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Epidemiology of vancomycin-resistant enterococci from France in 2012

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Abstract

Objectives:
The aim of the study was to describe recent epidemiological features of vancomycin-resistant enterococci (VRE) collected from French hospitals in 2012.

Methods:
The National Reference Center for Enterococci (NRC-Enc) received isolates suspected to be VRE from all French hospitals in 2012. All strains were identified by detection of species-specific *ddl* gene or sequencing of the *sodA* gene. Antimicrobial susceptibility testing was performed by the disc diffusion method, and following antibiotics were tested: ampicillin, streptomycin, kanamycin, gentamicin, erythromycin, lincomycin, pristinamycin, levofloxacin, chloramphenicol, doxycycline, vancomycin, teicoplanin, cotrimoxazole, linezolid, rifampicin and tigecycline. MICs of vancomycin, teicoplanin and daptomycin were determined by using E-test strips. Screening for all known *van* resistance genes was performed by multiplex PCR. All *vanA*- or *vanB*-positive *Enterococcus faecium* and *Enterococcus faecalis* isolates were typed by PFGE after *Sma*I restriction.

Results:
In 2012, 369 clinical isolates (including 262 VRE) were received by the NRC-Enc from 33 different French counties. Note that 9 strains were imported from foreign countries (i.e. Bulgaria, Greece, USA, Morocco, Portugal and Turkey). The species *E. faecium* was largely predominant (n = 252; 96.2%) whereas a few isolates were *E. faecalis* (n = 7; 2,7 %) or belonged to uncommon enterococcal species (*E. hirae*, n = 1; *E. durans*, n = 1; *E. gallinarum*, n = 1). *vanA* was the most frequent resistance gene (89.3%), followed by *vanB* (10.7%). Amongst *E. faecium* isolates, 227 (90.1%), 14 (9.6%) and 1 (0.3%) were positive for *vanA*, *vanB* and *vanD* respectively. The *vanA* gene was detected in 4 *E. faecalis*, 1 *E. hirae*, 1 *E. durans* and 1 *E. casseliflavus*, whereas 3 *E. faecalis* strains were positive for *vanB*. All (except five) *E. faecium* isolates were highly resistant to ampicillin, and high-level resistance to gentamicin was detected among 76% of isolates, this proportion being much higher than that of 2011 (45%) and previous years (ca. 20%). No strain was resistant to linezolid or tigecycline, and none exhibited MIC values higher than 4 mg/L for daptomycin. By PFGE analysis, 90 different profiles were identified for *E. faecium* (including 77 *vanA*-positive clones and 13 *vanB*-positive clones), of which some spread regionally in different hospitals.

Conclusion:
After an important peak in 2008-09, the number of VRE isolates received at the NRC-Enc has decreased and now remained stable. As described in previous years, some epidemic *E. faecium* clones diffuse at a regional level between closely located hospitals. Of note, there is a significant increase of gentamicin resistance in *E. faecium*, which should be kept under surveillance in the near future.

Introduction

Since its first description in 1988, emergence of VRE (vancomycin-resistant enterococci) has become one of the major threats to public health worldwide. In the United States, VRE became rapidly epidemic and then endemic in many hospitals (1) whereas VRE rates in clinical isolates increased in several European countries (2).

In France, a comprehensive national program for prevention of nosocomial infections has gradually been set up in France during the period from 1993 to 2004. Several recommendations targeted specifically VRE outbreaks and clinical microbiology laboratories were asked to send all isolates suspected to be a VRE to the reference laboratory for enterococci funded in 2006 (NRC-Enc) as part of the National Reference Center for Antimicrobial Resistance (3).

VRE rates in France were still low (1.4% in 2011) but several small-to-large outbreaks have occurred since 2004 (4).

The aim of the study was to describe recent epidemiological features of VRE clinical isolates collected from French hospitals in 2012.

Materials and methods

Bacterial strains
262 VRE were received at the NRC-Enc in 2012.

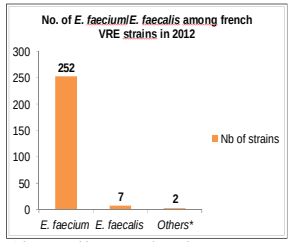
Identification
A multiplex PCR for detection of species-specific *ddl* gene as well as detection of all known *van* resistance genes was performed using specific primers, as previously described (5).

