Antimicrobial susceptibility of 6685 organisms isolated from Canadian hospitals: CANWARD 2007

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BACKGROUND: Antimicrobial resistance is a growing problem in North American hospitals as well as hospitals worldwide.

OBJECTIVES: To assess the antimicrobial susceptibility patterns of commonly used agents against the 20 most common organisms isolated from Canadian hospitals.

METHODS: In total, 7881 isolates were obtained between January 1, 2007, and December 31, 2007, from 12 hospitals across Canada as part of the Canadian Ward Surveillance Study (CANWARD 2007). Of these, 6685 isolates (20 most common organisms) obtained from bacteremic, urinary, respiratory and wound specimens underwent antimicrobial susceptibility testing. Susceptibility testing was assessed using the Clinical and Laboratory Standards Institute broth microdilution method.

RESULTS: The most active (based upon minimum inhibitory concentration [MIC]) agents against methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant Staphylococcus epidermidis (MRSE) were dalbavancin, daptomycin, linezolid, telavancin, tigecycline and vancomycin, with MIC90s required to inhibit the growth of 90% of organisms of 0.06 µg/mL and 0.06 µg/mL, 0.25 µg/mL and 0.25 µg/mL, 4 µg/mL and 1 µg/mL, 0.25 µg/mL and 0.25 µg/mL, and 1 µg/mL and 2 µg/mL, respectively. The most active agents against vancomycin-resistant enterococci were daptomycin, linezolid and tigecycline with MIC90s of 2 µg/mL, 4 µg/mL and 0.12 µg/mL, respectively. The most active agents against Escherichia coli were amikacin, cefepime, ertapenem, meropenem, piperacillin-tazobactam and tigecycline with MIC90s of 4 µg/mL, 2 µg/mL, 0.06 µg/mL or less, 0.12 µg/mL or less, 4 µg/mL and 1 µg/mL, respectively. The most active agents against extended-spectrum beta-lactamase-producing E coli were ertapenem, meropenem and tigecycline with MIC90s of 0.12 µg/mL or less, 0.12 µg/mL or less and 1 µg/mL, respectively. The most active agents against Pseudomonas aeruginosa were amikacin, cefepime, meropenem and piperacillin-tazobactam with MIC90s of 32 µg/mL, 32 µg/mL, 8 µg/mL, 8 µg/mL, and 64 µg/mL, respectively. The most active agents against Stenotrophomonas maltophilia were tigecycline and trimethoprim-sulfamethoxazole and levofloxacin with MIC90s of 8 µg/mL, 8 µg/mL and 8 µg/mL, respectively. The most active agents against Acinetobacter baumannii were amikacin, fluoroquinolones (eg, levofloxacin), meropenem, and tigecycline with MIC90s of 2 µg/mL or less, 1 µg/mL, 4 µg/mL and 2 µg/mL, respectively.

CONCLUSIONS: The most active agents versus Gram-positive cocci from Canadian hospitals were vancomycin, linezolid, daptomycin, tigecycline, dalbavancin and telavancin. The most active agents versus Gram-negative bacilli from Canadian hospitals were amikacin, cefepime, ertapenem (not P aeruginosa), meropenem, piperacillin-tazobactam and tigecycline (not P aeruginosa). Colistin (polymyxin E) was very active against P aeruginosa and A baumannii.

Key Words: Canadian hospitals; Resistance; Susceptibility

La susceptibilité aux antimicrobiens de 6 685 organismes isolés dans des hôpitaux canadiens : CANWARD 2007

HISTORIQUE : La résistance aux antimicrobiens est un problème croissant dans les hôpitaux nord-américains et du monde entier.

OBJECTIFS : Évaluer les modes de susceptibilité aux antimicrobiens d’agents souvent utilisés contre les 20 principaux organismes isolés dans des hôpitaux canadiens.

MÉTHODOLOGIE : Au total, on a recueilli 7 881 isolats entre le 1er janvier et le 31 décembre 2007 dans 12 hôpitaux du Canada, dans le cadre de l’étude CANWARD 2007 sur la surveillance des services aux hospitalisés canadiens. De ce nombre, 6 685 isolats (les 20 principaux organismes) prélevés dans des échantillons bactériémiques, urinaires, respiratoires et de plaies ont subi un test de susceptibilité aux antimicrobiens. On a évalué ce test au moyen de la méthode de microdilution en milieu liquide du Clinical and Laboratory Standards Institute.

RÉSULTATS : Les agents les plus actifs (d’après les données de concentration minimale inhibitrice [CMI] seulement) contre le staphylocoque doré méthicillinorésistant (MRSE) et le Staphylococcus epidermidis méthicillinorésistant (SERM) étaient la dalbavancine, la daptomycine, la linézolide, la télavancine, la tigécycline et la vancomycine, les CMI nécessaires pour inhiber la croissance de 90 % des organismes (CMI90) étant de 0.06 µg/mL et 0.06 µg/mL, 0.25 µg/mL et 0.25 µg/mL, 4 µg/mL et 1 µg/mL, 0.25 µg/mL et 0.25 µg/mL, 0.05 µg/mL et 0.25 µg/mL et 1 µg/mL et 2 µg/mL, respectivement. Les agents les plus actifs contre les écococus résistant à la vancomycine étaient la daptomycine, le linézolide et la tigécycline, avec une CMI90 de 2 µg/mL, 4 µg/mL et 0.12 µg/mL, respectivement. Les agents les plus actifs contre l’Escherichia coli étaient l’amikacine, le céfépine, l’értapénème, le méropénème, la piperacilline-tazobactam et la tigécycline, avec une CMI90 de 4 µg/mL, 2 µg/mL, 0.06 µg/mL ou moins, 0.12 µg/mL ou moins, 4 µg/mL et 1 µg/mL, respectivement. Les agents les plus actifs contre l’E coli producteur de...
bêta-lactamase à large spectre étaient l’ertapénème, le méropenème et la tigécycline, avec une CMI90 de 0,12 µg/mL ou moins, 0,12 µg/mL ou moins et 1 µg/mL, respectivement. Les agents les plus actifs contre le *Pseudomonas aeruginosa* étaient l’amikacine, le céfépime, le méropenème et la pipéracilline-tazobactam, avec une CMI90 de 32 µg/mL, 32 µg/mL, 8 µg/mL et 64 µg/mL, respectivement. Les agents les plus actifs contre le *Stenotrophomonas maltophilia* étaient la tigécycline, le triméthoprim-sulfaméthoxazole et la lévofloxacine, avec une CMI90 de 8 µg/mL, 8 µg/mL et 8 µg/mL, respectivement. Les agents les plus actifs contre l’*Acinetobacter baumannii* étaient l’amikacine, les fluoroquinolones (p. ex., la lévofloxacine), le méropénème et la tigécycline, avec une CMI90 de 2 µg/mL ou moins, 1 µg/mL, 4 µg/mL et 2 µg/mL, respectivement.

**CONCLUSIONS** : Les agents les plus actifs contre les cocci gram positifs des hôpitaux canadiens étaient la vancomycine, le linézolide, la daptomycine, la tigécycline, la dalbavancine et la téladévancine. Les agents les plus actifs contre les bacilles gram négatifs des hôpitaux canadiens étaient l’amikacine, le céfépime, l’ertapénème (sauf pour le *P aeruginosa*), le méropénème, la pipéracilline-tazobactam et la tigécycline (sauf pour le *P aeruginosa*). La colistine (polyoxypulse E) était très active contre le *P aeruginosa* et l’*A baumannii*.

