VRSA: A New and Unwelcome Arrival
Dr. Tammy Lundstrom
August 7, 2003

Slide 1

Vancomycin Resistant
Staphylococcus aureus

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Assistant Professor of Medicine
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VRSA
Clinical Background

Slide 3

Background
- Staphylococcus aureus remains a common
  cause of both community-acquired and
  nosocomial infections
- 1980s MRSA becomes an increasing problem
  in hospitals
- 1980s MRSA community acquired
  endocarditis prevalent in injection drug users
- 2000s community acquired MRSA in children

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**How is Vancomycin Resistance Defined?**
- Sensitive vancomycin MIC \(< 4 \mu g/mL\)
- Glycopeptide (vancomycin) intermediate (GISA) MIC between 4-8 \(\mu g/mL\)
- Glycopeptide (vancomycin) resistant (GRSA/VRSA) MIC \(> 8 \mu g/mL\)

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**Background**
- 1996
  - First Vancomycin-intermediate S. aureus (GISA) discovered in Japan
- July 1997
  - First US GISA patient described in Michigan
- June 2002
  - Total of 8 US patients with GISA known

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**Characteristics of GISA Cases**

<table>
<thead>
<tr>
<th>Date</th>
<th>State</th>
<th>Patient</th>
<th>Site</th>
<th>Contact</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/97</td>
<td>MI</td>
<td>857PD</td>
<td>Perit.</td>
<td>0</td>
<td>Cured</td>
</tr>
<tr>
<td>6/97</td>
<td>NJ</td>
<td>857HD</td>
<td>BS</td>
<td>0</td>
<td>Cured</td>
</tr>
<tr>
<td>4/99</td>
<td>IL</td>
<td>857HD</td>
<td>BS</td>
<td>0</td>
<td>Died</td>
</tr>
<tr>
<td>2/00</td>
<td>Nev</td>
<td>Choly</td>
<td>Bile</td>
<td>0</td>
<td>Cured</td>
</tr>
</tbody>
</table>

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Risk Factors for GISA
- Dialysis (PD or HD)
- Invasive devices
- Previous infection/colonization with S. aureus
- Multiple courses of antibiotics including vancomycin for extended time periods

***Multiple close contacts all culture negative

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Risk Factors for Staphylococcus aureus with Reduced Susceptibility to Vancomycin (MIC ≥ 4 ug/mL)

<table>
<thead>
<tr>
<th>19 cases</th>
<th>Adjusted OR (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin (per week) in prior 1 month</td>
<td>5.6 (2.2-14.3)</td>
</tr>
<tr>
<td>Previous MRSA culture in prior 2nd or 3rd month</td>
<td>15.5 (1.8-134.5)</td>
</tr>
</tbody>
</table>


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VRSA Case 1
July 2002

- 40 y/o female
- ESRD on hemodialysis
- Multiple and prolonged courses of vancomycin
- Chronic non-healing diabetic foot infection, requiring several serial amputations
- Several previous MRSA infections

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VRSA Case 1
July 2002
- Multiple skin/soft tissue infections since 1999 treated with a variety of antibiotics
- Total of 6.5 weeks of Vancomycin in the 6 months preceding discovery of VRSA

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VRSA Case 1
Timeline:
- 8/99 HD
- 3/01 R 5th MT; MSSA
- 5/01 Cellulitis MRSA
- 2/02 R 1st MT
- 4/02 R 4th MT MRSA BSI; Graft
- 5/23/02 Line out MRSA
- 6/06/02 Line out
- 6/14/02 Line out Exit Inf.

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VRSA Case 1
- 6/14/02 2 separate specimens to 2 different labs
- Catheter exit site and catheter tip grow VRSA (MIC ≥ 1024 micrograms/mL)
- 6/21/02 exit site healed
- Plantar ulcers cultured
- VRSA, VR E. faecalis, Klebsiella oxytoca, C. albicans
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<table>
<thead>
<tr>
<th>VRSA Case 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/28/02</td>
</tr>
<tr>
<td>- Negative swabs for VRSA</td>
</tr>
<tr>
<td>- Nares (VS-MRSA)</td>
</tr>
<tr>
<td>- Axilla</td>
</tr>
<tr>
<td>- Umbilicus (VS-MRSA)</td>
</tr>
<tr>
<td>- Catheter exit site</td>
</tr>
<tr>
<td>- Perirectal (VR E. faecalis)</td>
</tr>
</tbody>
</table>

