

Antibiotic activity against urinary tract infection (UTI) isolates of vancomycin-resistant enterococci (VRE): results from the 2002 North American Vancomycin Resistant Enterococci Susceptibility Study (NAVRESS)

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Background: The purpose of this study was to assess the prevalence of vancomycin-resistant enterococci (VRE) in urinary isolates in North America, and the activity of various antibiotics against VRE.

Materials and methods: Twenty-eight medical centres in the United States and 10 centres in Canada assessed the prevalence of VRE in urinary isolates in 2002. Each study site was asked to collect up to a maximum of 50 consecutive VRE (*Enterococcus faecium*, *Enterococcus faecalis* only) urinary isolates. Susceptibility was determined by NCCLS broth microdilution. The prevalence of *vanA* and *vanB* resistance genotypes was determined by multiplex PCR.

Results: From the 28 US medical centres, a total of 697 VRE (616 [88.4%] *E. faecium* and 81 [11.6%] *E. faecalis*) were received. Approximately 75% of all VRE (*E. faecium* and *E. faecalis*) isolates demonstrated a VanA phenotype (resistance to both vancomycin and teicoplanin). PCR detection of *vanA* and *vanB* resistance determinants showed that the *vanA* genotype was present in 584 of 697 (83.8%) VRE isolates, whereas 113 (16.2%) isolates possessed the *vanB* gene. The most active agents were linezolid, nitrofurantoin and chloramphenicol, with 0.3%, 0.6% and 2.4% resistance, respectively. The majority (77.8%) of vancomycin-resistant *E. faecium* isolates displayed the VanA phenotype, and 538 of these 616 (87.3%) isolates were PCR-positive for *vanA*; the *vanB* genotype was detected in 78 (12.7%) isolates. Resistance was lowest with linezolid, chloramphenicol and nitrofurantoin at 0.3%, 0.3% and 0.5%, respectively. Only three genetically indistinguishable *vanA*-positive *E. faecium* were isolated from the 10 Canadian medical centres.

Conclusion: VRE urinary isolates are common in the United States, are primarily of the *vanA* genotype and are very susceptible to linezolid, nitrofurantoin and chloramphenicol. In Canada, VRE urinary isolates remain uncommon.

Keywords: glycopeptide resistance, urinary isolates, *Enterococcus faecium*

Introduction

Enterococci are constitutive members of the intestinal flora of humans and animals and may also colonize the upper respiratory tract, biliary tracts and vaginas of otherwise healthy persons.^{1–4} Enterococci have been documented to cause infection of the urinary tract and other sites.^{4–7} Although more than one dozen species of *Enterococcus* have

been identified, *Enterococcus faecalis* and *Enterococcus faecium* account for approximately 85–90% and 5–10% of human enterococcal infections, respectively.^{1–4} Vancomycin-resistant enterococci (VRE), especially *E. faecium* are prevalent in hospitalized patient populations across the United States and are endemic in a number of healthcare institutions.^{2–4,8} In Canada, the prevalence of VRE infection and colonization is presently low (<1%).^{9,10}

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Vancomycin-resistant enterococci