**Antimicrobial susceptibility of organisms (CANWARD 2007)**

Hospitals in North America as well as hospitals worldwide are facing the growing presence of infections caused by antimicrobial-resistant as well as multidrug-resistant (MDR) pathogens (1-4). Pathogens including methicillin-resistant *Staphylococcus aureus* (MRSA; community-associated [CA-MRSA] and health care-associated [HA-MRSA]), vancomycin-resistant Enterococcus species (VRE), penicillin-resistant *Streptococcus pneumoniae*, extended-spectrum bêta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella* species, and fluoroquinolone-resistant and carbapenem-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* are growing in prevalence in Canada, the United States and globally (5-10). Treatment options of antimicrobial-resistant organisms can be severely limited because these organisms frequently display a MDR phenotype (3,4).

We recently reported on the antimicrobial activity of commonly used agents against 3931 organisms isolated from intensive care units in Canada (11). The purpose of the present study was to assess the in vitro activity (minimum inhibitory concentrations required to inhibit the growth of 50% and 90% of organisms [MIC50 and MIC90]) of commonly prescribed antimicrobials against the 20 most common organisms (6685 isolates) obtained from patients in hospitals across Canada.

**METHODS**

**Bacterial isolates**

Study isolates were obtained as part of the Canadian Ward Surveillance Study (CANWARD 2007). The CANWARD study included 12 medical centres from all regions of Canada (www.can-r.ca). The precise methods of isolate collection are explained in detail in the first paper of the present supplement (12). In brief, from January 1, 2007, to December 31, 2007, inclusive, each centre collected and submitted clinical isolates from patients attending hospital clinics, emergency rooms, medical and surgical wards, and intensive care units. Each centre was asked to submit clinical isolates (consecutive, one organism per infection site per patient) from blood (360 isolates collected as 30 consecutive/month for each of the 12 months), respiratory (n = 200), urine (n = 100), and wound/intravenous (n = 50) infections. All organisms were identified at the originating centre using local site criteria and were deemed clinically significant. In total, 7881 isolates were collected. 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 MIC testing was carried out.

**Antimicrobial susceptibilities**

Susceptibility testing was carried out using microbroth dilution in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines (11,13). For all antimicrobials tested, MIC interpretive standards were defined according to CLSI breakpoints (CLSI 2006). Susceptibility testing could not be performed with all agents due to lack of space on the susceptibility panels. Thus, susceptibility testing was not performed with *P aeruginosa* for ceftazidime, tobramycin and imipenem. The following interpretive breakpoints (Food and Drug Administration, USA) were used for tigecycline susceptible (S), intermediate (I) and resistant (R); *S aureus* (methicillin-susceptible [MSSA] and MRSA) 0.5 µg/mL or less (S); *Enterococcus faecalis* (vancomycin susceptible), 0.25 µg/mL or less (S); *Enterobacteriaceae*, 2 µg/mL or less (S), 4 µg/mL (I), and 8 µg/mL or greater (R). No breakpoints are presently available for dalbavancin and telavancin.

**Characterization of MRSA, ESBL-producing Enterobacteriaceae and VRE**

**MRSA**: Potential MRSA isolates were confirmed and tested as previously described (10). All isolates of MRSA were typed using pulsed-field gel electrophoresis following the Canadian standardized protocol to assess whether the isolates were CA-MRSA or HA-MRSA (9,10,14,15).

**ESBL testing**: Potential *E coli* or *Klebsiella* species. ESBL producers were identified and tested as previously described (10).

**VRE**: Potential VRE isolates were confirmed using CLSI vancomycin disk diffusion testing and underwent *vanA* and *vanB* polymerase chain reaction as well as DNA fingerprinting to assess genetic similarity, as previously described (7,10).

**RESULTS**

**Patient demographics and specimen types**

A total of 7881 organisms (the 20 most common organisms, representing 6685 isolates, underwent susceptibility testing) were obtained from bacteremic, urinary, respiratory and wound specimens from hospitals across Canada. The patient demographics associated with these isolates have been described (12).

**Most common organisms isolated from Canadian hospitals**

The 20 most common organisms isolated from hospitals across Canada included 3178 Gram-positive cocci: MSSA, *S pneumoniae*, MRSA, coagulase-negative staphylococci/*Staphylococcus epidermidis* and *Enterococcus* species, as well as 3507 Gram-negative bacilli including *E coli*, *P aeruginosa*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, *Enterobacter cloacae* and *Proteus mirabilis* (12).

**Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)**

In vitro activity of various antimicrobials against MSSA, MRSA (including HA-MRSA and CA-MRSA), coagulase-negative...
staphylococci/S. epidermidis (including both methicillin-susceptible [MSSE] and methicillin-resistant [MRSE] S. epidermidis), S. pneumoniae, Streptococcus pyogenes, Streptococcus agalactiae, Enterococcus faecalis and E. faecium including VRE is displayed in Table 1. Limited resistance was observed against MSSA with the exception of clarithromycin (26.2%), fluoroquinolones (range 9.5% to 12.0%) and clindamycin (8.6%) (Table 1). One hundred per cent susceptibility was observed with ceftazolin, daptomycin, ertapenem, linezolid, meropenem, piperacillin-tazobactam, tigecycline and vancomycin. Dalbavancin and telavancin were active with MIC_{90} of 0.06 µg/mL and 0.25 µg/mL, respectively. Resistance rates with MRSA were 87.9% to 89.0% to fluoroquinolones, 90.5% to clindamycin, 61.2% to clindamycin and 12.3% to trimethoprim-sulfamethoxazole (TMP-SMX). The most active agents tested against MRSA were vancomycin, daptomycin, linezolid and tigecycline with 100% susceptibility and MIC_{90} of 1 µg/mL, 0.25 µg/mL or less, respectively. Dalbavancin and telavancin demonstrated limited activity and MIC_{90} of 2 µg/mL, 0.25 µg/mL and 1 µg/mL, respectively (Table 1).  