NEJM 2003: 348; 1342-47

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<table>
<thead>
<tr>
<th>VRSA Case 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Hemodialysis Center A</td>
</tr>
<tr>
<td>- Utilized CDC Recommendations for Preventing Transmission of Infections Among Chronic Hemodialysis Patients</td>
</tr>
<tr>
<td>- Hospital A</td>
</tr>
<tr>
<td>- Utilized Universal Precautions-Broad</td>
</tr>
<tr>
<td>- Gloves for anticipated contact with non-intact skin or blood/body fluids</td>
</tr>
<tr>
<td>- Masks if splashing anticipated</td>
</tr>
<tr>
<td>- Gowns if soiling/splash anticipated</td>
</tr>
<tr>
<td>- Always use precautions for &quot;phenotypic shedders&quot;</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>VRSA Case 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>- VRSA susceptibilities</td>
</tr>
<tr>
<td>- Chloramphenicol</td>
</tr>
<tr>
<td>- Linezolid</td>
</tr>
<tr>
<td>- Minocycline</td>
</tr>
<tr>
<td>- Quinupristin-dalfopristin</td>
</tr>
<tr>
<td>- Tetracycline</td>
</tr>
<tr>
<td>- Trimethoprim-sulfamethoxazole</td>
</tr>
</tbody>
</table>

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VRSA Contact Screening

- Healthcare Contacts
  - Dialysis Center
  - Hospital A
  - Podiatry Clinic
- Social Contacts
  - Close Family
  - Nail Salon
- ***All Negative

MDCH/CDC

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VRSA Case 1
Clinical Resolution

- 7/2/02 outpatient surgical debridement
  - Met at entrance
  - Foot covered
  - Transmitted directly into OR isolation room
  - Gowns, gloves
  - Masks for surgical procedure
  - Recovered in isolation room and discharged

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VRSA Case 1
Clinical Resolution

- 14 day course TMP/SMX plus metronidazole
- Aggressive foot care
  - Evaluation twice weekly
  - Continued debridement
  - Gentian violet
  - Contact cast
  - Weekly culture
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VRSA Case 1
Clinical resolution

- 8/20/02
- Last positive culture for VRSA
- 12/02
- Foot ulcers healed
- 03/03
- Hospitalized with MRSA catheter tip positive and Pseudomonas aeruginosa bacteremia
- No evidence VRSA

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VRSA Case 2

- 9/20/02
- Pennsylvania
- Chronic foot ulcers, possible osteomyelitis
- VRSA susceptible to:
  - Chloramphenicol
  - Linezolid
  - Minocycline
  - Quinupristin-dalfopristin
  - Rifampin
  - Trimethoprim-sulfamethoxazole

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VRSA Case 2

- Multiple previous infections with MRSA and VRE
- No previous vancomycin (purported allergy)
- No recent hospitalizations
- Died of cardiac disease

SHEA Abstract
Conclusions

- Staphylococcus aureus most likely acquired vanA gene from E. faecalis cultured simultaneously from foot ulcer
- Prior vancomycin use and frequent MRSA infections were risk factors for the VRSA
- Aggressive local care cured the infection
- Routine infection control practices were adequate in this case to prevent spread

Investigators

Detroit MC/Wayne State
- William Brown
- Wasif Hafeez
- Elaine Flanagan
- Debbie Reid

MDCH
- Matthew Boulton
- Dawn Siefert
- G. Stoltman
- P. Somsel
- J. Hageman
- Lakeview Podiatry Associates
- Guy Rupp, DPM

CDC
- Scott Fridkin
- Soju Chang
- Fred Tenover
- Denise Cardo
- S. McAllister
- L. McDougal
- M. Kellum
- H. Holmes
- J. Chaitram
- P. Raney
- G. Foshiem
- L. Weigel
- M. Arduino

References

- MMWR 46(33) 1997
- MMWR 46(35) 1997
- MMWR 48(51) 2000
- Emerging Infectious Diseases 7(6) 2001
- MMWR 51(26) 2002
- MMWR 51(40) 2002
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VRSA
Epidemiological Investigation
CDC/MDCH/DMC Epidemiology

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Vancomycin Resistant S. aureus Infections: Contact Investigation
CDC
Division of Healthcare Quality Promotion

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Evolution of Drug Resistance in S. aureus

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Step 1: Identify and categorize potential contacts

- Extensive/Moderate/Minimal interaction:

Step 2: Culture patients and contacts

- Patients: anterior nares, wounds, and other clinically relevant sites (e.g., catheter exit site)
- Extensive Contacts: anterior nares, skin lesions
- Moderate or Minimal Contacts: anterior nares
- Priority given to those with extensive contact during the 2 weeks before VISA/VRSA culture date

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Step 3: Prospective Evaluation

- VISA/VRSA case-patient remains in healthcare facility
- Assess efficacy of infection control precautions
- Weekly nares cultures of extensive contacts

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VRSA Contact Investigation

- Objective: epidemiologic investigation to assess possible spread to healthcare workers (HCWS), patients, and other contacts.
- Methodology: swabbing of anterior nares and other clinically relevant sites (e.g., wounds, skin lesion, catheter exit sites)
- Identification of contacts: information obtained from HCWs, patients, family members

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Vancomycin-Resistant S. aureus (VRSA)

