



Antimicrobial Susceptibility of 56,936 Pathogens Isolated from Patients in Canadian Hospitals: 15 Years of the CANWARD Study 2007-2021

G.G. ZHANEL¹, M. BAXTER¹, A. GOLDEN¹, B. FUNK¹, P. LAGACÉ-WIENS¹, J. FULLER³, R. DAVIDSON⁴, J. BLONDEAU⁵, S. POUTANEN⁶, C. LAVALLÉE⁷, J. KARLOWSKY¹, R. TAYLOR¹,
A. WALKTY¹, D. BAY¹, F. SCHWEIZER¹, M.R. MULVEY^{1,2}, G. GOLDING^{1,2}, the CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE (CARA) and H. ADAM¹

¹University of Manitoba and ²National Microbiology Laboratory, Winnipeg, Canada; ³Western University, London, Canada; ⁴Queen Elizabeth II HSC, Halifax, Canada; ⁵Royal University Hospital, Saskatoon, Canada; ⁶Mount Sinai Hospital, Toronto, Canada, and ⁷Hôpital Maisonneuve-Rosemont, Montreal, Canada



University
of Manitoba

Dr. George G. Zhanel
MS673-820 Sherbrook Street
Winnipeg, MB R3A 1R9
CANADA
Email: ggzhanel@pcsinetnet.ca

Introduction

Antimicrobial-resistant Gram-positive organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA, community associated [CA] and healthcare associated [HA]), vancomycin-resistant *Enterococcus species* (VRE), penicillin-resistant *Streptococcus pneumoniae*, and Gram-negative bacilli such as extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella* species as well as fluoroquinolone-resistant and carbapenem-resistant Enterobacterales and *Pseudomonas aeruginosa* are increasing in prevalence in Canada and around the world (1, 2). Available therapeutic options for the treatment of these antimicrobial-resistant organisms are limited as these organisms frequently display a multidrug-resistant (MDR) phenotype and sometimes an extremely drug-resistant (XDR) phenotype (1, 2).

CANWARD (a collaboration between the Canadian Antimicrobial Resistance Alliance and the National Microbiology Laboratory) is a national ongoing surveillance study which assesses pathogens and antimicrobial resistance patterns in respiratory, bloodstream, urinary, and wound/IV site infection isolates from patients receiving care in medical/surgical wards, intensive care units, emergency rooms and outpatient clinics of Canadian hospitals.

Materials and Methods

Participating Sites

From January 2007 to October 2021, tertiary-care medical centres in major population centres in 8 of the 10 provinces in Canada were recruited (1, 2). These sites were geographically distributed in a population-based fashion.

Bacterial Isolates

Tertiary-care medical centres submitted pathogens from patients attending hospital clinics, emergency rooms, medical and surgical wards, and intensive care units. Each study site was asked to submit clinical isolates (consecutive, one per patient, per infection site) from inpatients and outpatients with respiratory, urine, wound, and bloodstream infections. Isolate identification was performed by the submitting site and confirmed at the reference site. Isolates were shipped on Amies semi-solid transport media to the coordinating laboratory (Health Sciences Centre, Winnipeg, Canada), subcultured onto appropriate media, and stocked in skim milk at -80°C until minimum inhibitory concentration (MIC) testing was carried out. From 2007-2021, between 2231 and 7718 isolates were collected in each year of the study (1, 2).

Antimicrobial Susceptibilities

The *in vitro* activity of selected antimicrobials was determined by broth microdilution in accordance with CLSI guidelines (3). MICs were determined using 96-well custom designed microtitre plates. These plates contained doubling antimicrobial dilutions in 100 μ L/well of cation adjusted Mueller-Hinton broth (or MHB supplemented with lysed horse blood, where required) and inoculated to achieve a final concentration of approximately 5 x 10⁵ CFU/mL. Colony counts were performed periodically to confirm inocula. Quality control was performed using ATCC QC organisms including *S. pneumoniae* 49619, *S. aureus* 29213, *E. faecalis* 29212, *E. coli* 25922, and *P. aeruginosa* 27853. MICs were interpreted using CLSI breakpoints (4).

