
George G Zhanel PhD1,2,3, Mel DeCorby MSc1,3, Kim A Nichol MSc3, Patricia J Baudry BSc1,3, James A Karlowsky PhD1,3, Philippe RS Lagace-Wiens MD1,2,3, Melissa McCracken MSc4, Michael R Mulvey PhD4, Daryl J Hoban PhD1,3;
The Canadian Antimicrobial Resistance Alliance (CARA)

BACKGROUND: Methicillin-resistant Staphylococcus aureus (MRSA), extended-spectrum beta-lactamase (ESBL)-producing Escherichia coli and vancomycin-resistant enterococci (VRE) are important hospital pathogens in Canada and worldwide.

OBJECTIVES: To genotypically and phenotypically characterize the isolates of MRSA, VRE and ESBL-producing E. coli collected from patients in Canadian intensive care units (ICUs) in 2005 and 2006.

METHODS: Between September 1, 2005, and June 30, 2006, 19 medical centres participating in the Canadian National Intensive Care Unit (CAN-ICU) study collected 4133 unique patient isolates associated with infections in ICUs. Isolates of MRSA underwent mecA polymerase chain reaction (PCR) and Panton-Valentine leukocidin analysis; they were typed using pulsed-field gel electrophoresis. All isolates of E. coli with ceftriaxone minimum inhibitory concentrations greater than or equal to 1 μg/mL were tested for the presence of an ESBL using the Clinical Laboratory Standards Institute double-disk diffusion method. Subsequently, PCR and sequence analysis were used to identify bla₅₃, and blaCTX-M. Isolates of VRE were tested for the presence of vanA and vanB genes by PCR.

RESULTS: Of the 4133 ICU isolates collected, MRSA accounted for 4.7% (193 of 4133) of all isolates. MRSA represented 21.9% (193 of 880) of all S. aureus collected during the study; 90.7% were health care-associated MRSA strains and 9.3% were community-associated MRSA strains. Resistance rates for the isolates of MRSA were 91.8% to levofloxacin, 89.9% to trimethoprim-sulfamethoxazole, 27.8% resistant to gentamicin and 26.3% resistant to doxycycline; all isolates were susceptible to ertapenem, meropenem and tigecycline. VRE accounted for 0.4% (17 of 4133) of all isolates and 6.7% (17 of 255) of enterococci isolates; 88.2% of VRE had the vanA genotype. Isolated VRE that were tested were uniformly susceptible to linezolid, tigecycline and daptomycin.

CONCLUSIONS: MRSA isolated in Canadian ICUs in 2005 and 2006 was predominately health care-associated (90.7%), ESBL-producing E. coli were all CTX-M producers (72% blaCTX-M and VRE primarily harboured a vanA genotype (88.2%). MRSA, ESBL-producing E. coli and VRE were frequently multidrug resistant.

Key Words: CAN-ICU; ESBL E. coli; Intensive care; MRSA; Resistance; VRE


HISTORIQUE : Le staphylocoque doré méthicillinorésistant (SARM), l’Escherichia coli producteur de bêta-lactamase à large spectre (BELS) et l’entérocoque vancomycinorésistant (EVR) sont des pathogènes importants dans les hôpitaux du Canada et d’ailleurs dans le monde.

OBJECTIFS : Caractériser le génotype et le phénotype des isolats de SARM, d’EVR et d’E. coli producteur de BELS prélevés chez des patients hospitalisés dans des unités de soins intensifs (USI) du Canada entre 2005 et 2006.

MÉTHODOLOGIE : Entre le 1er septembre 2005 et le 30 juin 2006, 19 centres médicaux participant à l’étude sur les unités de soins intensifs au Canada ont prélevé 4 133 isolats uniques chez des patients, associés à des infections à l’USI. Les isolats de SARM ont subi une réaction en chaîne de la polymérase mecA (PCR) et une analyse de la leucocidine de Panton-Valentine et ont été typés par électrophorèse en champ pulsé.