Table 1. United States and Canadian medical centres participating in NAVRESS

Investigator	Centre/city
<i>US study centres</i>	
Dr D. L. Sewell	Veterans Affairs Medical Center, Portland, OR
Dr G. Brooks	University of California, San Francisco, CA
Dr E. J. Baron	Stanford Hospital and Clinics, Stanford, CA
Dr D. A. Bruckner	UCLA Medical Center, Los Angeles, CA
Dr K. Carroll	ARUP Laboratories, Salt Lake City, UT
Dr S. J. Cavalieri	Creighton University Medical Center, Omaha, NE
Dr B. S. Reisner	University of Texas Medical Branch, Galveston, TX
Dr J. E. Clarridge	VA Medical Center, Houston, TX
Dr C. P. Cartwright	Hennepin County Medical Center, Minneapolis, MN
Dr A. Herring	Iowa Methodist Medical Center, Des Moines, IA
Dr W. M. Dunne	Barnes Jewish Hospital, St. Louis, MO
Dr S. Kehl	Froedtert Memorial Lutheran Hospital, Milwaukee, WI
Dr P. Schreckenberger	University of Illinois at Chicago Medical Center, Chicago, IL
Dr J. R. DiPersio	Summa Health System, Akron, OH
Dr M. R. Jacobs	University Hospitals of Cleveland, Cleveland, OH
Dr G. S. Hall	Cleveland Clinic Foundation, Cleveland, OH
Dr D. J. Hardy	University of Rochester Medical Center, Rochester, NY
Dr P. Della Latta	New York Presbyterian Hospital, New York, NY
Dr S. G. Jenkins	Mount Sinai Medical Center, New York, NY
Dr K. Van Horn	Westchester Medical Center, Valhalla, NY
Dr P. Bourbeau	Geisinger Medical Center, Danville, PA
Dr K. C. Hazen	University of Virginia Health System, Charlottesville, VA
Dr G. E. Steinkraus	New Hanover Regional Medical Center, Wilmington, NC
Dr P. Monroe	Medical Center of Central Georgia, Macon, GA
Dr Y. F. Wang	Grady Memorial Hospital, Atlanta, GA
Dr J. D. C. Yao	St. Luke's Hospital, Jacksonville, FL
Dr K. H. Rand	Shands Hospital, Gainesville, FL
Dr S. E. Sharp	Mount Sinai Medical Center, Miami Beach, FL
<i>Canadian centres</i>	
Dr P. Kibsey	Victoria General Hospital, Victoria, BC
Dr R. Rennie	University of Alberta Hospital, Edmonton, AB
Dr J. Blondeau	Royal University Hospital, Saskatoon, SK
Drs G. Zhanel/D. Hoban	Health Sciences Centre, Winnipeg, MB
Dr K. Ramotar	Ottawa General Hospital, Ottawa, ON
Dr D. Low	Mount Sinai Hospital, Toronto, ON
Dr M. Laverdiere	Maissoneuve-Rosemont, Montreal, QC
Dr M. Poisson	Hotel-Dieu of Montreal, Montreal, QC
Dr M. Kuhn	South East Health Care Corp., Moncton, NB
Dr R. Davidson	Queen Elizabeth II HSC, Halifax, NS

Urinary tract infections (UTI) are the most common nosocomial infections caused by enterococci, including vancomycin-resistant strains.^{1,4} Urinary tract infections have been reported to account for 34–46% of all infections in the hospital and occur at a rate of 12.9 cases/1000 discharges.⁶ In addition to UTI, vancomycin-resistant enterococci have also been associated with asymptomatic bacteriuria, colonization of the urinary tract and symptomatic disease such as cholecystitis, cholangitis, peritonitis, septicaemia, endocarditis, meningitis and simple wound infections.^{1–7} Management of VRE infections poses a clinical challenge as these organisms may be resistant to several antimicrobials with unique mechanisms of action.^{2,4,11} The purpose of this study was three-fold: 1) to assess the prevalence of urinary tract infections caused by VRE in major centres across North America; 2) to assess the activity of various antibiotics against urinary isolates of VRE and 3) to identify the genetic determinants of glycopeptide resistance.

Materials and methods

Study centres

Twenty-eight medical centres representing seven of nine regions of the United States Bureau of the Census and 10 Canadian centres representing all geographic regions were involved in this study (Table 1). To assess the prevalence of VRE in urinary isolates in US institutions, the chief clinical microbiologist was asked to provide information regarding the number of urine cultures processed per year in their institution, as well as the number of enterococcal species identified per year and the number of VRE (*E. faecalis*, *E. faecium*) obtained per year from urine cultures.

Collection of isolates

Each study site was asked to collect up to a maximum of 50 consecutive urinary isolates of VRE (*E. faecium*, *E. faecalis* only), one isolate per