### Table 1

Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

| % S | % I | % R | MIC_{50} | MIC_{90} | Range Min | Range Max |
|-----|-----|-----|----------|----------|-----------|-----------|
|     |     |     |          |          |           |           |
| **Methicillin-susceptible Staphylococcus aureus (n=1095)** | | | | | | |
| Cefazolin | 100 | >0.5 | 1 | ≤0.5 | 2 | |
| Cefepime | 99.8 | 0.2 | 4 | ≤1 | 16 | |
| Ceftriaxone | 99.6 | 0.4 | 4 | ≥1 | 16 | |
| Ciprofloxacin | 83.7 | 4.2 | 12 | ≤0.06 | >16 | |
| Clarithromycin | 73.2 | 0.6 | 26.2 | ≤0.25 | >16 | ≤0.03 | >32 |
| Clindamycin | 91 | 0.4 | 8.6 | ≤0.25 | ≤0.02 | ≤0.12 | >8 |
| Dalbavancin | No BP | 0.06 | 0.06 | ≤0.03 | 0.25 | |
| Daptomycin | 100 | 0.12 | 0.25 | ≤0.06 | 1 | |
| Ertapenem | 100 | 0.25 | 0.25 | 0.12 | 0.5 | |
| Levofloxacin | 89.7 | 0.3 | 10 | 0.25 | 4 | ≤0.06 | >32 |
| Linezolid | 100 | 2 | 4 | ≤0.12 | 0.4 | |
| Meropenem | 100 | ≤0.12 | 0.12 | ≤0.06 | 1 | |
| Moxifloxacin | 90 | 0.6 | 9.5 | ≤0.06 | 1 | ≤0.06 | >16 |
| Nitrofurantoin | 100 | 16 | 16 | ≤0.5 | 32 | |
| Piperacillin/Tazobactam | 100 | ≤1 | ≤1 | ≤1 | 0.25 | 2 | |
| **Methicillin-resistant S. aureus (MRSA) (n=385)** | | | | | | |
| Cefazolin | 100 | 0.0* | 64 | >128 | 0.5 | >128 |
| Cefepime | 99.8 | >0.12 | >128 | 2 | >256 | |
| Ceftriaxone | 99.6 | >0.12 | >256 | 2 | >256 | |
| Ciprofloxacin | 10.8 | 0.2 | 89 | >16 | 16 | 0.25 | >16 |
| Clarithromycin | 38.6 | 0.3 | 61.2 | >8 | >8 | ≤0.12 | >8 |
| Clindamycin | 9.5 | 90.5 | >16 | ≤32 | ≤0.12 | >32 | |
| Dalbavancin | No BP | 0.06 | 0.06 | ≤0.03 | 0.12 | |
| Daptomycin | 100 | 0.12 | 0.25 | 0.12 | 1 | |
| Ertapenem | 100 | 0.0* | 8 | ≤32 | 0.12 | >32 | |
| Levofloxacin | 11.6 | 88.4 | >32 | ≤32 | 0.12 | >32 | |
| Linezolid | 100 | 2 | 4 | 0.25 | 4 | |
| Meropenem | 100 | 0.0* | 8 | ≥32 | 0.12 | >64 | |
| Moxifloxacin | 11.6 | 0.5 | 87.9 | >16 | ≤0.06 | >16 | |
| Nitrofurantoin | 100 | 16 | 16 | 8 | 32 | |
| Piperacillin/Tazobactam | 100 | 0.0* | 32 | 128 | ≤1 | 256 | |
| **Health care-associated MRSA (n=285)** | | | | | | |
| Cefazolin | 100 | 0.0* | 128 | >128 | 1 | >128 | |
| Cefepime | 99.8 | >256 | >256 | 4 | >32 | |
| Ceftriaxone | 99.6 | >256 | >256 | 2 | >64 | |
| Ciprofloxacin | 2.1 | 97.9 | >16 | >16 | 0.25 | >16 | |
| Clarithromycin | 25.3 | 0.3 | 74.4 | >8 | >8 | ≤0.25 | >8 |
| Clindamycin | 3.2 | 96.8 | >16 | >16 | ≤0.12 | >16 | |
| Dalbavancin | No BP | 0.06 | 0.06 | ≤0.03 | 0.12 | |
| Daptomycin | 100 | 0.12 | 0.25 | 0.12 | 1 | |
| Ertapenem | 100 | 0.0* | 16 | ≤32 | 0.5 | >32 | |
| Levofloxacin | 2.1 | 97.9 | >32 | ≤32 | 0.12 | >32 | |
| Linezolid | 100 | 2 | 4 | 0.25 | 4 | |
| Meropenem | 100 | 0.0* | 8 | ≤32 | 0.25 | >32 | |

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### TABLE 1 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

|                     | % S | % I | % R | MIC<sub>50</sub> | MIC<sub>90</sub> | Range | Min | Max |
|---------------------|-----|-----|-----|------------------|------------------|-------|-----|-----|
| **Health care-associated MRSA (n=285)** – CONTINUED |     |     |     |                  |                  |       |     |     |
| Ciprofloxacin       | 39.9| 58.6| 8   | 0.03            | 128              | 2     | 58.6| 22.6| 18.8| 8   |
| Nitrofurantoin      | 60.1| 22.6| 18.8| 8               | 0.03             | 128   | 2   |
| Piperacillin/Tazobactam | 100.0*| 64 | 128 | 2 | 256 |
| Telavancin          | No BP| 0.25| 0.25| 0.12 | 1 |
| Tigecycline         | 100  | 0.25| 0.5 | 0.12 | 0.5 |
| TMP/SMX            | 83.9 | 16.1| ≤0.12| >8 | ≤0.12| >8 |
| Vancomycin         | 100  | 1   | 1 | ≤0.25 | 2 |
| **Community-associated MRSA (n=71)** |     |     |     |                  |                  |       |     |     |
| Cefazolin           | 100.0*| 8  | 32  | 1 | 128 |
| Cefepime            | 100.0*| 32| >32 | 8 | >32 |
| Ceftriaxone         | 100.0*| 32| >64 | 16 | >64 |
| Ciprofloxacin       | 38.1 | 14.6| 60.6| 16 | >16| 0.25 | >16 |
| Clindamycin         | 90.1 | 9.9 | ≤0.25| 16 | >0.25| >0.25| >8 |
| Clarithromycin      | 28.2 | 21.8| >16 | 16 | >16| >16 | >16 |
| Dalbavancin         | No BP| 0.06| 0.06| 0.03 | 0.12 |
| Daptomycin         | 100  | 0.12| 0.5 | 0.12 | 0.5 |
| Ertapenem          | 100.0*| 2 | 4 | 0.25 | 8 |
| Levofloxacin        | 42.3 | 57.7| 4  | 8 | 0.12| 16 |
| Linezolid           | 100  | 2  | 2 | 1 | 4 |
| Meropenem           | 100.0*| 1 | 4 | 0.25 | 8 |
| Moxifloxacin        | 42.3 | 14.5| 65.3| 2 | 2| 0.06 | 4 |
| Nitrofurantoin      | 100  | 16 | 16| 16 | 16 |
| Piperacillin/Tazobactam | 100.0*| 16 | 32 | 2 | 64 |
| Telavancin          | No BP| 0.25| 0.25| 0.12 | 0.5 |
| Tigecycline         | 100  | 0.25| 0.25| 0.06 | 0.25 |
| TMP/SMX            | 100  | ≤0.12| ≤0.12| 1 | ≤0.12| 1 |
| Vancomycin         | 100  | 1  | 1 | 0.5 | 1 |
| **Coagulase-negative staphylococci (n=182)** |     |     |     |                  |                  |       |     |     |
| Cefazolin           | 84.8 | 1.1 | 14.1| 1 | 64 | ≤0.5 | >128 |
| Cefepime            | 71.7 | 9.8 | 18.5| 4 | 128 | ≤1 | >128 |
| Ceftriaxone         | 69.4 | 14.3| 16.3| 8 | >256| 0.5| >256 |
| Ciprofloxacin       | 38.8 | 1 | 60.2| 16 | >16| 0.12| >16 |
| Clindamycin         | 43.9 | 2 | 54.1| 16 | >16| >16| >16 |
| Clarithromycin      | 71.4 | 28.6| ≤0.25| >8 | ≤0.12| >8 |
| Dalbavancin         | No BP| 0.03| 0.06| 0.03 | 0.12 |
| Daptomycin         | 100  | 0.12| 0.25| 0.06 | 0.5 |
| Ertapenem          | 83.3 | 16.7| 0.5 | >4 | 0.12| >4 |
| Levofloxacin        | 39.8 | 4.1 | 56.1| 8 | >32| ≤0.06| >32 |
| Linezolid           | 100  | 1  | 1 | 0.12 | 4 |
| Meropenem           | 75.5 | 9.2 | 15.3| 1 | 16 | ≤0.06| 32 |
| Moxifloxacin        | 42.9 | 6.1 | 51  | 2 | >16| ≤0.06| >16 |
| Piperacillin/Tazobactam | 88.8 | 11.2| 16 | 1 | 16 | ≤1 | 256 |
| Telavancin          | No BP| 0.12| 0.12| 0.06 | 0.12 |
| Tigecycline         | No BP| 0.25| 0.5 | 0.06 | 1 |
| TMP/SMX            | 64.3 | 35.7| 0.5 | 8 | ≤0.12| >8 |
| Vancomycin         | 100  | 1  | 2 | 0.5 | 2 |
| **Staphylococcus epidermidis (n=135)** |     |     |     |                  |                  |       |     |     |
| Cefazolin           | 83.1 | 1.5 | 15.4| 1 | 64 | ≤0.5| 128 |
| Cefepime            | 72.3 | 6.9 | 20.8| 8 | >32| ≤0.25| 128 |
| Ceftriaxone         | 58.6 | 22.6| 18.8| 8 | >64| ≤0.25| >256 |
| Ciprofloxacin       | 39.9 | 60.1| 8  | >16| ≤0.06| >16 |