1Department of Medical Microbiology, Faculty of Medicine, University of Manitoba; Departments of 2Medicine; 3Clinical Microbiology, Health Sciences Centre; 4Nosocomial Infections Branch, National Microbiology Laboratory, Winnipeg, Manitoba
Correspondence: Dr George G Zhanel, Clinical Microbiology, Health Sciences Centre, MS673-820 Sherbrook Street, Winnipeg, Manitoba R3A 1R9. Telephone 204-787-4902, fax 204-787-4699, e-mail ggzhanel@pcs.mb.ca
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The increasing prevalence of antimicrobial-resistant bacteria may threaten the ability of physicians to effectively treat infected patients and underscores the need for

continued surveillance (1-4). Antimicrobial-resistant pathogens, including methicillin-resistant Staphylococcus aureus (MRSA) (community-associated MRSA [CA-MRSA] and health care-associated MRSA [HA-MRSA]), extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae family such as Escherichia coli, and vancomycin-resistant enterococci (VRE), are increasing in prevalence in regions of Canada, the United States and globally (5-15). Available therapeutic options for the treatment of these antibiotic-resistant organisms are sometimes limited because these organisms frequently display a multidrug-resistant (MDR) phenotype (4,7,14,15).

The purpose of the present study was to genotypically and phenotypically characterize the isolates of MRSA, VRE and ESBL-producing E. coli collected from patients in Canadian intensive care units (ICUs) between 2005 and 2006.

METHODS

Bacterial isolates

Study isolates were obtained from the Canadian National Intensive Care Unit (CAN-ICU) study (www.can-icu.ca) (16). The CAN-ICU study included 19 medical centres across Canada (western Canada – British Columbia, Alberta, Saskatchewan and Manitoba; central Canada – Ontario and Quebec; and eastern Canada – Maritime provinces). The ICUs selected represented tertiary care medical centres from all regions of the country. Between September 2005 and June 2006, each centre collected a maximum of 300 consecutive, clinically significant isolates obtained from blood, urine, tissue or wound, and respiratory specimens (one pathogen per cultured site per patient) of ICU patients. Surveillance swabs; duplicate isolates; and eye, ear, nose and throat swabs were excluded, as were anaerobic bacteria and fungi. Isolates were shipped to the reference laboratory (Health Sciences Centre, Winnipeg, Manitoba) on Amies charcoal swabs, subcultured onto appropriate media and stocked in skim milk at –80°C until further testing was conducted.

Antimicrobial susceptibility testing

Following two subcultures from frozen stock, the in vitro activities of cefazolin, ceftriaxone, cefepime, ciprofloxacin, clarithromycin, clindamycin, dalbavancin, daptomycin,
doxycycline, erythromycin, gentamicin, levofloxacin, linezolid, meropenem, moxifloxacin, piperacillin-tazobactam, tigecycline, trimethoprim-sulfamethoxazole and vancomycin were determined by broth dilution in accordance with the 2006 Clinical Laboratory Standards Institute (CLSI) guidelines (M7-A7 and M100-S16) (16). Antimicrobial agents were obtained from pharmaceutical companies, and standard quality control organisms were defined according to the CLSI break points (M100-S16). For all antimicrobials tested, MIC interpretive standards were determined using double-tube broth microdilution in 100 μL/well of cation-adjusted Mueller-Hinton broth and were inoculated to achieve a final concentration of approximately 5×10^5 colony-forming units/mL. They were then incubated in ambient air for 24 h before reading. Colony counts were performed periodically to confirm inocula. Quality control was performed using American Type Culture Collection Quality Control organisms – Streptococcus pneumoniae 49619, S. aureus 29213, Enterococcus faecalis 29212, E. coli 25922 and Pseudomonas aeruginosa 27853.