Table 2. Prevalence of VRE in urinary isolates in the United States

Centre	No. urines/year	Enterococci/year		VRE/year		% VRE of all urines
		no.	(%)	no.	(%)	
1	14 615	746	(5.1)	195	(26.1)	1.33
2	13 000	2610	(20.1)	27	(1.0)	0.21
3	25 769	462	(1.8)	48	(10.4)	0.19
4	22 470	590	(2.6)	49	(8.3)	0.22
5	48 000	—	—	—	—	—
6	18 023	453	(2.5)	80	(17.7)	0.44
7	38 000	1500	(3.9)	250	(16.7)	0.66
8	16 000	800	(5.0)	28	(3.5)	0.18
9	6000	300	(5.0)	10	(3.3)	0.17
10	18 000	2500	(13.9)	45	(1.8)	0.25
11	24 098	872	(3.6)	228	(26.1)	0.95
12	19 000	1500	(7.9)	52	(3.5)	0.27
13	13 730	393	(2.9)	32	(8.1)	0.23
14	4800	270	(5.6)	48	(17.8)	1
15	19 850	510	(2.6)	72	(14.1)	0.36
16	32 454	742	(2.3)	99	(13.3)	0.3
17	29 000	1251	(4.3)	23	(1.8)	0.08
18	20 700	526	(2.5)	29	(5.5)	0.14
19	20 000	300	(1.5)	6	(2.0)	0.03
20	18 000	195	(1.1)	10	(5.1)	0.06
21	30 000	600	(2.0)	60	(10.0)	0.2
22	35 000	800	(2.3)	50	(6.2)	0.14
23	11 200	750	(6.7)	30	(4.0)	0.27
24	68 680	3768	(5.5)	311	(8.2)	0.45
25	18 000	1100	(6.1)	100	(9.1)	0.56
26	47 500	3107	(6.5)	444	(14.3)	0.93
27	64 308	—	—	92	—	0.14
28	8000	500	(6.3)	12	(2.4)	0.15
Mean \pm S.D.	24 150 \pm 15 953	1044 \pm 936	(5.0 \pm 4.1)	90 \pm 106	(9.2 \pm 7.2)	0.37 \pm 0.33
Range	4800–68 680	195–3768	(1.1–20.1)	6–444	(1.0–26.1)	0.03–1.33

patient. Study centres were asked to culture and identify significant VRE urinary isolates as per their standard laboratory practice. Isolates were transported to the coordinating laboratory (Health Sciences Centre, Winnipeg, Canada) on Amies charcoal swabs as previously described.¹² Upon receipt, isolates were cultured by the coordinating laboratory and isolate identities were confirmed.^{13,14} All isolates were stocked in skimmed milk and stored at -70°C awaiting reference antibiotic susceptibility testing.

Antibiotic susceptibility testing

Before antibiotic susceptibility testing, isolates were cultured twice onto blood agar. All antibiotics for susceptibility testing were obtained as laboratory-grade powders from their respective manufacturers. MICs were determined by standard NCCLS broth microdilution methods with Mueller–Hinton broth and were interpreted using NCCLS breakpoints.^{15,16} Specific MIC breakpoints (in mg/L) were as follows (S, susceptible; I, intermediate, and R, resistant): ampicillin, ≤ 8 and ≥ 16 ; vancomycin, ≤ 4 , 8–16 and ≥ 32 ; teicoplanin, ≤ 8 , 16 and ≥ 32 ; doxycycline, ≤ 4 , 8 and ≥ 16 ; ciprofloxacin, ≤ 1 , 2 and ≥ 4 ; chloramphenicol, ≤ 8 , 16 and ≥ 32 ; nitrofurantoin, ≤ 32 , 64 and ≥ 128 ; quinupristin/dalfopristin,

≤ 1 , 2 and ≥ 4 ; linezolid, ≤ 2 , 4 and ≥ 8 ; gentamicin, < 500 and ≥ 500 ; streptomycin, < 1000 and ≥ 1000 .

PCR for *vanA* and *vanB*

To determine the prevalence of *vanA* and *vanB* glycopeptide resistance genotypes among VRE, a multiplex PCR assay was carried out as described by Dutka-Malen *et al.*,¹⁷ with some modifications. PCR was carried out using a Perkin-Elmer GeneAmp PCR System 9700 with the following parameters: 94°C for 4 min, 30 cycles at 94°C for 1 min, 58°C for 45 s and 72°C for 1 min, and a final cycle at 72°C for 10 min.

