

Evaluation of the duration of *vanA* vancomycin-resistant *Enterococcus faecium* carriage and clearance during a large-scale outbreak in a region of eastern France

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A monthly follow-up evaluation of vancomycin-resistant *Enterococcus*-colonized patients conducted during an outbreak in France revealed that carriage can persist for an extended period. Recurrence was observed despite as many as 3 negative cultures. As a result, we propose another definition for VRE clearance.

Key Words: Duration of carriage; vancomycin-resistant *enterococcus*.

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The control of vancomycin-resistant *Enterococcus* (VRE) colonization during an outbreak is based on identifying and isolating VRE carriers in cohorting or gathering wards. Implementing these measures over an extended period is very difficult, however, due to human and material difficulties as well as high cost. Thus, to safely remove patients from isolation while following contact precautions, it is important to know the duration of VRE colonization.

In the United States, the Hospital Infection Control Practices Advisory Committee has recommended using culture of 3 consecutive negative rectal swabs (RSs) collected at least 1 week apart to define the clearance of VRE in a patient who was previously colonized or infected.¹ Some studies have concluded that these recommendations could effectively control the spread of VRE;^{2,3} however, others have shown that colonization

with VRE may persist despite 3 consecutive negative weekly surveillance stool cultures.^{4,5}

A large VRE colonization outbreak occurred in Lorraine, a region of eastern France, between 2005 and 2009.⁶ This outbreak was related to the clonal spread of a highly vancomycin- and teicoplanin-resistant *vanA* *Enterococcus faecium* strain. In an effort to detect any spontaneous decolonization or recurrence of VRE, we conducted a follow-up study of VRE carriers during hospitalization and after discharge.

METHODS

All VRE carriers identified during the outbreak were monitored on a monthly basis. In patients who were discharged, RSs were obtained following standard laboratory techniques⁶ at the patients' locations. *E faecium* was identified, and the *vanA* gene was detected simultaneously on suspected VRE isolates using polymerase chain reaction and a DNA strip assay (GenoType *Enterococcus*; Hain Lifescience, Nephren, Germany).⁷

Statistical analyses were performed using Stata version 9.2 (StataCorp, College Station, TX).

RESULTS

More than 70% of the 1,080 patients affected by the outbreak could not be included in this study, mainly because RSs were not obtained after patients were discharged to home. Data were collected from 300 patients who had at least 2 RS results over a minimum

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Table 1. Predictive value of positive RS cultures

Number of previous sequential negative cultures	Number of further positive cultures/number at risk (%)
1	19/223 (8.5)
2	13/180 (7.2)
3	8/102 (7.8)
4	4/70 (5.7)

course of 14 days. Overall, 2206 RSs were collected (mean \pm SD, 7 ± 8 per patient; range, 2-55). The median follow-up period after the first positive isolate/patient was 174 days (range, 16-1330 days). The mean age of the patient population was 77 ± 15 years, and the female/male sex ratio was of 1.7. Of the 257 patients for whom the residence was known after the first VRE-positive RS was identified, 26.7% had been discharged to home, 25.9% were in an assisted-living or nursing home, 21.9% were in a long-term care facility, 5.6% were in a rehabilitation facility, 14.3% were receiving chronic dialysis in a private or public hemodialysis unit, and 5.6% were hospitalized in an acute care facility.

To evaluate the duration of carriage (ie, time between the first and last positive RSs), we identified 82 patients with at least two positive RS results (mean, 4 positive RS results per patient) followed by at least one negative RS result. The median duration of carriage was 42 days (75th percentile, 101 days; 90th percentile, 221 days), and the maximum was 708 days.

When evaluating the rate and time of recurrence, we found that 19 (8.5%) of the 223 patients with a first negative follow-up RS culture had a positive culture at the next follow-up (Table 1). Among the patients who had two negative follow-up cultures, 7.2% became positive again after one further negative culture, 7.8% did so after two further consecutive negative cultures, and 5.7% did so after 3 further consecutive negative cultures. Moreover, 6 of the 45 VRE carriers (11%) who presented with at least 3 consecutive negative RS cultures over the course of at least 3 months developed recurrence.

DISCUSSION

This study demonstrates that VRE carriage can persist for months, even in patients discharged to home. Recurrences were observed in VRE carriers in whom 3 previously collected consecutive RSs obtained over a period of at least 3 months were negative. These results are similar to previously reported findings and confirm that recurrences can occur even after a long period with several negative RS cultures.^{2,4,5,8,9} Thus, the policy of

considering 3 consecutive negative RS cultures to indicate VRE clearance appears to be unsafe.

Given that pulsed-field gel electrophoresis analyses have shown that the emergence of VRE in Lorraine was due mainly to the spread of clonally related *vanA E faecium* strains,⁶ it was not possible to determine whether recurrences of VRE fecal colonization represented reinfections or relapses. However, taking into account that more than 25% of patients with recurrences have been discharged to home, and considering the overall low prevalence of VRE colonization among French nursing home residents as well as long-term care and rehabilitation facility patients, we believe that the recurrences observed in our study were more likely relapses, and that "relapse"-free periods were due to a decrease in VRE fecal density below the limits of detection rather than to a definitive clearance of VRE.

Antibiotic treatment may induce an increase in VRE fecal density and thereby promote "relapses."^{2,8-10} This prompted us to propose that a patient can be considered "cleared" of VRE if a RS obtained between 2 and 7 days after the cessation of at least 5 days of antibiotic treatment with drugs known to be selective for VRE (eg, third-generation cephalosporins, fluoroquinolones, carbapenems, imidazoles, glycopeptides) is negative. This definition was successfully implemented during the large-scale outbreak in our region.⁶ None of the cleared patients who were readmitted without contact precautions generated secondary cases. Nonetheless, further studies with higher numbers of cleared patients are needed to confirm the pertinence of the proposed criteria.

VRE carriage may persist for an extended period, and recurrences may be observed despite 3 or more negative RS cultures. We propose a definition of clearance that includes antibiotic therapy, the most important factor associated with the recurrence of high-density VRE RS cultures. We consider this definition safer than the existing recommendations for reducing the risk of VRE transmission.

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