Epidemiologic and Molecular Patterns of Hospital and Community-Associated MRSA

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Hosted by Bruce Gamage
Provincial Infection Control Network, BC

I have no disclosures relevant to this presentation
MRSA - a potpourri of recent cases

- 21 year old male with relapsing skin/soft tissue infection following long board crash
  ▪ Wound culture: MRSA, (R) clox, clinda, (S) vanco, doxy, tmp-smx
    • Rx wound management, IV vancomycin, step down to po doxycycline
- 45 yr old IDU, previous MRSA endocarditis, admitted after recent discharge AMA for recurrent MRSA endocarditis. At last discharge given po linezolid but may not have taken it
  ▪ Multiple blood cultures: MRSA, (R) clox, clinda, (S) vanco (MIC 1.0), linezolid

MRSA cases - continued

- 35 year old male with AML post Rx for Hodgkins Lymphoma. Multiple hospitalizations in multiple sites since 2008. Prior MRSA colonization. In hosp receiving chemotherapy, ANC <0.5. Developed abscess in axilla
  ▪ Culture: MRSA, (R) clox, clinda, (S) vanco, tmp-smx, doxy
Outline

- Evolution of betalactam resistance in *Staphylococcus aureus*
- *S. aureus* microbiology
  - Methicillin resistance in *S. aureus*
  - *S. aureus* toxins
  - Non-betalactam susceptibility
  - Genetic profiles of MRSA
  - Clinical profiles of MRSA strains
- Evolution of epidemiologic patterns of MRSA in hospital and community settings in North America
  - MRSA in Alberta

Evolution of antibiotic resistance in *S. aureus*
Chambers and Delo, Nat Rev Microbiol 2009

1. 1940’s – 1960’s: emergence and spread of penicillin resistance due to penicillinase production
2. 1959 – 1980’s: emergence and spread, primarily in Europe, of semisythetic penicillin (methicillin) resistance due to PBP mutation (PBP2’)
3. 1980’s: Emergence and spread of novel MDR strains of MRSA (such as USA100/CMRSA 2)
4. Late 1990’s: Emergence and spread of community based MRSA strains (such as USA300/CMRSA 10)
MRSA 101
Microbiology

- Methicillin resistance is a genetic trait in \textit{S. aureus} based on chromosomal \textit{mecA} gene
  - \textit{mecA} encodes a mutant Penicillin Binding Protein (PBP) 2 (a cell wall enzyme) designated PBP2’
  - \textit{mecA} is part of a larger a larger chromosomal cassette (SCC), with 8 types (SCC\textit{mecI-VIII})
  - Results in resistance to all betalactam antibiotics
  - Imposes no fitness burden on \textit{S aureus}

\textit{S aureus}: non-betalactam resistance

- Vancomycin
  - Very little full resistance (MIC $\geq 16$)
  - 'non-susceptible' isolates with elevated MIC ($\geq 2$) may fail Rx
    - A result of transient increase in cell wall thickness after prolonged non-curative vancomycin exposure
- Oral agents:
  - In the past hospital isolates typically MDR, community isolates have broader susceptibility
    - Clindamycin
      - Variable. Inducible resistance
    - Trimethoprim – sulfamethoxazole, Tetracyclines
      - Reasonable choices for non-invasive infections in susceptible strains. Ineffective for co-existing Streptococci
- Novel parenteral alternatives to vancomycin
  - Daptomycin
  - Telavancin
  - Ceftaroline
  - ...
MRSA typing & nomenclature

- Typing MRSA isolates is not required for clinical management, but is useful to explain and describe epidemiologic relationships: outbreaks or emerging epidemiologic patterns

- Typing methods:
  - Multilocus sequence typing (MLST)
  - Pulsed-field gel electrophoresis (PFGE)
  - spa-typing

- Nomenclature:
  - USA 100/CMRSA2 – classic HA-MRSA
  - USA 400/CMRSA7 – initial CA-MRSA, first described in children
  - USA 300/CMRSA10 – predominant CA-MRSA, unrelated to USA 400 or USA 100

Biologic distinctions between typical Community and typical Hospital MRSA strains