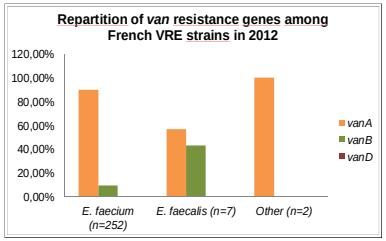
Antimicrobial susceptibility testing
Antibiotic susceptibility was determined by the disk method according to the Antibiogram Committee of the French Society for Microbiology (CA-SFM). MICs of glycopeptides and daptomycin were evaluated using E-test method.

Molecular Typing
PFGE analysis of the 262 VRE isolates was performed using the restriction endonuclease *Sma*I. Restriction fragments were separated by CHEF-III (Bio-Rad, France).

Results

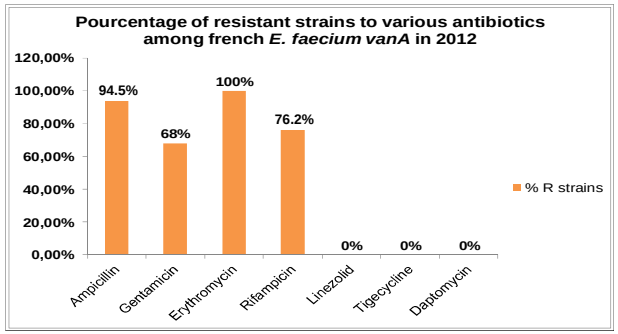
1) Repartition of *E. faecium*/*E. faecalis* and *van* resistance genes among french VRE in 2012





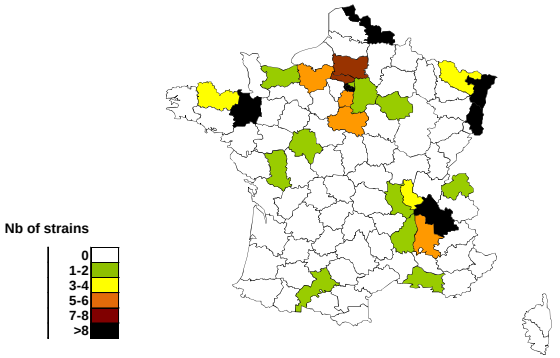
*Others : 1 *E. hirae vanA* and 1 *E. durans vanA*

2) Antimicrobial susceptibility profiles:



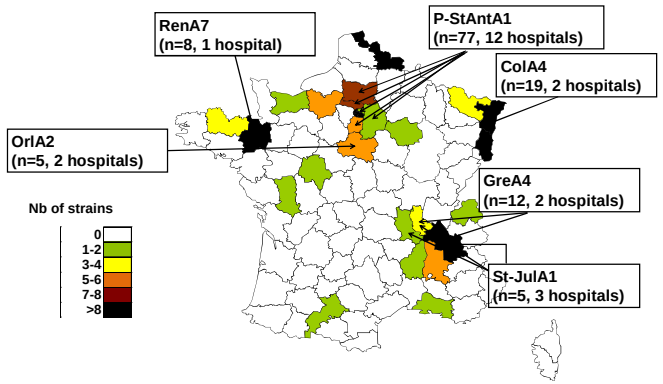
3) Geographic origin of French *vanA*- and *vanB*-positive *E. faecium* strains :

- 28 different French counties
- 9 strains were imported from foreign countries (Bulgaria, Greece, USA, Morocco, Portugal and Turkey)



4) PFGE pulsotypes

- *E. faecium vanA* (227 strains): 77 different clones
- *E. faecium vanB* (24 strains): 13 different clones
- 6 major clones in *E. faecium vanA* clones



Conclusions

- Stability of the number of VRE isolates since 2009 in France.
- Important number of pulsotypes, with a few major epidemic clones.
- Diffusion of *E. faecium* clones at the regional level, between closely located hospitals

(1) Sievert D. M.,Antimicrobial-Resistant Pathogens Associated with Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. Infection control and hospital epidemiology.
(2) Annual epidemiological report : Reporting on 2011 surveillance data and 2012 epidemic intelligence data. 2013. www.ecdc.europa.eu
(3) Avis du Comité technique des infections nosocomiales et des infections liées aux soins relatif à la maîtrise de la diffusion des entérocoques résistants aux glycopeptides dans les établissements de santé français, 6 octobre 2005. Bull Epidemiol Hebd. 2006; 13:88-9.
(4) Bilan des signalements d'infections nosocomiales pour entérocoques résistants aux glycopeptides (ERG) en France, 2005 -2011. http://www.invs.sante.fr/erg
(5) Depardieu F. Detection of the van alphabet and identification of enterococci and staphylococci at the species level by multiplex PCR. J Clin Microbiol. 2004 Dec;42(12):5857-60.