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Research Brief

Nosocomial outbreak of *vanD*-carrying vancomycin-resistant *Enterococcus faecium*

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Vancomycin-resistant enterococci (VRE) are an increasingly recognized cause of infection worldwide. The *vanD* operon has been found to be exclusively chromosomally encoded, and it is characterized by constitutive resistance to moderate levels of vancomycin and teicoplanin.[1] Strains of *Enterococcus faecium* harboring the *vanD* gene have been sporadically reported in the United States, Canada, Brazil, and Europe,[1–5] but nosocomial transmission of this genotype has not been described. We report the first nosocomial outbreak of *E. faecium* containing a *vanD* genotype in an orthopedic–neurosurgical ward at a Canadian tertiary-care center.

Sunnybrook Health Sciences Center is a 627-bed acute- and tertiary-care hospital located in Toronto, Ontario, Canada. Risk-factor–based screening for VRE using rectal swabs is performed for all patients on admission, and contact precautions and private room isolation are instituted for VRE-positive patients. Risk factors that prompt admission VRE screening include direct hospital transfer or prior admission within the last year, home healthcare services, hemodialysis, or patients unable to answer these questions. Patients with hospital stays >30 days receive repeat VRE screenings. Rectal swabs are plated on Brilliance VRE chromogenic agar (Oxoid, Nepean, Ontario), and all positive isolates are further characterized using pulsed-field gel electrophoresis (PFGE). Additionally, multiplex polymerase chain reaction (PCR) is performed for species identification (*E. faecalis, E. faecium*, *E. gallinarum*, and *E. casseliflavus*) and genotype (*vanA, vanB,* and *vanC*) detection. Over the past 4 years, ~40% of admissions have undergone VRE screening; among them, 0.5% were VRE positive on admission. Nosocomial transmission of VRE remained below 0.4 per 1,000 patient days over this period, with only 3 VRE bloodstream infections.

As part of an investigation of 2 nosocomially acquired cases of VRE (*vanA* subtype) in an inpatient unit, point prevalence screening performed by the Infection Prevention and Control program identified 2 nosocomial cases of VRE (*E. faecium*); both were negative by PCR for *vanA*, *vanB*, and *vanC*. In response, an outbreak was declared on May 7, 2017, and additional control measures were implemented: enhanced cleaning, hand hygiene audit-and-feedback, daily chlorhexidine gluconate bathing, dedicated equipment for isolated patients, and cohorting of healthcare providers to colonized patients.

Weekly point-prevalence screening identified 4 VRE (*E. faecium*) transmissions among patients with previously negative surveillance cultures, for a total of 6 cases in the unit between May 1, 2017, and May 15, 2017. Using PCR testing, the presence of *vanD* was confirmed in all 6 isolates.[5] Based on PFGE analysis, 4 of the isolates were indistinguishable, and 2 isolates were closely related, with <3 band differences (Table 1). Multilocus sequence typing of 7 housekeeping genes (*adk*, *atpA*, *ddI*, *gdh*, *gyd*, *purK*, and *pstD*) demonstrated a complete match with sequence type 117 (ST117) in all isolates.[6] Nucleic acid sequencing of the *vanD* gene indicated 100% shared identity with the *vanD4* gene.[3]

Of the 6 cases, 5 were linked to shared rooms with overlapping time periods. None of the patients colonized with *vanD E. faecium* developed a clinical infection. The outbreak was declared over on June 8, 2017, after no further cases were identified in 3 consecutive weekly point-prevalence screens. Upon review, 2 nosocomially acquired cases of *vanD*-carrying *E. faceium* were identified during routine surveillance screening on geographically separated units 4 months before the outbreak. Both isolates belonged to ST117 and had a PFGE pattern closely related to the outbreak strain.

To our knowledge, this is the first outbreak of nosocomial VRE transmission of the *vanD* genotype to be documented. The temporal and geographic clustering of cases suggests that transmission occurred through direct contact between healthcare providers with patients and the environment. The persistence of *vanD*-carrying VRE on environmental surfaces has not been studied, but this report provides evidence that nosocomial transmission can occur.