<table>
<thead>
<tr>
<th>Antimicrobial susceptibility</th>
<th>Presence of virulence factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA 100/CMRSA2: only reliably susceptible to vancomycin (and novel agents such as linezolid, daptomycin, telavancin, ceftaroline)</td>
<td>USA 300 has increased prevalence of:</td>
</tr>
<tr>
<td>USA300/CMRSA 10: typically also susceptible to tmp-smx, tetracycline, fusidic acid +/- clindamycin</td>
<td></td>
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<tr>
<td></td>
<td>▫ Paton Valentine Leucocidin (PVL)</td>
</tr>
<tr>
<td></td>
<td>▫ Associated with skin/soft tissue infection (“spider bite”) and severe-hemorrhagic pneumonia</td>
</tr>
<tr>
<td></td>
<td>▫ α-haemolysin</td>
</tr>
<tr>
<td></td>
<td>▫ Associated with endocarditis and pneumonia</td>
</tr>
</tbody>
</table>
Issues in MRSA Surveillance data

- Surveillance intensity
  - Numbers of cases you find can depend on how hard you look – especially colonization

- Clinical status
  - Some infections are treated without obtaining cultures
  - In lab based surveillance it can be difficult to distinguish infection from colonization
    - Eg - skin/wounds, sputum
    - No debate about significance of positive blood culture

- Source of MRSA
  - Hospital vs Community acquisition of MRSA is often speculative since acquisition is usually silent
  - Source of infection is easier to determine based on standard definition

MRSA - USA
Rhee et al Infect Control Hosp Epidemiol 36:1417 (2015)

- USA 100 has been present for many years in US hospitals. Since ~ 2007 it has been in relative decline in several regions (coincident with increased attention to IPC)
- USA 300 was introduced in the late 1990’s but did not emerge simultaneously: starting in western states and spreading east
  - Disproportionately affects children, incarcerated and inner city populations
MRSA BSI in a large Chicago hospital
2007-2013

Community Onset BSI

Hospital Onset BSI

Emergence of MRSA in a network of Canadian Hospitals (CNISP)
(Simor et al., ICHE, 2010)

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### Table 4: Laboratory Characterization of Canadian Strains of Methicillin-Resistant Staphylococcus aureus (MRSA) Identified in the Canadian Nosocomial Infection Surveillance Program, 1995–2007

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>PGGE genotype</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total no. of isolates typed</td>
<td>13,648</td>
<td>7,607</td>
<td>6,266</td>
<td>6,775</td>
<td></td>
</tr>
<tr>
<td>CMRSA-1 (USA300; ST45; CC45)</td>
<td>2,589 (19)</td>
<td>1,109 (43)</td>
<td>1,136 (47)</td>
<td>344 (5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CMRSA-2 (USA100/800; ST3; CC5)</td>
<td>6,370 (47)</td>
<td>373 (14)</td>
<td>2,051 (48)</td>
<td>3,846 (58)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CMRSA-3/6 (ST241/ST239; CC8)</td>
<td>1,603 (12)</td>
<td>622 (24)</td>
<td>437 (10)</td>
<td>544 (8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CMRSA-7 (USA400; ST1; CC1)</td>
<td>340 (12)</td>
<td>18 (1)</td>
<td>72 (2)</td>
<td>250 (4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CMRSA-10 (USA100; ST8; CC8)</td>
<td>1,175 (9)</td>
<td>1 (0.4)</td>
<td>32 (1)</td>
<td>1,142 (17)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Other types</td>
<td>1,571 (11)</td>
<td>484 (19)</td>
<td>538 (13)</td>
<td>549 (8)</td>
<td></td>
</tr>
<tr>
<td>SCCmec type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total no. of isolates typed</td>
<td>3,269</td>
<td>339</td>
<td>637</td>
<td>2,293</td>
<td></td>
</tr>
<tr>
<td>Type I</td>
<td>18 (1)</td>
<td>9 (3)</td>
<td>4 (1)</td>
<td>5 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Type II</td>
<td>1,765 (54)</td>
<td>202 (60)</td>
<td>434 (68)</td>
<td>1,129 (49)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Type III</td>
<td>283 (9)</td>
<td>64 (19)</td>
<td>71 (11)</td>
<td>148 (6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Type IV</td>
<td>1,151 (35)</td>
<td>63 (18)</td>
<td>96 (15)</td>
<td>992 (43)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Other types</td>
<td>52 (1)</td>
<td>1 (0.3)</td>
<td>32 (5)</td>
<td>19 (1)</td>
<td></td>
</tr>
</tbody>
</table>

### MRSA Infections/1,000 admissions in Sentinel Canadian Hospitals

Source: CNISP

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Healthcare Associated MRSA Infections in Sentinel Canadian Hospitals

MRSA BSI in Sentinel Canadian Hospitals/1000 Admissions
Community Acquired MRSA Infections in Sentinel Canadian Hospitals/1000 Admissions

Alberta

- Population 4.2 million (2014)
- 2 major urban centres (Edmonton, Calgary) with 68% of population
- 2 medical schools
- Academic medical centres in Edmonton and Calgary