Results

Prevalence of VRE survey

Responses regarding the prevalence of VRE urinary isolates were received from all 28 (100%) US medical centres studied and represented seven of nine geographic regions of the United States Bureau of the Census (Table 1). The mean \pm S.D. number of urine cultures processed per year was 24 150 \pm 15 953, from which 1044 \pm 936 (5.0 \pm 4.1%) enterococcal isolates were recovered (Table 2). The

Vancomycin-resistant enterococci

Table 3. Antibiotic activity against VRE from urinary isolates

Antibiotic	MIC ₅₀	MIC ₉₀	Range	S	I	R
All VRE (n = 697)						
teicoplanin	32	64	0.5–128	24.7%	18.8%	56.5%
ampicillin	64	128	1–256	14.2%		85.8%
chloramphenicol	4	8	1–64	96.6%	1.0%	2.4%
doxycycline	4	16	1–32	57.8%	26.0%	16.2%
vancomycin	256	512	8–512	0.0%	1.1%	98.9%
gentamicin	256	4096	16–4096	52.4%		47.6%
streptomycin	8192	8192	32–8192	30.7%		69.3%
linezolid	1	2	0.25–16	99.6%	0.1%	0.3%
quin/dalfo	1	8	0.25–128	67.3%	19.1%	13.6%
nitrofurantoin	32	32	1–128	96.1%	3.3%	0.6%
ciprofloxacin	64	64	1–64	0.1%	0.0%	99.9%
All VSE (n = 163)						
teicoplanin	0.5	0.5	0.5–1	100.0%	0.0%	0.0%
ampicillin	1	64	1–128	79.1%		20.9%
chloramphenicol	8	16	2–128	89.0%	6.7%	4.3%
doxycycline	8	16	1–32	47.2%	22.7%	30.1%
vancomycin	2	2	2–4	100.0%	0.0%	0.0%
gentamicin	16	4096	16–4096	73.6%		26.4%
streptomycin	512	8192	32–8192	63.2%		36.8%
linezolid	2	2	0.25–4	99.4%	0.6%	0.0%
quin/dalfo	8	16	0.25–32	19.0%	6.1%	74.8%
nitrofurantoin	8	32	2–128	96.3%	3.1%	0.6%
ciprofloxacin	32	64	1–64	38.0%	5.5%	56.4%
VRE (<i>E. faecium</i>) (n = 616)						
teicoplanin	32	32	0.5–128	22.2%	21.1%	56.7%
ampicillin	64	128	1–256	3.2%		96.8%
chloramphenicol	4	8	1–64	99.1%	0.6%	0.3%
doxycycline	4	16	1–32	60.7%	26.0%	13.3%
vancomycin	256	512	8–512	0.0%	0.5%	99.5%
gentamicin	16	4096	16–4096	56.8%		43.2%
streptomycin	8192	8192	32–8192	28.9%		71.1%
linezolid	1	2	0.25–16	99.5%	0.2%	0.3%
quin/dalfo	1	2	0.25–64	75.8%	20.8%	3.4%
nitrofurantoin	32	32	1–128	95.8%	3.7%	0.5%
ciprofloxacin	64	64	8–64	0.0%	0.0%	100.0%
VRE (<i>E. faecalis</i>) (n = 81)						
teicoplanin	64	128	0.5–128	43.2%	1.2%	55.6%
ampicillin	1	2	1–128	97.5%		2.5%
chloramphenicol	8	64	4–64	77.8%	3.7%	18.5%
doxycycline	8	16	1–32	35.8%	25.9%	38.3%
vancomycin	512	512	16–512	0.0%	6.2%	93.8%
gentamicin	4096	4096	16–4096	18.5%		81.5%
streptomycin	8192	8192	128–8192	44.4%		55.6%
linezolid	1	2	1–2	100.0%	0.0%	0.0%
quin/dalfo	8	32	1–128	2.5%	6.2%	91.4%
nitrofurantoin		8	8–128	98.8%	0.0%	1.2%
ciprofloxacin	32	64	1–64	1.2%	0.0%	98.8%
VSE (<i>E. faecium</i>) (n = 42)						
teicoplanin	0.5	1	0.5–1	100.0%	0.0%	0.0%
ampicillin	64	128	1–128	21.4%		78.6%
chloramphenicol	4	8	2–32	90.5%	7.1%	2.4%
doxycycline	1	8	1–32	73.8%	16.7%	9.5%
vancomycin	2	2	2–2	100.0%	0.0%	0.0%
gentamicin	16	2048	16–4096	78.6%		21.4%
streptomycin	4096	8192	32–8192	42.9%		57.1%
linezolid	2	2	0.25–4	97.6%	2.4%	0.0%

Table 3. (Continued)