Continued in next column
**TABLE 1 – CONTINUED**

Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

| % S | % I | % R | MIC<sub>50</sub> | MIC<sub>90</sub> | Range | Range | Max |
|-----|-----|-----|-----------------|-----------------|-------|-------|-----|
| **Methicillin-resistant S epidermidis (n=20)** – CONTINUED | | | | | | | |
| Telavancin | No BP | 0.25 | 0.25 | 0.12 | 0.25 | | |
| Tigecycline | No BP | 0.25 | 0.25 | 0.06 | 0.5 | | |
| TMP/SMX | 75 | 75 | 4 | 6 | ≤0.12 | 8 | |
| Vancomycin | 100 | 1 | 2 | 1 | 2 | | |
| **Streptococcus pneumoniae – all (n=702)** | | | | | | | |
| Amoxicillin/ | 99.4 | 0.4 | 0.2 | ≤0.06 | 0.12 | ≤0.08 | 8 | |
| Clavulanate | | | | | | | |
| Cefuroxime | 95.4 | 2.1 | 2.5 | ≤0.25 | ≤0.25 | ≤0.25 | >16 | |
| Ceftibuten | 99.7 | 1 | 0.2 | <0.06 | 0.12 | ≤0.06 | 4 | |
| Ciprofloxacin | 95.6 | 4.4 | 1 | 2 | ≤0.06 | >16 | | |
| Clarithromycin | 80.9 | 6 | 1 | 3 | ≤0.03 | 2 | ≤0.03 | >32 | |
| Clindamycin | 94 | 0.2 | 5.8 | ≤0.12 | ≤0.12 | ≤0.12 | >8 | |
| Dalbavancin | No BP | ≤0.03 | ≤0.03 | ≤0.03 | ≤0.12 | 0.12 | | |
| Daptomycin | No BP | 0.06 | 0.12 | 0.06 | 0.12 | | | |
| Doxycycline | 93 | 2.6 | 4.4 | ≤0.25 | 1 | ≤0.25 | >16 | |
| Ertapenem | 99.8 | 0.2 | 0.6 | ≤0.06 | ≤0.06 | ≤0.06 | 4 | |
| Levofloxacin | 99.4 | 0.6 | 0.5 | 1 | ≤0.06 | 32 | | |
| Linezolid | 100 | 0.5 | 1 | ≤0.12 | 2 | | | |
| Meropenem | 97.1 | 2.6 | 0.3 | ≤0.06 | ≤0.06 | ≤0.06 | 2 | |
| Moxifloxacin | 99.1 | 0.3 | 0.6 | 0.12 | 0.25 | 0.25 | 0.6 | |
| Penicillin | 79.1 | 1 | 5.7 | 0.06 | 0.25 | 0.03 | 8 | |
| Piperacillin/ | No BP | ≤1 | ≤1 | ≤1 | 4 | | | |
| Tazobactam | | | | | | | |
| Telavancin | No BP | ≤0.06 | ≤0.06 | ≤0.06 | 0.12 | | | |
| Telithromycin | 100 | 0.015 | 0.3 | ≤0.008 | 0.5 | | | |
| Tigecycline | No BP | ≤0.03 | ≤0.03 | ≤0.03 | 0.12 | | | |
| TMP/SMX | 86.2 | 6.7 | 7.1 | ≤0.12 | 1 | ≤0.12 | >8 | |
| Vancomycin | 100 | ≤0.25 | ≤0.25 | ≤0.25 | 0.5 | | | |
| **Streptococcus pyogenes (n=105)** | | | | | | | |
| Ceftriaxone | 100 | ≤0.06 | ≤0.06 | ≤0.06 | ≤0.06 | | | |
| Ciprofloxacin | No BP | 1 | 2 | 0.25 | 4 | | | |
| Clarithromycin | 90.4 | 9.6 | ≤0.03 | 0.12 | ≤0.03 | >32 | | |
| Clindamycin | 97.3 | 2.7 | ≤0.12 | ≤0.12 | ≤0.12 | >8 | | |
| Dalbavancin | No BP | ≤0.03 | ≤0.03 | ≤0.03 | ≤0.03 | | | |
| Daptomycin | 100 | ≤0.03 | 0.06 | ≤0.03 | 0.12 | | | |
| Ertapenem | 100 | ≤0.06 | ≤0.06 | ≤0.06 | ≤0.06 | | | |
| Levofloxacin | 98.6 | 1.4 | 0.5 | 1 | 0.25 | 4 | | |
| Linezolid | 100 | 1 | 1 | 0.5 | 2 | | | |
| Meropenem | 100 | ≤0.06 | ≤0.06 | ≤0.06 | ≤0.06 | | | |
| Moxifloxacin | No BP | 0.12 | 0.25 | 0.06 | 0.5 | | | |
| Piperacillin/ | No BP | ≤1 | ≤1 | ≤1 | ≤1 | | | |
| Tazobactam | | | | | | | |
| Telavancin | No BP | ≤0.06 | ≤0.06 | ≤0.06 | ≤0.06 | | | |
| Tigecycline | 100 | ≤0.03 | ≤0.03 | ≤0.03 | ≤0.12 | 0.12 | 0.25 | |
| TMP/SMX | No BP | ≤0.12 | ≤0.12 | ≤0.12 | 0.25 | | | |
| Vancomycin | 100 | 0.5 | 0.5 | 0.25 | 0.5 | | | |
| **Streptococcus agalactiae (n=116)** | | | | | | | |
| Ceftriaxone | 100 | ≤0.06 | ≤0.06 | ≤0.06 | 0.25 | | | |
| Ciprofloxacin | No BP | 1 | 2 | 0.5 | >16 | | | |
| Clarithromycin | 75 | 3.4 | 21.6 | ≤0.03 | >32 | ≤0.03 | >32 | |
| Clindamycin | 85.2 | 2.3 | 12.5 | ≤0.12 | >8 | ≤0.12 | >8 | |
| Dalbavancin | No BP | ≤0.03 | ≤0.03 | ≤0.03 | ≤0.03 | | | |
| Daptomycin | 100 | 0.12 | 0.12 | ≤0.03 | 0.12 | | | |
| Ertapenem | 100 | ≤0.06 | ≤0.06 | ≤0.06 | ≤0.06 | | | |