Table 1. Antimicrobial activity against the most common Gram-positive cocci isolated from Canadian hospitals

| Organism (no. tested) / Antimicrobial Agent | % S | % I | % R | MIC (μ g/mL) | | | |
|---|-------------------|------------------|------------------|-------------------|-------------------|--------------|-------------|
| | | | | MIC ₅₀ | MIC ₉₀ | Range Min | Range Max |
| | | | | | | | |
| Staphylococcus aureus, MSSA (9,397) | | | | | | | |
| Cefoxitin ^a | 100 | | | 4 | 4 | 0.12 | 4 |
| Ceftazidime ^b | 100 | | | ≤ 1 | ≤ 1 | ≤ 1 | 2 |
| Ceftriaxone | 100 | | | 4 | 4 | ≤ 1 | > 64 |
| Ciprofloxacin | 87.2 | 3.0 | 9.8 | 0.5 | 2 | ≤ 0.06 | > 16 |
| Clarithromycin | 75.6 | 0.6 | 23.7 | 0.25 | > 32 | ≤ 0.03 | > 32 |
| Clindamycin | 93.9 | 0.4 | 5.7 | ≤ 0.12 | ≤ 0.12 | ≤ 0.12 | > 8 |
| Daptomycin | 99.9 ^c | | | 0.1 ^d | 0.25 | 0.5 | ≤ 0.03 |
| Doxycycline | 98.9 | 0.7 | 0.4 | ≤ 0.12 | 0.25 | ≤ 0.12 | 32 |
| Entericidin | 98.2 | 0.1 | 1.7 | ≤ 0.5 | 0.5 | ≤ 0.5 | > 32 |
| Lefamulin | 98.4 | 1.6 | 0.12 | 0.12 | 0.03 | > 8 | |
| Levofloxacin | 90.1 | 0.3 | 9.6 | 0.25 | 1 | ≤ 0.06 | > 32 |
| Linezolid | 99.9 ^e | | | 0.1 | 2 | 4 | ≤ 0.12 |
| Nitrofurantoin | 99.9 | 0.1 ^f | 0.1 ^f | 16 | 16 | 0.5 | > 512 |
| Tigecycline ^g | 99.6 | 0.4 | 0.25 | 0.25 | 0.03 | 2 | |
| Trimethoprim Sulfamethoxazole | 99.5 | 0.5 | ≤ 0.12 | ≤ 0.12 | ≤ 0.12 | > 8 | |
| Vancomycin | 100 | | | 1 | 1 | ≤ 0.12 | 2 |
| Staphylococcus aureus, MRSA (2,513) | | | | | | | |
| Cefoxitin ^a | | 100 | | > 32 | > 32 | 8 | > 32 |
| Ceftazidime ^b | 100 | | | ≤ 1 | 2 | ≤ 1 | 4 |
| Ceftriaxone | | | | > 64 | > 64 | ≤ 1 | > 64 |
| Ciprofloxacin | 20.3 | 0.4 | 79.3 | > 16 | > 16 | ≤ 0.06 | > 16 |
| Clarithromycin | 17.4 | 0.5 | 82.1 | > 32 | > 32 | ≤ 0.03 | > 32 |
| Clindamycin | 58.8 | 0.1 | 41.1 | ≤ 0.12 | > 8 | ≤ 0.12 | > 8 |
| Daptomycin | 99.8 | | | 0.2 | 0.25 | 0.5 | 0.06 |
| Doxycycline | 97.8 | 0.9 | 1.4 | ≤ 0.12 | 1 | ≤ 0.12 | 16 |
| Entericidin | 93.4 | 0.4 | 6.2 | ≤ 0.5 | 1 | ≤ 0.5 | > 32 |
| Lefamulin | 98.9 | 1.1 | 0.12 | 0.25 | 0.03 | 0.5 | |
| Levofloxacin | 14.1 | 85.9 | > 32 | > 32 | 0.12 | > 32 | |
| Linezolid | 99.9 ^e | | | 1 | 2 | ≤ 0.12 | > 16 |
| Nitrofurantoin | 99.8 | 0.1 | 0.1 | 16 | 16 | 8 | 128 |
| Tigecycline ^g | 98.7 | 1.3 | 0.25 | 0.5 | ≤ 0.03 | 2 | |
| Trimethoprim Sulfamethoxazole | 94.7 | 5.3 | ≤ 0.12 | ≤ 0.12 | ≤ 0.12 | > 8 | |
| Vancomycin | 99.9 | 0.1 | | 1 | 1 | ≤ 0.12 | 4 |