Reports of *vanD*-carrying VRE have been sporadic in the literature. In addition to *E. faecium*, *vanD* has been identified in *E. faecalis*,[7] *E. avium*,[7] *E. gallinarum*,[8] and *E. raffinosus*.[9] Non-enterococcal bacteria can also harbor the *vanD* gene and may serve as an important reservoir.[10] A case of *vanD*-carrying

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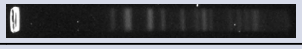
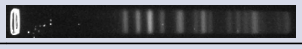
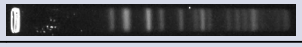
Table 1. Typing and Antimicrobial Susceptibility Testing of 6 *vanD Enterococcus faecium* Isolates Identified as Part of an Outbreak in a Canadian Neurosurgical Acute Care Ward and 2 Sporadic Isolates Identified 4 Months Prior

			Minimum Inhibitory Concentration (μg/mL)[a]									
	PFGE[b]	ST Type[c]	AMP	NIT	VAN	TEC	CIP	DAP	RIF	TET	TGC	LZD
Outbreak Cases												
1		117	> 32 (R)	64 (I)	≥ 32 (R)	24 (I)	≥ 8 (R)	2 (S)	> 4 (R)	≤ 1 (S)	≤ 0.12	2 (S)
2		117	> 32 (R)	64 (I)	≥ 32 (R)	6 (S)	≥ 8 (R)	2 (S)	> 4 (R)	≤ 1 (S)	≤ 0.12	2 (S)
3		117	> 32 (R)	64 (I)	≥ 32 (R)	6 (S)	≥ 8 (R)	2 (S)	> 4 (R)	≤ 1 (S)	≤ 0.12	2 (S)
4		117	> 32 (R)	32 (S)	≥ 32 (R)	24 (I)	≥ 8 (R)	2 (S)	> 4 (R)	≤ 1 (S)	≤ 0.12	2 (S)
5		117	> 32 (R)	64 (I)	≥ 32 (R)	32 (R)	≥ 8 (R)	2 (S)	> 4 (R)	≤ 1 (S)	≤ 0.12	2 (S)
6		117	NC	NC	≥ 32 (R)	24 (I)	≥ 8 (R)	2 (S)	> 4 (R)	≤ 1 (S)	≤ 0.12	2 (S)
Sporadic Cases												
7		117	> 32 (R)	64 (I)	≥ 32 (R)	NC	≥ 8 (R)	NC	NC	2 (S)	0.25	2 (S)
8		117	> 32 (R)	64 (I)	≥ 32 (R)	NC	≥ 8 (R)	NC	NC	≤ 1 (S)	≤0.12	2 (S)

Note. AMP, ampicillin; NIT, nitrofurantoin; VAN, vancomycin; TEC, teicoplanin; CIP, ciprofloxacin; DAP, daptomycin; RIF, rifampin; TET, tetracycline; TGC, tigecycline; LZD, linezolid; S, susceptible; I, intermediate; R, resistant; NC, not completed; ST, sequence type; PFGE, pulsed-field gel electrophoresis.
[a]Susceptibility testing was carried out using VITEK-2 antimicrobial susceptibility cards (bioMérieux, Marcy l'Etoile, France) and an in-house prepared microbroth dilution. Interpretative criteria provided in parentheses beside minimum inhibitory concentration values are based on CLSI M100-S27 performance standards for antimicrobial susceptibility testing.
[b]Isolates 1, 2, 5, and 6 were indistinguishable based on PFGE analysis.
[c]Isolate 8 was matched to ST117 with 5 of 7 matching housekeeping genes; all other isolates were matched to all housekeeping genes

E. faecium septicemia in a hematology ward reported by Starlander et al[2] identified 8 other patients (30%) with enterococci carrying the *vanD* gene, but no specific species were identified nor did dissemination occur.[2] The prevalence of *vanD* enterococcal carriage in the general population is unknown but may be underestimated because most microbiology laboratories do not routinely perform genotyping on VRE-positive patients.