For all antimicrobials tested, MIC interpretive standards were determined according to the CLSI break points (M100-S16). For tigecycline, the following susceptible, intermediate and resistant interpretive breakpoints (Food and Drug Administration) were used – S. aureus, less than or equal to 0.5 μg/mL (susceptible); Enterococcus species, less than or equal to 0.25 μg/mL (susceptible); and Enterobacteriaceae family, less than or equal to 2 μg/mL (susceptible), less than or equal to 4 μg/mL (intermediate), and greater than or equal to 8 μg/mL (resistant).

Characterization of MRSA, ESBL-producing Enterobacteriaceae family and VRE

MRSA: Potential MRSA isolates were confirmed using the CLSI disk-diffusion method and mecA polymerase chain reaction (PCR). All isolates of MRSA were tested for Panton-Valentine leukocidin and typed using pulsed-field gel electrophoresis following the Canadian standardized protocol to assess whether the isolates were CA-MRSA or HA-MRSA (10,11,17,18). Pulsed-field gel electrophoresis fingerprints were analyzed with BioNumerics version 3.5 (Applied Maths, Belgium) using a position tolerance of 1.0 and an optimization of 1.0. Strain relatedness was determined as previously described (19). Fingerprints were compared with the national MRSA fingerprint collection.
RESULTS

Patient demographics and specimen types

A total of 4133 organisms from 2580 patients (or 1.6 isolates per patient) were collected from ICUs across Canada in 2005 and 2006; they were taken during any time of the patient’s ICU admission. 59.3% (2451 of 4133) of isolates were collected from male patients, while 40.7% (1682 of 4133) were collected from female patients. Patient age breakdown was 17 years of age or younger, 13.7%; between 18 and 64 years of age, 46.7%; and 65 years of age or older, 39.6%. 54.8% of isolates belonged to the CMRSA-10 (USA300) genotype. The average age of patients with CA-MRSA was 43.2 years (range one to 75 years); CA-MRSA was more frequently isolated from male patients (72.2%, 13 of 18) than female patients. Also, 17 of 18 (94.4%) CA-MRSA isolates were positive for the PVL gene, and 61.1% (11 of 18) of isolates contained the SCCmec IV element, which made up 45% of all pathogens in ICUs. All MRSA, VRE and ESBL E coli underwent genotypic characterization and antimicrobial susceptibility studies.

MRSA

Of the 193 MRSA (21.9% of all S aureus) specimens isolated from ICUs, 175 (90.7%) were HA-MRSA genotypes, while 18 (9.3%) were CA-MRSA genotypes. HA-MRSA-associated genotypes included CMRSA-2 (USA100), 67.6%; CMRSA-6, 15.4%; CMRSA-1 (USA600), 5.9%; CMRSA-8, 4.4%; CMRSA-4 (USA200), 3.7%; CMRSA-3, 0.8%; and CMRSA-9, 0.7%. HA-MRSA genotypes occurred with similar frequencies in all regions of Canada (Table 2). The 18 CA-MRSA specimens were isolated from seven different cities in Canada; however, 15 of 18 (83.3%) were isolated from western Canada. Blood was the most common site from which CA-MRSA was isolated (50%, nine of 18), followed by respiratory (38.9%, seven of 18) and wounds (5.6%, one of 18). The average age of patients with CA-MRSA was 43.2 years (range one to 75 years); CA-MRSA was more frequently isolated from male patients (72.2%, 13 of 18) than female patients. Also, 17 of 18 (94.4%) CA-MRSA isolates were positive for the PVL gene, and 61.1% (11 of 18) of isolates belonged to the CMRSA-10 (USA300) genotype. The CMRSA-7 (USA400) genotype occurred in 38.9% (seven of 18) of isolates. All CMRSA-7 strains were reported from either Saskatchewan or Manitoba, while CMRSA-10 strains were primarily identified in British Columbia (eight of 11). The antimicrobial susceptibilities of the CMRSA and HA-MRSA isolates are shown in Table 3. CA-MRSA isolates were more susceptible than HA-MRSA isolates to fluoroquinolones (ciprofloxacin, levofloxacin and moxifloxacin), gentamicin and all beta-lactams, demonstrating lower MIC for 50% and 90% of isolates to cefazolin, cefepime, ceftriaxone, piperacillin-tazobactam and meropenem. Resistance rates were also lower for CA-MRSA isolates than HA-MRSA isolates for clarithromycin (66.6% versus 92.2%), clindamycin (27.8% versus 81.0%) and trimethoprim-sulfamethoxazole (0.0% versus 12.8%). No isolates of CA-MRSA or HA-MRSA were resistant to vancomycin, linezolid, tigecycline or daptomycin. Dalbavancin was active against all MRSA isolates, with MIC for 50% of isolates and MIC for 90% of isolates with values of 0.06 μg/mL. Of all MRSA, 88.8% were MDR (defined as resistant to three or more of the following: cefazolin and

