# Xpert® *vanA/vanB* Bibliography

Xpert® *vanA/ vanB*

### Cavalié, ECCMID 2009; Lalitagauri, DMID 2007

- The enterococci *E. faecium* (91%) and *E. faecalis* (7.8%) are commensal bacteria of the digestive tract which present sensitivity to glycopeptides in their wild phenotype

### Marner, DMID 2011

- Vancomycin-resistant enterococci (VRE)
  - are glycopeptide resistance enterococci, mainly due to the use of oral vancomycin for the treatment of patients with *C. difficile* infections, acquisition of van A & B genes
  - are increasingly problematic worldwide
  - plague health care with morbidity, mortality, increased length-of-stay and expenses

### APM Press release, 4 novembre 2008

- VRE infections cost a lot of money to institutions
- 6 months outbreaks in 3 wards of Beauvais hospital in France:
  - 40 000 € for health-care workers (HCWs) specifically hired for the VRE outbreak, 20 000 € for laboratory consumables, 374 000 € losses due to the cessation of admissions ; in total 430 000 € for 31 patients = 14 000 € per patients

### Taconnelli, IJAA 2008; Cavalié ECCMID 2009

- Transmission of VRE can occur through:
  - direct contact with colonized patients
  - infected patients
  - indirect contact via the hands of HCWs
  - contaminated patient care equipment or environmental surfaces (prolonged survival of VRE in the environment : N> 1 week)
- Antibiotic exposure plays an important role in the dynamic transmission of VRE

### Marner, DMID 2011; Cavalié, ECCMID 2009; Taconnelli, IJAA 2008; Domingo, JAC 2005

- Mainly *vanA* (which mediates resistance to Vancomycin and Teicoplanin) and *vanB* (which mediates resistance to Vancomycine only) contribute to acquired resistance to vancomycin in enterococci
- The dominant resistance factor in enterococci is *vanA* (eg : France *vanA* 71.3%- vanB 28.1%)
- 33.3% of other bacteria are carriers of *vanB* genes
- Enterococci have the ability to transfer vancomycin resistance to other bacteria (including methicillin-resistant *Staphylococcus aureus*)
- Target high-risk patients are located in intensive care (ICUs), pediatric ICU, oncology & haematology, and transplant (bone marrow) and nephrology units

### Calderwood, Infect Control Hosp Epidemiol 2008

- Bone marrow and stem cell transplant patients are at high risk for colonization and infection with antimicrobial-resistant pathogens, and particularly with VRE… 30% of transplant patients who are colonized with VRE will go on to experience overt infection

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## Marner, DMID 2011; Perencevich, CID 204; Bourdon, DMID 2011; Taconnelli, IJAA 2008; Gazin, EJCMID 2011; Stamper, JCM 2007

- Hospitals use many strategies to control nosocomial transmission of VRE
- "Passive surveillance": isolation of patients with known previous or current VRE colonization or infection
- "Active surveillance": uses admission screening, with subsequent isolation of patients who are found to be colonized with VRE
- "Outbreak management"
- Rapid and accurate microbiologic diagnosis of VRE leads to :
  - prompt identification of patients
  - rapid infection control intervention / contact precautions and appropriate barrier precautions
  - minimise transmission
  - better patient management and treatment
- Clinical laboratories use a variety of technics to detect VRE:
  - culture-based: direct / broth-enriched culture methods: "gold standard" but time-consuming and costly to implement
  - molecular methods (BD GeneOhm, Abbott M2000 van R, Xpert *vanA/vanB*), are sensitive and cost-effective (Taconnelli, IJAA 2008)

## Xpert *vanA/vanB* Package Insert

- Xpert *vanA/vanB* is a qualitative in vitro diagnostic test designed for rapid detection of vancomycin-resistance (*van A/van B*) genes from rectal and perianal swab specimens in patient at risk for intestinal colonization of vancomycin resistant bacteria