*Continued in next column*
TABLE 1 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

| Enterococcus faecium (n=60) | % S | % I | % R | **MIC**<sub>50</sub> | **MIC**<sub>90</sub> | Range <br>Min | Range <br>Max |
|---------------------------|-----|-----|-----|-------------------|-------------------|-------------|-------------|
| Ceftriaxone                | No BP | >64 | >256 | 0.5 | >256 |
| Ciprofloxacin             | 12.1 | 5.1 | 82.8 | >16 | >16 | 1 | >16 |
| Clarithromycin            | No BP | >32 | >32 | 0.5 | >32 |
| Clindamycin               | No BP | >8 | >8 | ≤0.12 | >8 |
| Dalbavancin               | No BP | 0.12 | 0.25 | ≤0.03 | >16 |
| Daptomycin                | 100 | 1 | 0.12 | 2 |
| Ertapenem                 | No BP | >32 | >32 | 4 | >32 |
| Levofloxacin              | 17.2 | 3.5 | 79.3 | >32 | >32 | 1 | >32 |
| Linezolid                 | 91.4 | 8.6 | 2 | 2 | 1 | 4 |
| Meropenem                 | No BP | >32 | >64 | 4 | >64 |
| Moxifloxacin              | No BP | >16 | >16 | ≤0.25 | >16 |
| Nitrofurantoin            | 40.6 | 32.4 | 27 | 64 | 128 | 8 | 128 |
| Piperacillin/ Tazobactam  | No BP | >512 | >512 | 2 | >512 |
| Telavancin                | No BP | 0.12 | 0.5 | ≤0.06 | 4 |
| Tigecycline               | 100 | 0.12 | 0.12 | 0.06 | 0.5 |
| Vancomycin                | 88.3 | 11.7 | 0.5 | >8 | ≤0.25 | >8 |
| **Vancomycin-resistant enterococci (n=8)**<sup>†</sup> | | | | | | | |
| Cefazolin                 | No BP | >128 | >128 | >128 | >128 |
| Cefepime                  | No BP | >128 | >128 | >128 | >128 |
| Ceftriaxone               | No BP | >256 | >256 | >64 | >256 |
| Ciprofloxacin             | 100 | >16 | >16 | >16 | >16 |
| Clarithromycin            | No BP | >16 | >32 | 2 | >32 |
| Clindamycin               | No BP | >8 | >8 | ≤0.25 | >8 |
| Dalbavancin               | No BP | 0.5 | >16 | 0.06 | >16 |
| Daptomycin                | 100 | 1 | 0.25 | 2 |
| Ertapenem                 | No BP | >32 | >32 | >32 | >32 |
| Levofloxacin              | No BP | >100 | >32 | >32 | >32 |
| Linezolid                 | 75 | 25 | 2 | 4 | 1 | 4 |
| Meropenem                 | No BP | >64 | >64 | >32 | >64 |
| Moxifloxacin              | No BP | >16 | >16 | >16 | >16 |
| Nitrofurantoin            | 50 | 50 | 64 | 128 | 64 | 128 |
| Piperacillin/ Tazobactam  | No BP | >512 | >512 | >512 | >512 |
| Telavancin                | No BP | 0.12 | 4 | 0.12 | 4 |
| Tigecycline               | 100 | 0.06 | 0.12 | 0.06 | 0.12 |
| Vancomycin                | 100 | >8 | >8 | >8 | >8 |

<sup>†</sup>Based upon oxacillin susceptibility; <sup>†</sup>5 vanA and 3 vanB, I intermediate, Max Maximum; **MIC**<sub>50/90</sub> Minimum inhibitory concentrations (in µg/mL) required to inhibit 50%/90% of organisms; Min Minimum; No BP No Clinical and Laboratory Standards Institute (or Food and Drug Administration for tigecycline) -approved breakpoints defined; R resistant; S susceptible

activity against VRE with **MIC**<sub>90</sub> of greater than 16 µg/mL and 4 µg/mL, respectively.

**Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-negative bacilli)**

The in vitro activity of various antimicrobials against *E coli* (including ESBL-producing *E coli*), *P aeruginosa*, *K pneumoniae*, *H influenzae*, *E cloacae*, *P mirabilis*, *Serratia marcescens*, *S maltophilia*, *Klebsiella oxytoca*, *Moraxella catarrhalis* and *A babamnii* is displayed in Table 2. For *E coli*, resistance rates were: TMP-SMX 26.6%, ciprofloxacin and levofloxacin 24.5% and 23.6%, respectively, and cefazolin 14.2% (Table 2). Limited resistance occurred with ceftazidime 8.9%, gentamicin 10.6%, nitrofurantoin 1.2%, piperacillin-tazobactam 1.3% and cefepime 2.0%. One hundred per cent susceptibility was observed with ertapenem and meropenem, while 99.8% of *E coli* were susceptible to tigecycline (Table 2). Thus, the most active agents against *E coli* were amikacin, amoxicillin-clavulanate, cefepime, meropenem, piperacillin-tazobactam and tigecycline with **MIC**<sub>90</sub> of 4 µg/mL, 8 µg/mL, 2 µg/mL, 0.06 µg/mL or less, 0.12 µg/mL or less, 4 µg/mL and 1 µg/mL, respectively. ESBL-producing *E coli* displayed 92.5% resistance to ciprofloxacin, 67.9% resistance to TMP-SMX and 58.5% resistance to gentamicin. All ESBL-producing *E coli* were susceptible to ertapenem, meropenem, nitrofurantoin and tigecycline, with **MIC**<sub>90</sub> of 0.12 µg/mL, 0.12 µg/mL or less, 32 µg/mL and 1 µg/mL, respectively. The most active agents tested against *P aeruginosa* were piperacillin-tazobactam, meropenem, colistin (polymyxin E) and amikacin, with 92.7%, 87.8%, 87.6% and 85.4% susceptibility and **MIC**<sub>90</sub> of 64 µg/mL, 8 µg/mL, 4 µg/mL and 32 µg/mL, respectively (Table 2). Resistance with *P aeruginosa* was high with fluoroquinolones 23.4% to 25.1% and gentamicin 20.8%. All agents were active against *H influenzae* except TMP-SMX, with 12.1% resistance. For *K pneumoniae*, resistance rates were: TMP-SMX 8.8%, ceftazolin 7.0%, fluoroquinolones 4.2% to 6.6%, piperacillin-tazobactam 2.0%, tigecycline 1.7% and ceftriaxone 3.1%. One hundred per cent susceptibility occurred with ertapenem and meropenem as well as 99.6% with amikacin (Table 2). With *E cloacae*, resistance rates were: ceftazolin 91.0%, ceftriaxone 18.1%, TMP-SMX 8.4%, piperacillin-tazobactam 9.1%, gentamicin 3.6%, fluoroquinolones 3.0% to 7.8% and tigecycline 1.2%. One hundred per cent susceptibility occurred with amikacin, cefepime, ertapenem and meropenem (Table 2). With *P mirabilis*, resistance rates were: ceftazolin 5.0%, TMP-SMX 9.2%, fluoroquinolones 7.6% to 9.2% and gentamicin 3.4%. One hundred per cent susceptibility occurred with cefepime, ceftriaxone, ertapenem, meropenem and piperacillin-tazobactam (Table 2). With *S marcescens*, resistance rates were: ceftazolin 99.1%, TMP-SMX 2.8%, fluoroquinolones 4.7% to 7.5%, ceftriaxone 2.8%, amikacin (Table 2). With *S maltophilia* were suscept-