MI, June 2002
- 40 y female, hemodialysis
- Diabetes, neuropathic ulcers
- Catheter exit-site and foot wound infected
- Outpatient dialysis
- Healed 3 months

PA, September 2002
- 70 y male, morbid obesity
- Venous stasis ulcers
- Heel wound infected
- Outpatient
- Died 11 weeks

CDC

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Contact Investigation
VRSA, MI
- Personal contacts: family members, friends
- Community contacts: nail salon
- Healthcare contacts: healthcare workers and patients (current and past)
  - Dialysis Center 1
  - Dialysis Center 2
  - Vascular Clinic
  - Hospital: hemodialysis unit, 2 wards, ED
- Environmental samples

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Contact Investigation in Healthcare Settings: VRSA MI

<table>
<thead>
<tr>
<th>Contacts</th>
<th># Available</th>
<th>S. aureus</th>
<th>MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staff &amp; HCWs</td>
<td></td>
<td></td>
<td>571%</td>
</tr>
<tr>
<td>Concurrent patients</td>
<td>56 (100%)</td>
<td>38 (68%)</td>
<td>7 (12%)</td>
</tr>
<tr>
<td>Previous patients</td>
<td>26 (25%)</td>
<td>20 (77%)</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>Dialysis Centers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCWs</td>
<td>6 (100%)</td>
<td>5 (83%)</td>
<td>0</td>
</tr>
<tr>
<td>Concurrent patients</td>
<td>115 (85%)</td>
<td>99 (86%)</td>
<td>13 (11%)</td>
</tr>
<tr>
<td>Outpatient office</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCWs</td>
<td>2 (100%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Previous patients</td>
<td>11 (50%)</td>
<td>5 (45%)</td>
<td>0</td>
</tr>
</tbody>
</table>

CDC

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Contact Investigation in Social Settings VRSA, MI

<table>
<thead>
<tr>
<th>Contacts</th>
<th># Available</th>
<th>S. aureus</th>
<th>MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Household/family</td>
<td></td>
<td></td>
<td>5 (50%)</td>
</tr>
<tr>
<td>Social contacts</td>
<td>2 (100%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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Contact Investigation VRSA, MI

- Total contacts anticipated: 547
- Total contacts swabbed: 371 (68%)
- Total positive cultures for S. aureus: 110 (30%)
- Total positive cultures for MRSA: 28 (8%)
- No VRSA

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Contact Investigation
VRSA, MI

- Prospective evaluation: continued swabbing until patient was negative for 3 weeks
- VRSA Case-Patient – weekly
- Dialysis Center 1: dedicated nurses – weekly
- Vascular Hospital: primary physicians – weekly
- VRSA Investigator – weekly
- Dialysis Center 1: patients – 2 months (Aug & Sept)

Infection Control at Dialysis Center After Identification of VRSA

- Staff of VRSA patient
  - Dedicated (technician and nurse)
  - Glove, gown, and mask, hand hygiene between tasks
- VRSA-Patient
  - Last shift, dedicated equipment (except scale), remote module
  - Foot dressing inspected and wrapped before entering unit
  - Wash hands and graft with chlorohexidine soap
  - Foot care at home:
    - change dressings with gloves, hand hygiene before/after
    - restrict care to single room

VRSA, PA
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Contact Investigation
VRSA, PA

- *S. aureus* carriage study of contacts
- Primary contact: physical contact with case-patient
- Secondary contact: disruption of skin integrity & received care from primary contact on same day
- Environmental sampling

CDC

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Contact Investigation
VRSA, PA

<table>
<thead>
<tr>
<th>Contact Type(#)</th>
<th># Cultured</th>
<th>#Colonized with MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary (220)</td>
<td>205 (93%)</td>
<td>14 (7%)</td>
</tr>
<tr>
<td>Secondary (63)</td>
<td>57 (90%)</td>
<td>7 (12%)</td>
</tr>
<tr>
<td>Total (283)</td>
<td>262 (93%)</td>
<td>21 (8%)</td>
</tr>
</tbody>
</table>

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Contact Investigation
VRSA, PA

- No VRSA identified among contacts
- No VRSA identified among *S. aureus* clinical isolates
- No VRSA identified in case-patient’s home

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VRSA PA: Infection Control

- Hospital/in-patient: as per HICPAC guidelines
- Out-patient/household:
  - Dedicated care-taker
  - Schedule as last appointment
  - Minimize contact; contact precautions
  - Dedicated, disposable equipment
  - Hand hygiene

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Public Health Evaluation

- Definitions
- Laboratory surveillance and diagnostics
- Contact investigation
- Decolonization
- Infection control issues
- Hospital
- Dialysis
- Home healthcare

www.cdc.gov/ncidod/hip/vanco/vanco.htm

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PREVENTION IS PRIMARY!

Protect patients... protect healthcare personnel... promote quality healthcare!
Division of Healthcare Quality Promotion

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