| Staphylococcus epidermidis (1,253) | | | | | | | |
| Amox-Clav | | | | 1 | 8 | ≤ 0.06 | 32 |
| Cefazolin | | | | 1 | 32 | ≤ 0.5 | > 128 |
| Cefepime | | | | 4 | 64 | ≤ 0.25 | > 32 |
| Cefoxitin | | | | 8 | > 32 | ≤ 0.06 | > 32 |
| Ceftazidime | | | | ≤ 1 | ≤ 1 | ≤ 1 | 4 |
| Ceftriaxone | | | | 8 | > 64 | ≤ 1 | > 64 |
| Ciprofloxacin | 47.4 | 1.5 | 51.0 | 4 | > 16 | ≤ 0.06 | > 16 |
| Clarithromycin | 34.3 | 1.3 | 64.4 | 32 | > 32 | ≤ 0.03 | > 32 |
| Clindamycin | 59.3 | 1.4 | 39.3 | ≤ 0.12 | > 8 | ≤ 0.12 | > 8 |
| Daptomycin | 99.8 | | | 0.2 | 0.25 | 0.25 | 0.03 |
| Doxycycline | 95.2 | 2.4 | 2.4 | 0.5 | 1 | ≤ 0.12 | 32 |
| Ertapenem | | | | 2 | > 32 | ≤ 0.03 | > 32 |
| Entericidin | 61.5 | 5.6 | 32.8 | ≤ 0.5 | > 32 | ≤ 0.5 | > 32 |
| Levofloxacin | 44.2 | 1.6 | 54.2 | 4 | > 32 | 0.12 | > 32 |
| Linezolid | 100 | | | 1 | 1 | ≤ 0.12 | 4 |
| Meropenem | | | | 1 | 32 | ≤ 0.12 | > 32 |
| Meropenem | 48.0 | 8.8 | 43.2 | 1 | > 16 | ≤ 0.06 | > 16 |
| Moxifloxacin | | | | | | | |
| Pip-Tazo | | | | ≤ 1 | 16 | ≤ 1 | 256 |
| Tigecycline ^g | | | | 0.12 | 0.5 | ≤ 0.03 | 2 |
| Trimethoprim Sulfamethoxazole | 61.6 | | | 38.4 | 0.5 | 8 | ≤ 0.12 |
| Vancomycin | 100 | | | 1 | 2 | ≤ 0.12 | 4 |
| Streptococcus pneumoniae (3,068) | | | | | | | |
| Amox-Clav | 97.6 | 1.3 | 1.0 | ≤ 0.06 | 0.12 | ≤ 0.06 | 16 |
| Ceftazidime | | | | ≤ 0.06 | ≤ 0.06 | ≤ 0.06 | 1 |
| Ceftriaxone | 99.4 | 0.4 | 0.2 | ≤ 0.12 | ≤ 0.12 | ≤ 0.12 | 4 |
| Cefuroxime | 91.9 | 1.2 | 6.9 | ≤ 0.25 | 0.5 | ≤ 0.25 | > 16 |
| Chloramphenicol | 97.5 | | | 2.5 | 2 | 4 | ≤ 0.12 |
| Ciprofloxacin | | | | 1 | 2 | ≤ 0.06 | > 16 |
| Clarithromycin | 78.3 | 3.2 | 18.6 | ≤ 0.03 | 4 | ≤ 0.03 | > 32 |
| Clindamycin | 92.4 | 0.5 | 7.1 | ≤ 0.12 | ≤ 0.12 | ≤ 0.12 | > 64 |
| Daptomycin | | | | 0.06 | 0.12 | | |
| Doxycycline | 86.3 | 1.2 | 12.6 | ≤ 0.25 | 2 | ≤ 0.25 | > 16 |
| Ertapenem | 90.0 | 0.9 | 0.1 | ≤ 0.06 | 0.12 | ≤ 0.06 | 4 |
| Entericidin | 93.0 | 5.0 | 1.9 | ≤ 0.03 | 0.06 | ≤ 0.03 | 1 |
| Lefamulin | 100 | | | 0.06 | 0.12 | ≤ 0.015 | 0.25 |
| Levofloxacin | 99.1 | 0.1 | 0.7 | 1 | 1 | ≤ 0.06 | 32 |
| Linezolid | 99.9 ^e | | | 0.1 ^f | 1 | ≤ 0.12 | 4 |
| Meropenem | 94.9 | 3.2 | 1.9 | ≤ 0.06 | 0.12 | ≤ 0.06 | 2 |
| Penicillin | 82.5 | 12.9 | 4.7 | ≤ 0.03 | 0.25 | ≤ 0.03 | > 8 |
| Pip-Tazo | | | | ≤ 1 | ≤ 1 | ≤ 1 | 16 |
| Tigecycline ^g | 99.7 | 0.3 | 0.03 | 0.06 | ≤ 0.015 | 0.25 | |
| Trimethoprim Sulfamethoxazole | 85.0 | 6.1 | 8.9 | ≤ 0.12 | 2 | ≤ 0.12 | > 8 |