**DISCUSSION**

The CANWARD study was the first national, prospective surveillance study assessing antimicrobial activity against pathogens from Canadian hospitals, including hospital clinics.
### TABLE 2
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-negative bacilli)

| Organism                        | % S | % I | % R | MIC<sub>50</sub> | MIC<sub>90</sub> | Range | Max |
|---------------------------------|-----|-----|-----|------------------|------------------|-------|-----|
| **Escherichia coli** (n=1701)   |     |     |     |                  |                  |       |     |
| Amikacin                        | 99.5| 0.4 | 0.1 | ≤2               | 4                | ≤2    | >64 |
| Amoxicillin/Clavulanate         | 90.3| 8.5 | 1.2 | 4                | 8                | 0.5   | 32  |
| Cefazolin                       | 82.1| 3.7 | 14.2| 2                | 64               | ≤0.5  | >128|
| Cefepime                        | 95.2| 2.6 | 1  | 2               | ≤0.25            | ≤0.25 | >128|
| Cefotaxime                      | 92.4| 3.8 | 3.8| 4               | ≤0.06            | ≤0.06 | >128|
| Ceftriaxone                     | 89.2| 1.9 | 8.9| 1               | ≤0.25            | ≤0.25 | >256|
| Ciprofloxacin                   | 75.2| 0.3 | 24.5| ≤0.06           | >16              | ≤0.06 | >16 |
| Colistin                        | No BP|     |     |                  |                  |       |     |
| Ertapenem                       | 100 |     |     | ≤0.06           | ≤0.06            | ≤0.06 | >16 |
| Gentamicin                      | 88.9| 10.6| 0.5| 16              | ≤0.5             | ≤0.5  | >32 |
| Levofloxacin                    | 75.7| 0.8 | 23.6| 16              | ≤0.06            | ≤0.06 | >32 |
| Meropenem                       | 100 |     |     | ≤0.12           | ≤0.12            | ≤0.12 | >16 |
| Moxifloxacin                    | No BP|     |     | ≤0.06           | >16              | ≤0.06 | >16 |
| Nitrofurantoin                  | 95.7| 3.1 | 1.2| 16              | ≤0.5             | ≤0.5  | >256|
| Piperacillin/Tigecycline        | 97.6| 1.1 | 1.3| 2               | ≤1               | ≤1    | >512|
| Tigecycline                     | 99.8| 0.2 | 0.25| 1               | 0.06             | 0.06  | 4   |
| TMP/SMX                         | 73.4| 26.0| 1.2| >8              | ≤0.12            | ≤0.12 | >8  |
| **Extended-spectrum beta-lactamase E coli** (n=53) |     |     |     |                  |                  |       |     |
| Amikacin                        | 94.3| 3.8 | 1.9| 4               | 16              | ≤2    | >64 |
| Amoxicillin/Clavulanate         | 60.4| 37.7| 1.9| 8               | 16              | 4     | 16  |
| Cefazolin                       | 100 | 128 | >128| 128            | >128            | >128  | >128|
| Cefepime                        | 45.3| 30.2| 24.5| 16              | >32             | ≤32   | >128|
| Cefotaxime                      | 92.4| 5.7 | 1.9| 8               | 4               | 8     | >32 |
| Ceftriaxone                     | 3.8 | 15.1| 81.1| >64            | >64             | 4     | >64 |
| Ciprofloxacin                   | 7.5 | 92.5| >16 | >16             | ≤0.06           | >16   | >16 |
| Colistin                        | No BP|     |     | 1               | 0.25            | 2     |     |
| Ertapenem                       | 100 |     |     | ≤0.06           | 0.12            | ≤0.06 | 0.25|
| Gentamicin                      | 41.5| 58.5| 32 | 32             | ≤32             | ≤32   | >32 |
| Levofloxacin                    | 7.5 | 92.5| 16 | 32             | ≤0.06           | ≤0.06 | >32 |
| Meropenem                       | 100 |     |     | ≤0.12           | ≤0.12           | ≤0.12 | >16 |
| Moxifloxacin                    | No BP|     |     | >16             | ≤0.06           | >16   | >16 |
| Nitrofurantoin                  | 96.2| 3.8 | 16 | 32             | 8               | 32    | 8   |
| Piperacillin/Tigecycline        | 92.4| 5.7 | 1.9| 4               | ≤1              | ≤1    | >512|
| Tigecycline                     | 100 |     | 0.5 | 1              | 0.25            | 2     |     |
| TMP/SMX                         | 32.1| 67.9| >8 | >8             | ≤0.12           | >8    | >8  |
| **Pseudomonas aeruginosa** (n=633) |     |     |     |                  |                  |       |     |
| Amikacin                        | 85.4| 7   | 7.6| 8               | 32              | ≤2    | >64 |
| Amoxicillin/Clavulanate         | No BP|     | >32 | >32            | 1               | >32   | >32 |
| Cefazolin                       | No BP|     | >128| >128           | 16             | >128  | >128|
| Cefepime                        | 67.4| 20.9| 11.7| 8              | 32              | ≤0.25 | >128|
| Cefotaxime                      | No BP|     | >32 | >32            | 2               | >32   | >32 |
| Ceftriaxone                     | 23.9| 40.9| 35.2| 32             | 256             | ≤0.25 | >256|
| Ciprofloxacin                   | 66 | 10.6| 23.4| 0.5            | 16              | ≤0.06 | >16 |
| Colistin                        | 87.6| 12.4| 2 | 4              | 0.5            | >16   | >16 |
| Ertapenem                       | No BP|     | 8   | 32             | 0.12            | ≤32   | >32 |
| Gentamicin                      | 60.2| 20.8| 1.9| 4               | ≤0.5            | ≤0.5  | >32 |
| Levofloxacin                    | 61.5| 13.4| 25.1| 2               | 16              | ≤0.06 | >64 |
| Meropenem                       | 87.8| 4.1 | 8.1| 0.5            | ≤0.06           | ≤0.06 | >64 |
| Moxifloxacin                    | No BP|     | 4   | >16            | ≤0.06           | >16   | >16 |