### Table 1

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Organism</th>
<th>Isolates, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Staphylococcus aureus – MSSA</td>
<td>687 (16.6)</td>
</tr>
<tr>
<td>2</td>
<td>Escherichia coli</td>
<td>493 (11.9)</td>
</tr>
<tr>
<td>3</td>
<td>Pseudomonas aeruginosa</td>
<td>419 (10.1)</td>
</tr>
<tr>
<td>4</td>
<td>Haemophilus influenzae</td>
<td>329 (8.0)</td>
</tr>
<tr>
<td>5</td>
<td>CNS – Staphylococcus epidermidis</td>
<td>273 (6.6)</td>
</tr>
<tr>
<td>6</td>
<td>Enterococcus species</td>
<td>255 (6.2)</td>
</tr>
<tr>
<td>7</td>
<td>Streptococcus pneumoniae</td>
<td>244 (5.9)</td>
</tr>
<tr>
<td>8</td>
<td>Klebsiella pneumoniae</td>
<td>224 (5.5)</td>
</tr>
<tr>
<td>9</td>
<td>S aureus – MRSA</td>
<td>193 (4.7)</td>
</tr>
<tr>
<td>10</td>
<td>Enterobacter cloacae</td>
<td>164 (4.0)</td>
</tr>
<tr>
<td>11</td>
<td>Stenotrophomonas maltophilia</td>
<td>108 (2.7)</td>
</tr>
<tr>
<td>12</td>
<td>Serratia marcescens</td>
<td>100 (2.4)</td>
</tr>
<tr>
<td>13</td>
<td>Moraxella catarrhalis</td>
<td>78 (1.9)</td>
</tr>
<tr>
<td>14</td>
<td>Klebsiella oxytoca</td>
<td>77 (1.8)</td>
</tr>
<tr>
<td>15</td>
<td>Streptococcus pyogenes</td>
<td>49 (1.2)</td>
</tr>
<tr>
<td>16</td>
<td>Enterobacter aerogenes</td>
<td>47 (1.1)</td>
</tr>
<tr>
<td>17</td>
<td>Citrobacter freundii</td>
<td>39 (0.9)</td>
</tr>
<tr>
<td>18</td>
<td>Streptococcus agalactiae</td>
<td>39 (0.9)</td>
</tr>
<tr>
<td>19</td>
<td>Proteus mirabilis</td>
<td>38 (0.9)</td>
</tr>
<tr>
<td>20</td>
<td>Acinetobacter baumannii</td>
<td>28 (0.7)</td>
</tr>
<tr>
<td>Other*</td>
<td></td>
<td>249 (6.0)</td>
</tr>
</tbody>
</table>

Notes: CNS Coagulase-negative staphylococci. MRSA Methicillin-resistant S aureus; MSSA Methicillin-susceptible S aureus; *Other – Acinetobacter species, Burkholderia species, Bacillus species, Citrobacter species, Corynebacterium species, Enterobacter species, Haemophilus species, Micrococcus species, Morganella species, Neisseria species, Pseudomonas species, Salmonella species, Serratia species, Staphylococcus species and Streptococcus species.
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TABLE 2
Characteristics of 18 community-associated methicillin-resistant Staphylococcus aureus (MRSA) isolates from patients in Canadian intensive care units in 2005 and 2006

