surgical wounds, sputum, urine, and blood cultures; strain CMRSA-4 was more likely to be isolated from sputum than were the other strains. In colonized patients, all strains were commonly recovered from nasal mucosa, skin, and rectal or perineal sites. All of these MRSA strains were typically resistant to erythromycin, clindamycin (Dalacin C, Pharmacia & Upjohn, Mississauga, Ontario) and ciprofloxacin (Cipro, Bayer Inc, Etobicoke, Ontario). CMRSA-1 and CMRSA-3 were generally resistant to trimethoprim/sulphamethoxazole, whereas CMRSA-2 and CMRSA-4 were usually susceptible to this agent. No strains with reduced susceptibility to vancomycin have been detected thus far.

CMRSA strains are available upon request from the Laboratory Centre for Disease Control, Health Canada.

#### DESCRIPTION OF CANADIAN EPIDEMIC STRAINS OF MRSA

**CMRSA-1:** The strain designated as CMRSA-1 has been most widely found in the province of Ontario, where it accounts for the majority of strains identified in the province's hospitals; it has commonly been referred to as the 'Ontario epidemic strain'. However, this strain has also been isolated sporadically from patients hospitalized in British Columbia, Alberta, Manitoba



**Figure 2)** Dendrogram of *Sma*I digested DNA profiles obtained by pulsed field gel electrophoresis of Canadian epidemic methicillin-resistant *Staphylococcus aureus* (CMRSA) strains (CMRSA-1, CMRSA-2, CMRSA-3, CMRSA-4) with representative subtype variations

and Newfoundland. In addition, the strain has been identified in the United States and some European countries. Laboratory identification of this strain is often problematic because the organism's colonial morphology may resemble that of coagulase-negative staphylococci and because the isolate may have weak or negative test results with rapid slide agglutination assays (5,6). Detection of coagulase activity may also be weak or delayed, often requiring overnight incubation. Most CMRSA-1 isolates have been determined to be a phage-type 95, although some isolates are nontypeable and, in about 30% of isolates, other phage types have been identified (7). *Sma*I macrorestriction of chromosomal DNA followed by PFGE has identified at least five closely related DNA profiles (Figures 1,2).

**CMRSA-2:** This strain is the most widespread of current Canadian strains, although CMRSA-1 and CMRSA-3 are more frequently encountered in some parts of the country. In the CNISP surveillance in 1995, CMRSA-2 was reported from 12 of 16 sentinel hospital sites and from all areas of the country. The strain has also been reported in the United States and Argentina. This strain has the typical colonial morphology of *S aureus* in culture, and it is reliably positive when tested with rapid agglutination assays. CMRSA-2 exhibits variable phage-typing results: The strain generally reacts with Group III phages, but it may also be nontypeable. PFGE with *Sma*I yields a variety of closely related DNA profiles, with as many as 15 variants identified to date (Figures 1,2).

**CMRSA-3:** CMRSA-3 was first identified in Canada in 1993 in a patient transferred directly from a hospital in the Punjab region of India to a hospital in British Columbia. Therefore, the strain has also been referred to as the 'Punjabi strain'. Since then, it has spread to other hospitals in British Columbia and in Manitoba (8). Sporadic cases with CMRSA-3 have also been reported in Alberta and in one patient transferred directly to an Ontario hospital from the Punjab. The colonial morphology of CMRSA-3 is typical of that for *S aureus*, and the strain has the expected positive reaction with rapid agglutination tests. Variable phage types are associated with CMRSA-3, although most

isolates appear to react with group III phages. A representative DNA profile is shown in Figure 1.

**CMRSA-4:** Most CMRSA-4 isolates have been recovered from patients in Ontario, particularly from a small number of Toronto hospitals. This strain has also been identified in Alberta, Quebec, Nova Scotia and Newfoundland. The strain has the typical colonial morphology of *S aureus* and gives a positive reaction with rapid agglutination assays. CMRSA-4 has been associated with many variable phage types. DNA macrorestriction with *Sma*I has identified two predominant closely related molecular subtypes (Figures 1,2).

## SUMMARY

We hope that standardized nomenclature for identifying epidemic MRSA strains prevalent in Canadian hospitals will be helpful to physicians and infection control practitioners attempting to understand and control the spread of the organism in health care facilities. It is anticipated that, as MRSA continues to evolve in Canadian health care facilities, other strains may be recognized as 'epidemic'; as these strains become better characterized, they may be added to those designated above. We invite laboratory physicians and infection control personnel to submit strains that may warrant characterization and designation as a Canadian epidemic strain to the Laboratory Centre for Disease Control, Health Canada, Winnipeg, Manitoba.

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## CLINICAL VIGNETTE

# Diagnosis?

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A 15-month-old African-Canadian male was referred for consultation because of a recent febrile illness associated with abdominal distension, decreased appetite, fever and lethargy for one week. His mother noted that he had not been himself for about six months, over which time he became increasingly irritable, lost interest in play and had a weight loss of 3 kg. He was constipated, and defecation was painful. There was no history of sweats, cough, rhinorrhea, discharge from eyes or ears, rash, arthralgia or arthritis, or urinary symptoms. He was unable to walk or crawl but could sit unsupported and scoot around the floor. He had a five-word vocabulary. He was born at 40 weeks gestation by induced vaginal delivery. There was history of oligohydramnios, but the pregnancy, labour and delivery were otherwise unremarkable. He was on no medications and his immunizations were up to date. He had a history of three skin infections of the diaper, scalp and periorbital area as well as pimples that were treated effectively with topical fucidin. He had been hospitalized for treatment of cervical adenitis at age three months, and for gastroenteritis and dehydration at 14 months.

The boy lived with his family in a small town in the Maritimes. They had travelled to Barbados in the previous year while the father engaged in agricultural employment. Animal

exposures included domestic cats, a dog and a goldfish. The family history was notable only for irritable bowel syndrome and hypertension.

On examination, he looked chronically ill. Temperature was 38.3°C, pulse 170 beats/min and respiration 55 breaths/min. Blood pressure was normal. Height was 75 cm (fifth to 10th percentile), the weight 7.8 kg (less than fifth percentile) and the head circumference 47.5 cm (25th to 50th percentile). His abdomen was protuberant and tympanic, and bowel sounds were heard. The liver was palpable 3 cm below the costal margin; there was no splenomegaly or adenopathy. The rest of his examination was unremarkable. A complete blood count revealed a hypochromic, microcytic anemia (hemoglobin 68 g/L) with a normal total white and platelet count. Aspartate aminotransferase was slightly elevated at 78 U/L). An abdominal ultrasound revealed three cystic masses in the liver of mixed echogenicity; the largest was 7×6 cm and had a necrotic centre. Numerous smaller lesions were also present. Radiological appearance was consistent with a hepatoblastoma. Stools for culture, ova and parasite examination, and occult blood were negative.

What is the diagnosis?

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