Continued in next column
| Organism                        | % S | % I | % R | MIC50  | MIC90  | Range | Max | Range | Max |
|--------------------------------|-----|-----|-----|--------|--------|-------|-----|-------|-----|
| Enterobacter cloacae (n=166)   |     |     |     |        |        |       |     |       |     |
| Moxifloxacin                   | No BP | >16 | >16 | ≤0.06  | >16    | >16   | >16 |
| Nitrofurantoin                 | >16 | >16 | >16 | >16    | >16    | >16   | >16 |
| Cefepime                       | ≤1  | ≤1  | ≤1  | ≤0.25  | ≥0.12  | ≥0.12 | ≥0.12 |
| Ciprofloxacin                  | ≤0.06 | >16 | >16 | >16    | >16    | >16   | >16 |
| Colistin                       | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Gentamicin                     | ≤0.06 | >16 | >16 | >16    | >16    | >16   | >16 |
| Levofloxacin                   | ≤0.06 | >16 | >16 | >16    | >16    | >16   | >16 |
| Moxifloxacin                   | ≤0.06 | >16 | >16 | >16    | >16    | >16   | >16 |
| Tigecycline                    | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Nitrofurantoin                 | >16 | >16 | >16 | >16    | >16    | >16   | >16 |
| Tigecycline                    | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Proteus mirabilis (n=119)      |     |     |     |        |        |       |     |       |     |
| Amikacin                       | 99.2 | 9.8 | 0.8 | ≤0.06  | >16    | >16   | >16 |
| Cefuroxime                     | 96.6 | 8.4 | 1.9 | ≤0.25  | ≥0.12  | ≥0.12 | ≥0.12 |
| Cefoxitin                      | 95.8 | 9.8 | 4.5 | ≤0.25  | ≥0.12  | ≥0.12 | ≥0.12 |
| Ciprofloxacin                  | 95.8 | 9.8 | 4.5 | ≤0.25  | ≥0.12  | ≥0.12 | ≥0.12 |
| Colistin                       | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Gentamicin                     | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Levofloxacin                   | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Moxifloxacin                   | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Tigecycline                    | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Nitrofurantoin                 | >16 | >16 | >16 | >16    | >16    | >16   | >16 |
| Tigecycline                    | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Serratia marcescens (n=108)    |     |     |     |        |        |       |     |       |     |
| Amikacin                       | 99.1 | 9.9 | 0.9 | ≤0.06  | >16    | >16   | >16 |
| Cefuroxime                     | 96.6 | 8.4 | 1.9 | ≤0.25  | ≥0.12  | ≥0.12 | ≥0.12 |
| Cefoxitin                      | 95.8 | 9.8 | 4.5 | ≤0.25  | ≥0.12  | ≥0.12 | ≥0.12 |
| Ciprofloxacin                  | 95.8 | 9.8 | 4.5 | ≤0.25  | ≥0.12  | ≥0.12 | ≥0.12 |
| Colistin                       | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Gentamicin                     | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Levofloxacin                   | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Moxifloxacin                   | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Tigecycline                    | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Nitrofurantoin                 | >16 | >16 | >16 | >16    | >16    | >16   | >16 |
| Tigecycline                    | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Stenotrophomonas maltophilia (n=107) |     |     |     |        |        |       |     |       |     |
| Amikacin*                      | 16   | >16 | ≤0.06 | >16 >16 | >16    | >16 |
| Cefuroxime*                    | >32  | >16 | >16 | >16    | >16    | >16   | >16 |
| Cefoxitin*                     | >128 | >128 | >128 | >128    | >128    | >128   | >128 |
| Ciprofloxacin                  | >128 | >128 | >128 | >128    | >128    | >128   | >128 |
| Colistin                       | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Gentamicin                     | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Levofloxacin                   | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Moxifloxacin                   | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Tigecycline                    | No BP | >16 | >16 | >16    | >16    | >16   | >16 |
| Nitrofurantoin                 | >16 | >16 | >16 | >16    | >16    | >16   | >16 |

Continued on next page
TABLE 2 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-negative bacilli)

| Organism                  | % S | % I | % R | MIC<sub>50</sub> | MIC<sub>90</sub> | Range Min | Range Max |
|---------------------------|-----|-----|-----|------------------|------------------|-----------|-----------|
| Acinetobacter baumannii   | 92  | 8   | ≤2  | ≤2 ≤2 ≤2         | ≥ >64            | 8 ≤0.5    | 2 >128    |
| Amoxicillin/Clavulanate   | No BP | 8  | 32  | 2 >32            |                  |           |           |
| Ceftazolin                | No BP | >128 | >128 | 64 >128         |                  |           |           |
| Cefepime                  | 84  | 8   | 16  | 8 ≤1 >128       |                  |           |           |
| Cefoxitin                 | No BP | >32  | >32  | 8 >32           |                  |           |           |
| Ceftriaxone               | 8  | 32  | 16  | 8 ≤2 >32       |                  |           |           |
| Ciprofloxacin             | 88  | 12  | 0.25| 4 ≤0.12 >32    |                  |           |           |
| Colistin                  | 1   | 2   | 1   | 2               |                  |           |           |
| Ertapenem                 | No BP | 4   | 8   | 2 >32           |                  |           |           |
| Gentamicin                | 92  | 8   | ≤0.5| 1 ≤0.12 >32    |                  |           |           |
| Levofloxacin              | 92  | 8   | 0.25| 0.25 ≤0.12 >32 |                  |           |           |
| Meropenem                 | 92  | 8   | 0.4 | ≤0.12 >32      |                  |           |           |
| Moxifloxacin              | No BP | 0.12| 0.12| 0.06 >32       |                  |           |           |
| Nitrofurantoin            | No BP | >256| >256| >256 >256      |                  |           |           |
| Piperacillin/TMP/SMX       | 76  | 12  | 4   | ≥ >128 s1      |                  |           |           |
| Ticarcillin               | No BP | 0.5 | 2   | 0.12 >4        |                  |           |           |
| Tazobactam                | 84  | 16  | ≤0.12| ≥ >8          |                  |           |           |

*Non-Enterobacteriaceae breakpoints used: Colistin (polymyxin E): Intermediate; Max Maximum; MIC<sub>50</sub> Minimum inhibitory concentrations (in µg/mL) required to inhibit 50%/90% of organisms; Min Minimum; No BP No Clinical and Laboratory Standards Institute (or Food and Drug Administration for tigecycline) approved breakpoints defined. R Resistant; S Susceptible; TMP-SMX Trimethoprim-sulfamethoxazole

emergency rooms, medical and surgical wards, and intensive care units. A total of 7881 organisms were obtained between January 1, 2007, and December 31, 2007, inclusive. Of the 7881 organisms, 6885 (87.4%) represented the 20 most common organisms isolated from hospitals in Canada and underwent antimicrobial susceptibility testing.

The most active agents (based upon MIC data only) against the 3178 Gram-positive organisms tested were vancomycin, linezolid, dalbavancin, tigecycline, and tigecycline. Tigecycline was active against MSSA and MRSA with 100% of isolates demonstrating susceptibility with MICs of 1 µg/mL or less (Table 1). No difference in linezolid activity was observed between HA-MRSA and CA-MRSA. Linezolid was more active against MSSE and MRSE in comparison with MSSA and MRSA, with all isolates demonstrating linezolid MICs of 1 µg/mL or less (Table 1). Linezolid’s continued excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (11,16,17). As has been previously documented, linezolid continues to be active against Strepococcus species with all isolates displaying MICs of 2 µg/mL or less (11,17). Linezolid was less active against E faecalis and E faecium, with 1.3% and 8.6% of strains demonstrating intermediate resistance, respectively. This rate of linezolid resistance in E faecium is consistent with previous reports (17-19).

Daptomycin was active against MSSA and MRSA with 100% of isolates demonstrating susceptibility, with MICs of 1 µg/mL or less (Table 1). No difference in daptomycin activity was observed between HA-MRSA and CA-MRSA. Daptomycin was equally active against MSSE and MRSE compared with MSSA and MRSA, with all isolates demonstrating daptomycin MICs of 0.25 µg/mL or less. Daptomycin’s excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (11,16). As has been previously reported (11,16), daptomycin was active against Streptococcus species with isolates displaying MICs of 0.12 µg/mL or less. Daptomycin was active against E faecalis, E faecium, and VRE, with 100% susceptibility and all isolates displaying MICs of 2 µg/mL or less (Table 1). Daptomycin-resistant enterococci species continue to be rare (18) and have not been documented in Canada. From these data, it is clear daptomycin is a very active agent against all Gram-positive organisms causing infections in Canadian hospitals.