<table>
<thead>
<tr>
<th>Isolate number</th>
<th>City (direction)</th>
<th>Specimen source</th>
<th>Age (years)</th>
<th>Sex</th>
<th>PVL</th>
<th>Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>58173</td>
<td>Winnipeg (W)</td>
<td>Respiratory</td>
<td>1</td>
<td>F</td>
<td>+</td>
<td>CMRSA-7 (USA400)</td>
</tr>
<tr>
<td>61592</td>
<td>Vancouver (W)</td>
<td>Blood</td>
<td>39</td>
<td>M</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
<tr>
<td>62697</td>
<td>Saskatoon (W)</td>
<td>Blood</td>
<td>5</td>
<td>M</td>
<td>+</td>
<td>CMRSA-7 (USA400)</td>
</tr>
<tr>
<td>62825</td>
<td>Regina (W)</td>
<td>Blood</td>
<td>25</td>
<td>F</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
<tr>
<td>62996</td>
<td>Victoria (W)</td>
<td>Blood</td>
<td>21</td>
<td>F</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
<tr>
<td>63307</td>
<td>Winnipeg (W)</td>
<td>Respiratory</td>
<td>58</td>
<td>M</td>
<td>+</td>
<td>CMRSA-7 (USA400)</td>
</tr>
<tr>
<td>64195</td>
<td>Halifax (E)</td>
<td>Blood</td>
<td>75</td>
<td>F</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
<tr>
<td>64914</td>
<td>Saskatoon (W)</td>
<td>Respiratory</td>
<td>39</td>
<td>M</td>
<td>+</td>
<td>CMRSA-7 (USA400)</td>
</tr>
<tr>
<td>65226</td>
<td>Victoria (W)</td>
<td>Respiratory</td>
<td>56</td>
<td>M</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
<tr>
<td>65667</td>
<td>Victoria (W)</td>
<td>Blood</td>
<td>48</td>
<td>M</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
<tr>
<td>66065</td>
<td>Saskatoon (W)</td>
<td>Respiratory</td>
<td>67</td>
<td>M</td>
<td>+</td>
<td>CMRSA-7 (USA400)</td>
</tr>
<tr>
<td>66122</td>
<td>Halifax (E)</td>
<td>Blood</td>
<td>69</td>
<td>F</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
<tr>
<td>66303</td>
<td>Vancouver (W)</td>
<td>Respiratory</td>
<td>38</td>
<td>M</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
<tr>
<td>67442</td>
<td>Victoria (W)</td>
<td>Respiratory</td>
<td>36</td>
<td>M</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
<tr>
<td>67878</td>
<td>Victoria (W)</td>
<td>Wound</td>
<td>40</td>
<td>M</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
<tr>
<td>67884</td>
<td>Victoria (W)</td>
<td>Blood</td>
<td>39</td>
<td>M</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
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<tr>
<td>68300</td>
<td>Saskatoon (W)</td>
<td>Blood</td>
<td>49</td>
<td>M</td>
<td>–</td>
<td>CMRSA-7 (USA400)</td>
</tr>
<tr>
<td>68584</td>
<td>Sydney (E)</td>
<td>Wound</td>
<td>73</td>
<td>M</td>
<td>+</td>
<td>CMRSA-10 (USA300)</td>
</tr>
</tbody>
</table>

TABLE 3
Antimicrobial susceptibilities of community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) and healthcare-associated MRSA (HA-MRSA) isolated from patients in Canadian intensive care units in 2005 and 2006