Antibiotic	MIC ₅₀	MIC ₉₀	Range	S	I	R
quin/dalfo	1	4	0.25–16	69.0%	14.3%	16.7%
nitrofurantoin	32	64	8–128	88.1%	9.5%	2.4%
ciprofloxacin	64	64	1–64	9.5%	2.4%	88.1%
VSE (<i>E. faecalis</i>) (n = 121)						
teicoplanin	0.5	0.5	0.5–0.5	100.0%	0.0%	0.0%
ampicillin	1	1	1–64	99.2%		0.8%
chloramphenicol	8	16	2–128	8.4%	6.6%	5.0%
doxycycline	8	16	1–32	38.0%	24.8%	37.2%
vancomycin	2	2	2–4	100.0%	0.0%	0.0%
gentamicin	16	4096	16–4096	71.9%		28.1%
streptomycin	512	8192	128–8192	70.2%		29.8%
linezolid	2	2	0.5–2	100.0%	0.0%	0.0%
quin/dalfo	8	16	1–32	1.7%	3.3%	95.0%
nitrofurantoin	8	16	2–64	99.2%	0.8%	0.0%
ciprofloxacin	2	64	1–64	47.9%	6.6%	45.5%

quin/dalfo = quinupristin/dalfopristin.

prevalence of VRE varied from as low as 1% to as high as 26.1% (mean $9.2 \pm 7.2\%$). VRE-positive urinary isolates represented 0.37% ($\pm 0.33\%$) of all urine cultures processed.

VRE isolates and demographics

From the 28 US medical centres, a total of 697 VRE (616 [88.4%] *E. faecium* and 81 [11.6%] *E. faecalis*) were received, along with 163 vancomycin-susceptible enterococci (VSE) (121 [74.2%] *E. faecalis* and 42 [25.8%] *E. faecium*) (Table 3). Of the 697 VRE, 74.2% were inpatient urinary isolates, 24.8% were outpatient isolates and 1% were unknown. In total, 69.9% of all urinary isolates were obtained from female patients, whereas 30.1% were obtained from male subjects. Breakdown of isolates by age was as follows: ≤ 16 years, 1.0%; 17–64 years, 42.8%; ≥ 65 years, 53.8%; unknown, 2.4%. The 10 Canadian medical centres isolated and submitted a total of three VRE. All three organisms were obtained from the same centre, were identified as *vanA*-positive *E. faecium* and were genetically indistinguishable by pulsed-field gel electrophoresis (data not shown).

Antibiotic susceptibility and PCR determination of VRE

The activity of various antibiotics against VRE is displayed in Table 3. Approximately 75% of all VRE (*E. faecium* and *E. faecalis*) isolates demonstrated a *VanA* phenotype, characterized by resistance to both vancomycin and teicoplanin. PCR detection of *vanA* and *vanB* resistance determinants showed that the *vanA* genotype was present in 584 of 697 (83.8%) VRE isolates (Table 4). One hundred and thirteen (16.2%) isolates possessed the *vanB* gene. The most active agents were linezolid, nitrofurantoin and chloramphenicol, with 0.3%, 0.6% and 2.4% resistance, respectively. Quinupristin/dalfopristin and doxycycline maintained good activity, with 13.6% and 16.2% resistance, respectively. The majority (77.8%) of vancomycin-resistant *E. faecium* isolates were co-resistant to vancomycin and teicoplanin (*VanA* phenotype), and 538 of these 616 (87.3%) isolates were PCR-positive for *vanA*. The *vanB* genotype was detected in the remaining 78 (12.7%) isolates. In 25 of 28 (89.3%) centres, the majority (60–100%) of vancomycin-resistant *E. faecium* isolates were *vanA*-