Tigecycline was active against MSSA and MRSA with 100% of isolates demonstrating susceptibility, with MICs of 0.5 µg/mL or less (Table 1). No difference in tigecycline activity was observed between HA-MRSA and CA-MRSA. Tigecycline was equally active against MSSE and MRSE compared with MSSA and MRSA, with all isolates demonstrating tigecycline MICs of 0.25 µg/mL or less (11,16,17). As has been previously documented, tigecycline is a very active agent against all Strepococcus species with isolates displaying MICs of 1 µg/mL or less (9,16). Tigecycline was less active against E faecalis and E faecium with 0% and 11.7% of strains resistant, respectively. As has been reported elsewhere, the predominant VRE genotype in North America continues to be vanA (4,7).

Linezolid was active against MSSA and MRSA with 100% of isolates demonstrating susceptibility with MICs of 4 µg/mL or less (Table 1). No difference in linezolid activity was observed between HA-MRSA and CA-MRSA. Linezolid was more active against MSSE and MRSE in comparison with MSSA and MRSA, with all isolates demonstrating linezolid MICs of 1 µg/mL or less (Table 1). Linezolid’s continued excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (11,16,17). As has been previously documented, linezolid continues to be active against Strepococcus species with all isolates displaying MICs of 2 µg/mL or less (11,17). Linezolid was less active against E faecalis and E faecium, with 1.3% and 8.6% of strains demonstrating intermediate resistance, respectively. This rate of linezolid resistance in E faecium is consistent with previous reports (17-19).

Daptomycin was active against MSSA and MRSA with 100% of isolates demonstrating susceptibility, with MICs of 1 µg/mL or less (Table 1). No difference in daptomycin activity was observed between HA-MRSA and CA-MRSA. Daptomycin was equally active against MSSE and MRSE compared with MSSA and MRSA, with all isolates demonstrating daptomycin MICs of 0.25 µg/mL or less. Daptomycin’s excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (11,16). As has been previously reported (11,16), daptomycin was active against Streptococcus species with isolates displaying MICs of 0.12 µg/mL or less. Daptomycin was active against E faecalis, E faecium, and VRE, with 100% susceptibility and all isolates displaying MICs of 2 µg/mL or less (Table 1). Daptomycin-resistant enterococci species continue to be rare (18) and have not been documented in Canada. From these data, it is clear daptomycin is a very active agent against all Gram-positive organisms causing infections in Canadian hospitals.
MICs of 0.12 µg/mL or less. Dalbavancin’s excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (11,20). As has been previously reported (11,20), dalbavancin was active against Strepococcus species with isolates displaying MICs of 0.12 µg/mL or less. Dalbavancin was active against E faecalis, but displayed less activity against E faecium and VRE (Table 1).

Telavancin was active against MSSA and MRSA with 100% of isolates demonstrating MICs of 1 µg/mL or less (Table 1). No difference in telavancin activity was observed between HA-MRSA and CA-MRSA. Telavancin was equally active against MSSA and MRSE, with all isolates demonstrating MICs of 0.25 µg/mL or less. Telavancin’s excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (20,21). As has been previously reported (21), telavancin was active against Strepococcus species with isolates displaying MICs of 0.12 µg/mL or less. Telavancin was active against E faecalis, but displayed less activity against E faecium and VRE (Table 1). It has been previously documented that telavancin is active against VanB Enterococcus species, but not VanA Enterococcus species (21).

The most active (based on MIC only) agents against the 3507 Gram-negative bacilli obtained from Canadian hospitals were amikacin, cefepime, ertapenem (not P aeruginosa), meropenem, piperacillin-tazobactam and tigecycline (not P aeruginosa) (Table 2). Amikacin was very active against E coli (including ESBL-producing strains) with 99.5% of strains testing susceptible with an MIC90 of 4 µg/mL. Likewise, amikacin proved to be very active against all other Enterobacteriaceae tested (Table 2). Against P aeruginosa, amikacin proved to be one of the most active agents tested, with 85.4% of strains testing susceptible with MIC90 of 32 µg/mL. Against A baumannii, amikacin P aeruginosa was very active with 92.0% of strains being susceptible with MIC90 of 2 µg/mL or less. The excellent activity of amikacin against both Enterobacteriaceae as well as nonfermenters isolated from patients in hospitals, including in the intensive care unit, is not surprising because the reduced usage of aminoglycosides in favour of fluoroquinolones over the past 15 years has resulted in maintained activity of aminoglycosides in the setting on increasing fluoroquinolone resistance (4,19,22). Thus, amikacin represents a potential option for the treatment of infections caused by Gram-negative bacilli resistant to other less toxic agents.

In the present study, we reported that cefepime, ertapenem, meropenem and piperacillin-tazobactam were very active against Gram-negative bacilli isolated from patients in Canadian hospitals. These agents were active against Enterobacteriaceae including against E coli (only ertapenem and meropenem were active against ESBL-producing strains). Against P aeruginosa, resistance was piperacillin-tazobactam 7.3%, meropenem 8.1% and cefepime 11.7%. Previous investigators have reported the ongoing excellent activity of these agents versus Gram-negative bacilli isolated from hospitalized patients (4,19,22). Colistin was found to be very active against E coli (including ESBL strains) with MIC90 of 1 µg/mL. Colistin was also very active against Klebsiella species, E cloacae and P mirabilis. Against P aeruginosa, resistance to colistin was 12.4% with an MIC90 of 4 µg/mL (Table 2). Against A baumannii, colistin was also very active, with an MIC90 of 2 µg/mL (Table 2). These data are consistent with other reports of the promising potential of colistin for Gram-negative bacilli such as P aeruginosa and A baumannii (23,24).

Tigecycline demonstrated 99.8% susceptibility versus E coli (100% versus ESBL-producing strains) and was also active against other Enterobacteriaceae including K pneumoniae, E cloacae, S marcescens and K oxytoca (Table 2). Tigecycline was not active against P mirabilis and P aeruginosa. Tigecycline also proved to be active against S maltophilia and A baumannii organisms frequently resistant to other antimicrobial classes (Table 2). The activity of tigecycline against Gram-negative bacilli (with the exception of P aeruginosa) has been previously reported and supports the potential to use this agent for the treatment of infections caused by non-Pseudomonas Gram-negative bacilli in hospitalized patients (11,19).

The present study has several limitations, including the fact that we can not be certain that all clinical specimens represented active infection. In the CANWARD study, we asked centres to obtain ‘clinically significant’ specimens from patients with a presumed infectious disease. Although all of the isolates may not represent actual infection from patients, we believe that most do because we excluded all surveillance swabs and duplicate swabs, as well as eye, ear, nose and throat swabs and genital cultures. In addition, we do not have admission date data for each patient/clinical specimen, thus were not able to provide a more accurate description of community versus nosocomial onset. Finally, susceptibility testing was not performed for all antimicrobial agents due to lack of space on the susceptibility panels utilized. It is recognized that data on antimicrobials such a ceftazidime, imipenem, tobramycin and others would be beneficial, because different hospital formularies stock these and other antimicrobials not tested in this study.

CONCLUSIONS

The most active agents versus Gram-positive cocci from Canadian hospitals were vancomycin, linezolid, daptomycin, tigecycline, dalbavancin and telavancin. The most active agents versus Gram-negative bacilli from Canadian hospitals were amikacin, cefepime, ertapenem (not P aeruginosa), meropenem, piperacillin-tazobactam and tigecycline (not P aeruginosa). Colistin was very active against P aeruginosa and A baumannii.

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