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>CA-MRSA (n=18)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>HA-MRSA (n=175)</th>
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<tbody>
<tr>
<td></td>
<td>MIC50 (μg/mL)</td>
<td>MIC90</td>
<td>Range</td>
<td>S</td>
<td>I</td>
<td>R</td>
<td>S</td>
<td>I</td>
<td>R</td>
<td>S</td>
<td>I</td>
<td>R</td>
<td>S</td>
<td>I</td>
<td>R</td>
<td>S</td>
<td>I</td>
<td>R</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>16.0</td>
<td>16.0</td>
<td>0.25–16.0</td>
<td>38.9</td>
<td>–</td>
<td>61.1</td>
<td>32.0</td>
<td>32.0</td>
<td>0.25–16.0</td>
<td>5.1</td>
<td>–</td>
<td>94.9</td>
<td>Clarithromycin</td>
<td>&gt;16.0</td>
<td>&gt;16.0</td>
<td>≤0.25–16.0</td>
<td>38.9</td>
<td>–</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>&gt;16.0</td>
<td>&gt;16.0</td>
<td>≤0.25–16.0</td>
<td>33.4</td>
<td>–</td>
<td>66.6</td>
<td>&gt;16.0</td>
<td>&gt;16.0</td>
<td>≤0.25–16.0</td>
<td>7.8</td>
<td>–</td>
<td>92.2</td>
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<tr>
<td>Clindamycin</td>
<td>0.25</td>
<td>&gt;8.0</td>
<td>≤0.25–8.0</td>
<td>72.2</td>
<td>–</td>
<td>27.8</td>
<td>&gt;8.0</td>
<td>&gt;8.0</td>
<td>≤0.25–8.0</td>
<td>19.0</td>
<td>–</td>
<td>81.0</td>
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<tr>
<td>Dalbavancin</td>
<td>0.06</td>
<td>0.06</td>
<td>≤0.03–0.06</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.06</td>
<td>0.06</td>
<td>≤0.03–0.12</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Daptomycin</td>
<td>0.25</td>
<td>0.25</td>
<td>0.12–0.25</td>
<td>100.0</td>
<td>–</td>
<td>0.0</td>
<td>0.12</td>
<td>0.25</td>
<td>0.12–0.5</td>
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<tr>
<td>Gentamicin</td>
<td>≤0.25</td>
<td>1.0</td>
<td>≤0.25–32</td>
<td>94.4</td>
<td>–</td>
<td>5.6</td>
<td>0.5</td>
<td>1.0</td>
<td>≤0.25–64.0</td>
<td>83.7</td>
<td>–</td>
<td>16.3</td>
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<tr>
<td>Levofloxacin</td>
<td>4.0</td>
<td>8.0</td>
<td>0.12–8.0</td>
<td>38.9</td>
<td>–</td>
<td>61.1</td>
<td>&gt;32.0</td>
<td>&gt;32.0</td>
<td>0.12–32.0</td>
<td>5.1</td>
<td>–</td>
<td>94.9</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>2.0</td>
<td>2.0</td>
<td>1.0–2.0</td>
<td>100.0</td>
<td>–</td>
<td>0.0</td>
<td>2.0</td>
<td>2.0</td>
<td>1.0–4.0</td>
<td>100.0</td>
<td>–</td>
<td>0.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>1.0</td>
<td>2.0</td>
<td>≤0.06–4.0</td>
<td>38.9</td>
<td>11.1</td>
<td>50.0</td>
<td>8.0</td>
<td>&gt;18.0</td>
<td>≤0.06–16</td>
<td>5.0</td>
<td>–</td>
<td>95.0</td>
<td></td>
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<tr>
<td>Tigecycline</td>
<td>0.12</td>
<td>0.25</td>
<td>0.12–0.25</td>
<td>100.0</td>
<td>–</td>
<td>0.0</td>
<td>0.12</td>
<td>0.5</td>
<td>0.06–0.5</td>
<td>100.0</td>
<td>–</td>
<td>0.0</td>
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<tr>
<td>SXT</td>
<td>0.12</td>
<td>0.12</td>
<td>0.12–0.5</td>
<td>100.0</td>
<td>–</td>
<td>0.0</td>
<td>≤0.12</td>
<td>16.0</td>
<td>≤0.12–32.0</td>
<td>87.2</td>
<td>–</td>
<td>12.8</td>
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<td>Vancomycin</td>
<td>1.0</td>
<td>1.0</td>
<td>0.5–1.0</td>
<td>100.0</td>
<td>–</td>
<td>0.0</td>
<td>1.0</td>
<td>1.0</td>
<td>≤0.25–1.0</td>
<td>100.0</td>
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I Intermediate; MIC Minimum inhibitory concentration; MIC50 MIC for 50% of isolates; MIC90 MIC for 90% of isolates; R Resistant; S Susceptible; SXT Trimethoprim-sulfamethoxazole

