VRSA

VANCOMYCN
THE LAST LINE OF DEFENSE

BUG KILLER

VANCOMYCN
Hобразный выстреливающий объект, армейский танк и фигуры в военной форме с нацеленными на оружие.
A tale of two friends (fiends) - Awe Maduka MD

- VRE had a distant cousin called MRSA. VRE & MRSA liked each other a lot and usually hung out together.
- MRSA was a capable guy. He could resist the entire β-lactam group of poisons humans sent his way.
- But when humans used vanco, MRSA was done.
- VRE, though, knew how to deal with vanco.
- VRE shared his resistance gene (vanA) with his cousin, MRSA, → VRSA was born.
- What does vanA do? Changes the binding target of vanco so vanco cannot bind.
- MRSA had to change his name to VRSA but VRE didn’t mind- they had won after all.
The MRSA-VRE-VRSA saga

- All VRSA isolated so far also had *mecA* gene (i.e., they are MRSA) in addition to newly acquired *vanA*
- Most patients with VRSA had been exposed to (prolonged) treatment with vancomycin
- A few had not been exposed to vanco but had exposure to other antimicrobials (the trigger for genetic transfer may not be vanco exposure alone)
- Note that **VISA** has a different mechanism of resistance: Vanco gets trapped in thickened cell wall
<table>
<thead>
<tr>
<th>Case</th>
<th>State</th>
<th>Year</th>
<th>Age</th>
<th>Source</th>
<th>Diagnosis</th>
<th>Underlying Conditions</th>
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<tbody>
<tr>
<td>1</td>
<td>MI</td>
<td>2002</td>
<td>40</td>
<td>Plantar ulcers and Catheter tip</td>
<td>Plantar soft tissue infection</td>
<td>Diabetes, dialysis</td>
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<td>Obesity</td>
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<td>63</td>
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<td>Multiple sclerosis, Diabetes, kidney stones</td>
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<td>Gangrene</td>
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<td>58</td>
<td>Surgical site wound after panniculectomy</td>
<td>Surgical site infection</td>
<td>Obesity</td>
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<td>6</td>
<td>MI</td>
<td>2005</td>
<td>48</td>
<td>Plantar ulcer</td>
<td>Osteomyelitis</td>
<td>MVA, chronic ulcers</td>
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<td>Diabetes, dialysis, chronic ulcers</td>
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<td>Surgical site wound after foot amputation</td>
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<td>Diabetes, hepatic encephalopathy</td>
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<td>2009</td>
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<td>Plantar soft tissue infection</td>
<td>Diabetes, obesity, lupus, rheumatoid arthritis</td>
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<td>2010</td>
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<td>Wound drainage</td>
<td>Prosthetic joint infection</td>
<td>Diabetes, end-stage renal disease, dialysis</td>
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<td>2010</td>
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<td>Vaginal discharge</td>
<td>Chronic recurrent C. difficile infection, chronic UTIs, vesicoenteric fistula</td>
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FEB 2015: 4th DE Case; 14th U.S. Case

• 67 yo female
• Chronic great toe ulcer
• Multiple comorbidities: Diabetes, end-stage renal disease, dialysis, CVA (wheelchair bound), morbid obesity, CHF
• Lives alone (?)
• Dialysis 3x/week; Wound Center
• Most recent hospitalization – August 2014
• Vanco usage – March & July 2014 (6 doses each month during dialysis)
Laboratory History

• 2/27/15 – Hospital cx toe ulcer (vanR, Etest MIC >256)
  – Also MRSA, VRE, Candida
• 3/3/15 – DPHL (Vitek2 MIC >32; Etest MIC >256)
• 3/10/15 – CDC Confirmation – MIC 512; Etest MIC >256
• 3/23/15 – CDC PFGE – USA100 (healthcare strain)
Delaware VRSA Strains

- 1\textsuperscript{st} (U.S. 11\textsuperscript{th}) – USA100 (healthcare)
- 2\textsuperscript{nd} (U.S. 12\textsuperscript{th}) – USA100 (healthcare)
- 3\textsuperscript{rd} (U.S. 13\textsuperscript{th}) – USA1100 (community)
  - Associated MRSA USA500 – atypical healthcare strain
- 4\textsuperscript{th} (U.S. 14\textsuperscript{th}) – USA100 (healthcare)
Goals of Epi Investigation

• Look for evidence of transmission--evaluate those with extensive & moderate interaction w/ case patient:
  • Healthcare worker contacts
  • Other patients in close contact settings
  • Family/close contacts
  • Home health agencies
  • Outpatient settings
  • Others as identified

• Education of all disciplines regarding Infection Prevention (strict contact precautions)

• Note: No person-to-person transmission has ever been documented among all 14 confirmed VRSA cases.
  • Documented for VISA: 43 VISAs from 43 pts in Taiwan hospital shown to be from same clone (Hsueh et al Int J Antimicrob Agents, 2010)
Epi Investigation

• Collection of surveillance swabs from:
  • Wound Center staff (nares/groin cultures)
  • Dialysis Center staff & dialysis patients on same shift as case patient (nares cultures)
  • Infectious disease provider staff (nares/groin cultures)
  • Home contacts
  • Home health (if visited after Jan 1, 2015)
  • Case patient (nares/groin or perirectal/wound)