| Vancomycin | 100 | | | 0.25 | 0.25 | ≤ 0.12 | 1 |
| Streptococcus agalactiae (904) | | | | | | | |
| Amox-Clav | | | | ≤ 0.06 | 0.12 | ≤ 0.06 | 0.25 |
| Ceftazidime | | | | ≤ 0.06 | ≤ 0.06 | ≤ 0.06 | ≤ 0.06 |
| Ceftriaxone | 100 | | | ≤ 0.12 | ≤ 0.12 | ≤ 0.12 | 0.5 |
| Cefuroxime | | | | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | 0.5 |
| Chloramphenicol | 97.3 | 2.3 | 0.4 | 4 | 4 | 0.5 | 64 |
| Ciprofloxacin | | | | 0.5 | 1 | 0.25 | > 16 |
| Clarithromycin | 64.3 | 3.4 | 32.3 | ≤ 0.03 | > 32 | ≤ 0.03 | > 32 |
| Clindamycin | 80.2 | 0.8 | 19.0 | ≤ 0.12 | > 64 | ≤ 0.12 | > 64 |
| Daptomycin | | | | 0.25 | 0.25 | ≤ 0.03 | 1 |
| Doxycycline | | | | 8 | 16 | ≤ 0.25 | > 16 |
| Ertapenem | 100 | | | ≤ 0.06 | ≤ 0.06 | ≤ 0.06 | 0.12 |
| Entericidin | | | | ≤ 0.03 | ≤ 0.03 | ≤ 0.03 | 0.12 |
| Levofloxacin | 96.7 | | | 3.3 | 1 | 0.25 | > 32 |
| Linezolid | 97.9 | | | 2.1 | 1 | 2 | ≤ 0.12 |
| Meropenem | | | | ≤ 0.06 | ≤ 0.06 | ≤ 0.06 | 0.12 |
| Moxifloxacin | | | | 0.12 | 0.25 | ≤ 0.06 | 16 |
| Penicillin | 99.8 | 0.2 | 0.06 | 0.12 | 0.12 | ≤ 0.03 | 0.25 |
| Pip-Tazo | | | | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 |
| Tigecycline ^g | 99.8 | 0.2 | 0.06 | 0.06 | ≤ 0.015 | 1 | |
| Trimethoprim Sulfamethoxazole | | | | ≤ 0.12 | ≤ 0.12 | ≤ 0.12 | 1 |
| Vancomycin | 100 | | | 0.5 | 0.5 | ≤ 0.25 | 1 |
| Streptococcus pyogenes (808) | | | | | | | |
| Amox-Clav | | | | ≤ 0.06 | ≤ 0.06 | ≤ 0.06 | 1 |
| Ceftazidime | | | | ≤ 0.06 | ≤ 0.06 | ≤ 0.06 | 0.5 |
| Ceftriaxone | 100 | | | ≤ 0.12 | ≤ 0.12 | ≤ 0.12 | 0.25 |
| Cefuroxime | | | | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | 1 |
| Chloramphenicol | 97.4 | 2.1 | 0.5 | 2 | 4 | 0.5 | 64 |
| Ciprofloxacin | | | | 0.5 | 1 | ≤ 0.06 | > 16 |
| Clarithromycin | 89.1 | 1.7 | 9.2 | ≤ 0.03 | 0.5 | ≤ 0.03 | > 32 |
| Clindamycin | 97.8 | 0.1 | 2.1 | ≤ 0.12 | ≤ 0.12 | ≤ 0.12 | > 64 |
| Daptomycin | | | | 0.06 | 0.12 | ≤ 0.03 | 0.25 |
| Doxycycline | | | | ≤ 0.25 | 1 | ≤ 0.25 | > 16 |
| Ertapenem | 100 | | | ≤ 0.06 | ≤ 0.06 | ≤ 0.06 | 1 |
| Entericidin | | | | ≤ 0.03 | ≤ 0.03 | ≤ 0.03 | 0.25 |
| Levofloxacin | 99.7 | 0.1 | 0.1 | 0.5 | 1 | ≤ 0.06 | 16 |
| Linezolid | 99.4 | 0.6 | 1 | 2 | ≤ 0.12 | 4 | |
| Meropenem | | | | ≤ 0.06 | ≤ 0.06 | ≤ 0.06 | 0.25 |
| Moxifloxacin | | | | 0.12 | 0.25 | ≤ 0.06 | 4 |
| Penicillin | 99.9 | 0.1 | ≤ 0.03 | ≤ 0.03 | ≤ 0.03 | 0.25 | |
| Pip-Tazo | | | | | | | |