positive. In two of 28 (7.1%) centres, 87.0% and 93.8% of isolates were *vanB*-positive. Isolates in the remaining centre were approximately 50% *vanA*-positive and 50% *vanB*-positive. Resistance was lowest with linezolid, chloramphenicol and nitrofurantoin at 0.3%, 0.3% and 0.5%, respectively. Quinupristin/dalfopristin and doxycycline were also quite active, with 3.4% and 13.3% resistance, respectively. In contrast to vancomycin-resistant *E. faecium*, only half of all vancomycin-resistant *E. faecalis* isolates demonstrated a *VanA* phenotype. *vanA* and *vanB* genotypes were detected in 56.8% and 43.2% of these isolates, respectively. In six of the 13 (46.2%) centres that submitted vancomycin-resistant *E. faecalis*, 60–100% of the isolates were *vanA*-positive. Similarly, the majority of isolates in six other institutions were *vanB*-positive. Nine *vanA*-positive and nine *vanB*-positive VRE were detected in the remaining centre. The most active agents against vancomycin-resistant *E. faecalis* were linezolid, nitrofurantoin and ampicillin, with 0.0%, 1.2% and 2.5% resistance, respectively. As expected, quinupristin/dalfopristin resistance amongst these isolates was fairly high (91.4%). Chloramphenicol remained active, with a resistance rate of 18.5%.

Discussion

Several US studies have reported dramatic increases in the colonization and prevalence of infections caused by VRE.^{4,8,18} Very few studies, however, have described the epidemiology and clinical importance of VRE in urinary isolates. In one 18 month evaluation of patients with positive urine cultures at a tertiary care hospital, 13 of 98 (13.3%) patients with positive cultures had symptomatic UTIs, giving an overall rate of 2.8 VRE UTI per 10 000 patient admissions.¹⁹ Another study of 28 VRE-infected patients found that only seven (28%) had UTI,²⁰ whereas a recent prospective culture prevalence survey of residents in 25 long-term care facilities found that 124 of 373 (33.2%) urine cultures were positive for enterococci and that 32 (25.8%) of those 124 enterococcal isolates were vancomycin-resistant.²¹ Our study demonstrated that vancomycin-resistant enterococci urinary isolates are present throughout most regions of the United States and represent approximately 9.2% of all enterococci

Table 4. Distribution of *vanA* and *vanB* glycopeptide resistance genotypes among vancomycin-resistant enterococci in the United States

Centre	<i>E. faecium</i>					<i>E. faecalis</i>					Total VRE				
	no. of isolates	genotype [no. (%)]				no. of isolates	genotype [no. (%)]				no. of isolates	genotype [no. (%)]			
		<i>vanA</i>	<i>vanB</i>				<i>vanA</i>	<i>vanB</i>				<i>vanA</i>	<i>vanB</i>		
1	10	6	(60.0)	4	(40.0)	0	–	–	–	–	10	6	(60.0)	4	(40.0)
2	23	3	(13.0)	20	(87.0)	0	–	–	–	–	23	3	(13.0)	20	(87.0)
3	16	1	(6.2)	15	(93.8)	0	–	–	–	–	16	1	(6.2)	15	(93.8)
4	45	39	(86.7)	6	(13.3)	2	2	(100.0)	0	(0.0)	47	41	(87.2)	6	(12.8)
5	15	15	(100.0)	0	(0.0)	0	–	–	–	–	15	15	(100)	0	(0.0)
6	7	3	(42.9)	4	(57.1)	0	–	–	–	–	7	3	(42.9)	4	(57.1)
7	3	3	(100.0)	0	(0.0)	0	–	–	–	–	3	3	(100.0)	0	(0.0)
8	10	10	(100.0)	0	(0.0)	0	–	–	–	–	10	10	(100.0)	0	(0.0)
9	6	6	(100.0)	0	(0.0)	0	–	–	–	–	6	6	(100.0)	0	(0.0)
10	15	15	(100.0)	0	(0.0)	0	–	–	–	–	15	15	(100.0)	0	(0.0)
11	36	34	(96.6)	2	(3.4)	8	7	(87.5)	1	(12.5)	44	41	(93.2)	3	(6.8)
12	6	6	(100.0)	0	(0.0)	0	–	–	–	–	6	6	(100.0)	0	(0.0)
13	10	9	(90.0)	1	(10.0)	3	2	(66.7)	1	(33.3)	13	11	(84.6)	2	(15.4)
14	20	19	(95.0)	1	(5.0)	1	0	(0.0)	1	(100.0)	21	19	(90.5)	2	(9.5)
15	43	32	(74.4)	11	(25.6)	3	0	(0.0)	3	(100.0)	46	32	(69.6)	14	(30.4)
16	46	40	(87.0)	6	(13.0)	2	0	(0.0)	2	(100.0)	48	40	(83.3)	8	(16.7)
17	35	35	(100.0)	0	(0.0)	2	2	(100.0)	0	(0.0)	37	37	(100.0)	0	(0.0)
18	31	31	(100.0)	0	(0.0)	18	9	(50.0)	9	(50.0)	49	40	(81.6)	9	(18.4)
19	27	27	(100.0)	0	(0.0)	19	5	(26.3)	14	(73.7)	46	32	(69.6)	14	(30.4)
20	43	43	(100.0)	0	(0.0)	5	2	(40.0)	3	(60.0)	48	45	(93.8)	3	(6.2)
21	37	29	(78.4)	8	(21.6)	0	–	–	–	–	37	29	(78.4)	8	(21.6)
22	23	23	(100.0)	0	(0.0)	0	–	–	–	–	23	23	(100.0)	0	(0.0)
23	34	34	(100.0)	0	(0.0)	16	16	(100.0)	0	(0.0)	50	50	(100.0)	0	(0.0)
24	21	21	(100.0)	0	(0.0)	0	–	–	–	–	21	21	(100.0)	0	(0.0)
25	12	12	(100.0)	0	(0.0)	0	–	–	–	–	12	12	(100.0)	0	(0.0)
26	10	10	(100.0)	0	(0.0)	1	1	(100.0)	0	(0.0)	11	11	(100.0)	0	(0.0)
27	29	29	(100.0)	0	(0.0)	1	0	(0.0)	1	(100.0)	30	29	(96.7)	1	(3.3)
28	3	3	(100.0)	0	(0.0)	0	–	–	–	–	3	3	(100.0)	0	(0.0)
Total	616	538	(87.3)	78	(12.7)	81	46	(56.8)	35	(43.2)	697	584	(83.8)	113	(16.2)