To date, 5 distinct *vanD* alleles have been reported in enterococci (*vanD1* to *vanD5*). While previous *vanD*-carrying VRE reported in Canada have included strains N97-330 (*vanD3* allele) and N03-0072 (*vanD5* allele),[5] this outbreak represents the first Canadian cases of *vanD4*-carrying VRE. The *vanD4* gene was initially identified in an *E. faecium* (isolate 10/96A, ST281) from a 9-year-old girl with aplastic anemia in Brazil.[3] The finding of 100% sequence homology with *vanD4*, yet different sequence types between the outbreak and the *E. faecium* 10/96A isolate, suggests acquisition of resistance through horizontal gene transfer rather than clonal expansion.

The index case in this outbreak was a patient hospitalized for more than a year who received multiple courses of antibiotics with no travel history to Brazil. We suspect that this patient acquired the organism from the hospital environment in the context of selective pressure. With the identification of a related *vanD* isolate 4 months prior, unrecognized nosocomial transmission of this strain likely took place months before the outbreak.

This report describes the first documented nosocomial outbreak of *vanD*-carrying *E. faecium*. Many institutions do not routinely perform genotyping on VRE isolates; therefore, *vanD* transmission in hospitalized patients may be underrecognized.

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References

1. Depardieu F, Kolbert M, Pruul H, *et al. VanD*-type vancomycin-resistant *Enterococcus faecium* and *Enterococcus faecalis*. *Antimicrob Agents Chemother* 2004;48:3892–3904.
2. Starlander G, Tellgren-Roth C, Melhus Å. Fatal acquisition of *vanD* gene during vancomycin treatment of septicaemia caused by *Enterococcus faecium*. *J Hosp Infect* 2016;92:408–412.
3. Camargo IL, Dalla Costa LM, Woodford N, Gilmore MS, Darini AL. Sequence analysis of *Enterococcus faecium* strain 10/96A (VanD4), the original vancomycin-resistant *E. faecium* strain in Brazil. *J Clin Microbiol* 2006;44:2635–2637.
4. Boyd DA, Kibsey P, Roscoe D, Mulvey MR. *Enterococcus faecium* N03-0072 carries a new *VanD*-type vancomycin resistance determinant: characterization of the *VanD5* operon. *J Antimicrob Chemother* 2004;54:680–683.
5. Boyd DA, Lalancette C, Lévesque S, Golding GR. Characterization of a genomic island harbouring a new *vanD* allele from *Enterococcus faecium* N15-508 isolated in Canada. *J Antimicrob Chemother* 2016;71:2052–2054.

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6. Homan WL, Tribe D, Poznanski S, *et al*. Multilocus sequence typing scheme for *Enterococcus faecium*. *J Clin Microbiol* 2002;40: 1963–1971.
7. Depardieu F, Foucault ML, Bell J, *et al*. New combinations of mutations in *VanD*-Type vancomycin-resistant *Enterococcus faecium*, *Enterococcus faecalis*, and *Enterococcus avium* strains. *Antimicrob Agents Chemother* 2009;53:1952–1963.
8. Boyd DA, Miller MA, Mulvey MR. *Enterococcus gallinarum* N04-0414 harbors a *VanD*-type vancomycin resistance operon and does not contain a D-alanine:D-alanine 2 (ddl2) gene. *Antimicrob Agents Chemother* 2006;50:1067–1070.
9. Tanimoto K, Nomura T, Maruyama H, *et al*. First VanD-Type vancomycin-resistant *Enterococcus raffinosus* isolate. *Antimicrob Agents Chemother* 2006;50:3966–3967.
10. Domingo MC, Huletsky A, Giroux R, *et al*. High prevalence of glycopeptide resistance genes *vanB*, *vanD*, and *vanG* not associated with enterococci in human fecal flora. *Antimicrob Agents Chemother* 2005;49:4784–4786.

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