ESBL-producing E coli

ESBL-producing E coli accounted for 3.7% (18 of 493) of all E coli isolates collected. Although ESBL-producing E coli were obtained from a variety of Canadian cities, 88.9% (16 of 18) were obtained from central and eastern Canada, whereas only 11.1% (two of 18) were obtained from western Canada (Table 4). The mean age of patients with ESBL-producing E coli was 54.1 years (range 25 to 85.5 years), with 10 of 18 (61.1%) isolates from female patients and eight of 18 (44.4%) isolates from male patients. The most common sources of ESBL-producing E coli included the urinary tract (50.0%, nine of 18) followed by blood (27.8%, five of 18), and respiratory and wound sites, both at 11.1% (two of 18). The most common genotype of the ESBL-producing E coli was CTX-M-15 at 72.2% (13 of 18); followed by CTX-M-2 at 11.1% (two of 18); and CTX-M-1 at CTX-M-9 and CTX-M-14 each at 5.6% (one of 18 each) (Table 4). The TEM-1 gene (not an ESBL) was identified in 61.1% (11 of 18) of isolates. ESBL-producing E coli frequently displayed an MDR phenotype, with 77.8% of isolates demonstrating concomitant resistance to ciprofloxacin, 55.6% demonstrating resistance to trimethoprim-sulfamethoxazole, 27.8% demonstrating resistance to gentamicin and 26.3% of isolates being resistant to piperacillin-tazobactam, ciprofloxacin, clarithromycin, clindamycin, linezolid, vancomycin and tigecycline, compared with only 2.3% of MSSA.
demonstrating resistance to doxycycline (data not shown). No isolates were resistant to meropenem, ertapenem (data not shown), or tigecycline (Table 4).

VRE
Of the 17 VRE isolated, 52.9% (nine of 17) occurred in eastern Canada, 41.2% (seven of 17) in western Canada and 5.9% (one of 17) in central Canada (Table 5); 76.5% (13 of 17) of isolates were Enterococcus faecium, while 23.5% (four of 17) were Enterococcus faecalis. The mean patient age was 62.1 years (range 26 to 83 years), and 64.7% (11 of 17) of isolates were from female patients. The source was primarily wound (52.9%, nine of 17), followed by both blood and urine at 17.6% (three of 17) each, and respiratory sites at 5.9% (one of 17). The most common genotype was tunA (88.2%, 15 of 17). All isolates were resistant to ciprofloxacin. No isolates were resistant to linezolid, daptomycin or tigecycline.

**DISCUSSION**

The CAN-ICU study was the first national prospective surveillance study assessing antimicrobial resistance in Canadian ICUs. It determined that more than one-half of all infections in the ICUs were respiratory in origin, irrespective of patient age and sex (16). Bloodstream, wound or intravenous origin, and urinary tract infections were less common than respiratory infections in ICU patients, as has been previously documented (21).

The CAN-ICU study documented that MSSA and MRSA are important pathogens causing respiratory tract infections, bacteremia, and wound or intravenous infections in ICUs in Canada. MRSA accounted for 21.9% of all S. aureus, and 9.3% of all MRSA causing infections in the ICU were CA-MRSA genotypes. This has not been previously documented in Canada and shows the infiltration of CA-MRSA into Canadian ICUs. All 18 of the CA-MRSA isolates were either USA400 (CMRSA-7) or USA300 (CMRSA-10) genotypes. These two genotypes are the two primary CA-MRSA genotypes reported across North America (11,18,22-24). It appears that infections in Canadian ICUs caused by CA-MRSA are primarily occurring in western Canada, with USA400 (CMRSA-7) the predominant genotype in Saskatchewan or Manitoba, and USA300 (CMRSA-10) the predominant genotype in British Columbia (Table 2).