387

Vancomycin-resistant enterococci

isolated as well as 0.37% of all urine cultures processed. Actual VRE prevalence rates, however, were highly variable from centre to centre, ranging from 1.0% to as high as 26.1% in some centres.

In Canada, the prevalence of VRE infection and colonization is still very low (<1%). For this reason, published studies frequently study colonization rather than infection.^{9,10} In this study, 10 Canadian geographically dispersed centres isolated and submitted only three VRE isolates, suggesting that VRE continues to be isolated infrequently in Canada. These data are consistent with previous studies, which have consistently reported a low prevalence of VRE colonization and infection throughout Canada.^{9,10}

Vancomycin-resistant enterococci obtained from urinary isolates were primarily vancomycin-resistant *E. faecium* (88.4%) and approximately 75% of these strains displayed a VanA phenotype;²² 83.8% of all VRE and 87.3% of vancomycin-resistant *E. faecium* were shown by PCR to carry the *vanA* gene. Although the majority of VRE isolates were *vanA*-positive, *vanB* was the predominant genotype in two of 28 (7.1%) centres. These data indicate that despite the predominance and widespread distribution of the *vanA* resistance determinant, the *vanB* genotype has become well established and shows remarkable stability in some US institutions. The most active agents against all VRE isolates (*E. faecium* and *E. faecalis*) were linezolid, nitrofurantoin and chloramphenicol, with 0.3%, 0.6% and 2.4% resistance, respectively. Specifically against urinary isolates of vancomycin-resistant *E. faecium*, the most active agents were linezolid, chloramphenicol and nitrofurantoin, with 0.3%, 0.3% and 0.5% resistance, respectively. The excellent activity of linezolid and nitrofurantoin against VRE has been previously reported.^{5,10,23} Against vancomycin-resistant *E. faecium*, quinupristin/dalfopristin maintained activity in the majority of patients, with only 3.5% resistance. Ampicillin and ciprofloxacin, however, displayed almost universal resistance. The poor activity of fluoroquinolones and ampicillin against vancomycin-resistant *E. faecium* has been reported previously.¹¹ Two isolates of vancomycin-resistant *E. faecium* demonstrated high level resistance to linezolid (MIC, 16 mg/L) which, although rare, has been previously reported.²⁴

In conclusion, VRE urinary isolates are present throughout the United States, as reported by every medical centre in this study, and are very susceptible to linezolid, nitrofurantoin and chloramphenicol. In Canada, VRE urinary isolates are rare. Glycopeptide susceptibilities and PCR show that the *vanA* genotype is widely disseminated amongst VRE isolated in North America.

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