– CDC increased recommendation from traditional nares culture to 2 swabs per contact due to growing concerns about extra-nasal sources
Laboratory testing by DPHL

- 49 total swabs collected by Epi during this investigation & cultured by DPHL
  - Dialysis staff (12 individuals - nares/groin)
  - Dialysis patients (12 patients - nares; case patient - nares/axilla [peri-rectal or groin not possible]
  - Wound Center staff (2 individuals – nares/groin)
  - Infectious disease staff (3 individuals – nares/groin)
Algorithm for Testing *S. aureus* with Vancomycin (VA)

**Acceptable Primary Test Methods Include:**

- MIC method (plus VA screen plate)
- Disk diffusion plus VA screen plate

**Clinical and Laboratory Standards Institute**

*S. aureus*/Vancomycin Breakpoints
- Susceptible: ≤2 µg/ml (VSSA)
- Intermediate: 4-8 µg/ml (VISA)
- Resistant: ≥16 µg/ml (VRSA)

**Steps:**

1. **CHECK for purity**
2. **CONFIRM isolate ID**
3. **RETEST using an MIC method**
4. **SAVE ISOLATE**
5. **NOTIFY** infection control, physician, local health department and CDC of “possible VISA/VRSA”
6. **SEND S. aureus with vancomycin MIC ≥8 to CDC** for MIC confirmation and van gene detection

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**Important Footnotes:**
- Laboratories using automated MIC methods that have not been validated for VRSA detection and laboratories using disk diffusion should add a commercial BHI VA agar screen plate (6 µg/ml).
- Disk diffusion will not differentiate VISA (MICs 4-8) from susceptible strains (MICs 0.5-2). The vancomycin disk test will detect VRSA isolates containing the vanA resistance gene by showing no zone of inhibition around the disk (zone = 6 mm). VA screen plate will not reliably detect strains for which MIC<4 µg/ml.
- If concerned about a result based on a patient’s history, send to a reference lab for MIC testing.

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DPHL Results

- Of the 49 surveillance specimens received, only the index patient was colonized with methicillin resistant S. aureus (MRSA).
- DPHL began screening using a vancomycin screening agar (Hardy Diagnostics, cat #G14). No contacts identified with VRSA.
- CDC requested further identification for vancomycin resistant Enterococcus (VRE) and MRSA to make a molecular epidemiological link to the VRSA identified from the index patient.
- CDC received VRE isolate from submitting hospital on specimen initial identified with VRSA. DPHL identified MRSA from index patient of the 49 specimens received for testing.
- “The MRSA from the index patient is a match with the VRSA, but the VRSA appears to contain markers for the VRE plasmid and not the MRSA plasmid. All of this points to the VRE and MRSA contributing directly to formation of the VRSA.” –Brandi Lambago, CDC Deputy Chief of Clinical and Environmental Microbiology Branch, Division of Healthcare Quality Promotion
DPHL Results

- Publications on precursor surveillance from MI’s VRSA isolates for reference.
CDC Resources

• Division of Healthcare Quality Promotion (DHQP)
  • Drs. Alex Kallen, Maroya Walters, Brandi Limbago & a host of others
CDC Reminds Clinical Laboratories and Healthcare Infection Preventionists of their Role in the Search and Containment of Vancomycin-Resistant Staphylococcus aureus (VRSA)

The Centers for Disease Control and Prevention (CDC) has recently confirmed the 13th case of vancomycin resistant *Staphylococcus aureus* (VRSA) infection since 2002 in the United States. This serves as a reminder about the important role of clinical laboratories in the diagnosis of VRSA cases to ensure prompt recognition, isolation, and management by infection control personnel. This is an important opportunity for all laboratories to revisit their step-by-step problem-solving procedure or algorithm for detecting VRSA that is specific for their laboratory. A sample algorithm is available and highlights the recommended testing methodologies for detecting VRSA and actions based on testing results.

Furthermore, because of exchange of genetic material from vancomycin-resistant enterococci (VRE) to methicillin-resistant *Staphylococcus aureus* (MRSA) in the emergence of VRSA, CDC is asking clinical laboratories, when patients are identified with suspected or confirmed VRSA, to ensure that all VRE, MRSA, and VRSA isolates from these patients are saved. Following confirmation of VRSA, CDC recommends that all three isolate types (i.e., VRE, MRSA, and VRSA) be shared with clinical and public health officials.
Healthcare-associated Infections (HAIs)

Laboratory Detection of Vancomycin-Intermediate/Resistant *Staphylococcus aureus* (VISA/VRSA)

- What is the difference between vancomycin-susceptible *S. aureus*, VISA and VRSA?
- What is CLSI (formerly, NCCLS)?
- What are glycopeptide-intermediate *S. aureus* (GISA)?
- Why are VISA and VRSA isolates important?
- Can routine susceptibility tests detect VISA and VRSA?
- What is the vancomycin agar screen test?
- Should repeat testing include any specific antimicrobial agents that might not be included in the routine panel?
- How should local clinical laboratories save presumptive VISA or VRSA isolates?
- Are VISA and VRSA isolates resistant to oxacillin?
- What are the mechanisms of resistance for VRSA and VISA?
- Should VISA and VRSA be reported to the infection control