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Alberta Health Services (AHS)

- As in other Canadian provinces all medically necessary healthcare is provided publicly
- AHS founded in 2009 to provide all medically necessary hospital care in Alberta
- Currently (2015) provides 3.1 million annual inpatient days through
  - 2 tertiary hospitals
  - 2 pediatric hospitals
  - 1 cancer hospital
  - 7 large urban hospitals
  - 7 regional hospitals
  - 82 small suburban / rural hospitals

MRSA in Alberta: a retrospective cohort study
Bush et al
Antimicrobial Resistance and Infection Control, 2015

Methods:
- Incident MRSA in AHS hospitals between 01/04/2011 and 31/03/2013
- Epidemiologic definitions of source of MRSA
  - Hospital Acquired
    - Identified >48 hr after hospital admission
  - Healthcare Associated (HCA)
    - <48 hr after admission, healthcare risk (e.g. LTC, hemodialysis)
  - Community Acquired
- Spa-typing and PFGE of a subset of isolates
Results

- 4818 incident MRSA cases
  - 32.7% clinical, 67.4% screening
  - 41.1% HA, 20.8% HCA, 38.1% CA
  - 43.4% large urban, 23.6% small suburban rural
- 2248 (46.7%) isolates available for typing
Epidemiology of MRSA BSI in Alberta
Taylor et al
J Hosp Infect, 2015

Background

- Focus is on infection
  - By surveying only BSI, avoids problems related to surveillance intensity, definition of clinical status and permits comparison to other jurisdictions
- Source = source of BSI not MRSA

Methods

- MRSA blood culture isolates between 04/11-03/13 were assessed by site based ICP’s
- Isolates were spa-typed

<table>
<thead>
<tr>
<th>Table I</th>
<th>Metillin-resistant Staphylococcus aureus (MRSA) bloodstream infections (BSI) in Alberta, Canada in 2011-2013 by location and setting of BSI acquisition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospital acquired</td>
</tr>
<tr>
<td>Sex</td>
<td>N (%)</td>
</tr>
<tr>
<td>Male</td>
<td>60 (60.6)</td>
</tr>
<tr>
<td>Age</td>
<td>64.6 (16.6)</td>
</tr>
<tr>
<td>Facility type, N (%)</td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td>36 (36.4)</td>
</tr>
<tr>
<td>Large urban</td>
<td>34 (34.3)</td>
</tr>
<tr>
<td>Regional</td>
<td>19 (19.2)</td>
</tr>
<tr>
<td>Small suburban/rural</td>
<td>7 (7.1)</td>
</tr>
<tr>
<td>Paediatric</td>
<td>3 (3.0)</td>
</tr>
<tr>
<td>Geographic zone, N (%)</td>
<td></td>
</tr>
<tr>
<td>Calgary</td>
<td>48 (48.5)</td>
</tr>
<tr>
<td>Edmonton</td>
<td>30 (30.3)</td>
</tr>
<tr>
<td>Remaining zones</td>
<td>21 (21.2)</td>
</tr>
</tbody>
</table>

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Conclusions

- MRSA epidemiology is in transition and varies geographically
- Across North America, there has been a decline in traditionally hospital acquired MRSA
- Community sourced MRSA is variable, but well established/predominant in several areas
- In Alberta, MRSA BSI is predominantly community onset
- While USA 300/CMRSA 10 is still predominantly a community strain and USA 100/CMRSA 2 is still predominantly a hospital strain, presumption of source of MRSA based on strain type is no longer viable
Epidemiologic and Molecular Patterns of Hospital and Community-Associated MRSA
Prof. Geoffrey Taylor University of Alberta
A Webber Training Teleclass

February 17  (Free WHO Teleclass ... North America)
SUCCESSFUL IMPLEMENTATION STRATEGY FOR THE
PREVENTION OF SURGICAL SITE INFECTIONS
Prof. Sean Berenholtz, Johns Hopkins Schools of Medicine, Baltimore

February 24  (South Pacific Teleclass)
PATIENT EMPOWERMENT AS PART OF AN ASIAN HAND HYGIENE
PROGRAMME
Prof. Yee Chun Chen, National Taiwan University Hospital and College of Medicine

March 3  MERS-COV: IMPLICATIONS FOR HEALTHCARE FACILITIES
Prof. Sotirios Tsiodras, University of Athens Medical School, Greece

March 10  (FREE Teleclass)
BARRIERS TO TB INFECTION CONTROL IN DEVELOPING COUNTRIES
Dr. Eltony Mugomeri, National University of Lesotho

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