## Bourdon, DMID 2011 (Performance of Xpert *vanA/vanB*)

- 804 rectal swab specimens
- Xpert *vanA/vanB* compared to enriched culture: sensitivity and negative predictive value of this method were 100%
- Turn Around Time (TAT) : Broth aerobe cultures 24 h, subculture onto chromogenic agar plates incubated aerobically, and lecture after 24, 48, and 72h / in total from 48h to 5 days

## Marner, DMID 2011 (Active surveillance with Xpert *vanA/vanB*)

- VRE screening for all hospital admissions to the ICU and weekly screening of patients in the bone marrow transplant ward
- Performance comparison of Xpert *vanA/vanB* with direct and broth-enriched culture methods from perianal swabs
- Compared to the combined reference standard, sensitivity was 96.4%, specificity 93.0%, PPV 92.0% and
- NPV 96.9%, and total agreement was 94.6% (n = 184)
- The 95% limit of detection was 100 colony-forming units (CFU)/mL for *vanA* and 114 CFU/mL for *vanB*
- Sample types (rectal versus perirectal or perianal swabs) may account for some variability between reported assay performance
- Patients often refused to allow rectal or perirectal swab collection, leading to evaluate in this study the use of perianal swabs with Xpert *vanA/vanB*
- The use of perianal swabs for active VRE surveillance offered :
  - improved specificity
  - minimally invasive sampling
  - limited risk of false-positive results due to *vanB*-bearing stool anaerobes
  - limited PCR inhibition (rarely contaminated with stool which limits the need for repeat testing)
  - rapid and accurate results
- The use of Xpert *vanA/vanB* offers improved sensitivity over that of direct cultures and eliminates the need for tedious and labor-intensive broth enrichment cultures



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## Cavalié, ECCMID 2009 (Outbreak screening with Xpert *vanA/vanB*)

- Outbreak of *E. faecium* resistant to Vancomycin (VRE) of *vanB* type in Toulouse University Hospital (October 2008 to April 2009)
- Perianal sampling with double swabs and implementation of conventional screening (culture, subculture, identification; TAT 5 days) and Xpert *vanA/vanB* screening (on-demand testing, TAT 45')
- Screening in nephrological intensive care unit (N=1000)
- Screening of all the contacts or admitted patients + set up of extra contact precautions and cohorting with 3 dedicated area (carriers, contacts and admitted)
- Negative Xpert results were reported without culture confirmation, and the clinicians stopped isolation and put the patients in a double room
- Positive Xpert were cultured from the other swab in accordance with Cepheid recommendations
- The isolation was continued until the definitive culture result
- The VRE screening by Xpert is very attractive thanks to its high NPV, especially in an outbreak situation
- A negative result can be obtained in less than one hour and thereby limiting the need for isolation of newly admitted patients, whereas culture can take up to 5 days

## Badaby, JCM 2012

- First reported evaluation of the Xpert® *vanA** test in a patient population at high risk for VRE colonization : transplant patient
- The clinical sensitivity, specificity, positive predictive value and negative predictive value of the Xpert *vanA* PCR assay were 100%, 96.9%, 91.3% and 100%, respectively, when tested on 300 consecutively collected rectal swabs for routine surveillance of vancomycin-resistant enterococci (VRE) from rectal swabs in patients at high risk for VRE carriage

## Stamper, JCM 2007

- The sensitivity of the direct culture method was much lower (84.9%), and the false-negative rate (15.5%) was too high to effectively support active surveillance efforts based on agar culture alone

## Mehta et al., 2008; Sloan et al., 2004; Stamper et al., 2007

- Some studies published for active surveillance and detection of VRE reported issues with false-positive results due to *vanB* and suggest follow-up culture be performed on any *vanB*-positive results

**Xpert vanA is a product commercialized by Cepheid in the USA only, in EU the test commercialized is Xpert vanA/vanB.*


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