The present study is the first to document that ESBL-producing *E. coli* are becoming more common than ESBL-producing Klebsiella species in Canadian ICUs. While 3.7% of *E. coli* were ESBL-producing *E. coli*, and 1.8% of Klebsiella species were ESBL-producing Klebsiella species (data not shown), the relative abundance of ESBL-producing *E. coli* (89.5%) was primarily obtained in central and eastern Canada from urine, blood, the respiratory tract and wounds. All 18 ESBL-producing *E. coli* that were isolated displayed an MDR phenotype, with 77.8% demonstrating concomitant resistance to fluoroquinolones and 55.6% demonstrating resistance to trimethoprim-sulfamethoxazole. The study showed that CTX-M with bla*CTX-M-15* was the predominant genotype (72%) of ESBL-producing *E. coli* in Canada. Other studies (8,9,12,13) assessing ESBL-producing *E. coli* have shown that the CTX-M genotype is spreading rapidly in both community and hospital settings. Pitout et al (13) investigated the molecular epidemiology of ESBL-producing *E. coli* collected between 2000 and 2005 in the Calgary Health Region in Alberta. These investigators reported...
that 64% (354 of 552) of ESBL-producing *E coli* were PCR-
positive for *bla*_{CTX-M} genes, with CTX-M-14 (59.6%) and
CTX-M-15 (36.2%) reported most commonly. This study
highlights the rapid spread of MDR ESBL CTX-M-15 
*E coli* in Canadian ICUs. This genotype is likely spreading rapidly
due to the extensive use of third-generation cephalosporins and
fluoroquinolones.

The CAN-ICU study showed that VRE represented 6.7% of
all enterococci tested, with the vanA genotype (mostly *
E faecium*) making up 88.2% of VRE. This relatively low level
of VRE across Canada has been previously documented and
likely reflects the active surveillance programs in Canadian
hospitals (14). Such programs have been reported to prevent
VRE colonization and bacteremia (25). Previous data (5,14)
have suggested that the *E faecium* carrying vanA is the
predominant genotype in North America.

Resistance rates of MRSA were high with fluoroquinolones
and macrolides, such as clarithromycin and clindamycin (range
76.1% to 91.8%); they were lower, at 11.7%, with trimethoprim-
sulfamethoxazole. Thus, trimethoprim-sulfamethoxazole still
represents a reasonable empirical treatment for mild to moderate
infections caused by CA-MRSA or HA-MRSA. It should be
noted that the study found a significant difference between the
susceptibilities of CA-MRSA and HA-MRSA. Like others, we
report that CA-MRSA was more susceptible to beta-lactams,
trimethoprim-sulfamethoxazole, macrolides, clindamycin and
fluoroquinolones than HA-MRSA (11). All CA-MRSA and
HA-MRSA isolates were susceptible to vancomycin, linezolid,
tigecycline and daptomycin. Likewise, all VRE in the study
proved to be susceptible to linezolid, tigecycline and daptomycin.
MDR ESBL-producing *E coli* isolates were all susceptible to the
carbenapenem, ertapenem, metronem and tigecycline. Because
nosocomial infections in the ICU are frequently MDR
(frequently associated with prior antimicrobial use [6]), some
have suggested that involvement of an infectious diseases
specialist may help to improve, cure and minimize further resist-
ance development (2).

CONCLUSIONS

MRSA isolated in Canadian ICUs in 2005 and 2006 was pre-
dominately HA-MRSA (90.7%), ESBL-producing *E coli* were
all CTX-M producers (72% *bla*_{CTX-M-15}) and VRE primarily
harboured a vanA genotype (88.2%). MRSA, ESBL-producing *E coli* and VRE were frequently MDR.

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