What’s New in MRSA?

An Update on Legislative Mandates and MRSA in the Obstetrics/Gynecology Patient

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Overview

- New CA state legislation: MRSA active surveillance testing
- The epidemiology of MRSA: community vs. health care associated MRSA infections
- MRSA in the obstetrics-gynecology patient
Active Surveillance Cultures (ASC) for MRSA

California state law now mandates active surveillance cultures for MRSA within 24 hours of admission:

- Patients scheduled for inpatient surgery
- Discharge from acute care hospital within 30 days
- Admitted to an ICU
- Receives inpatient dialysis
- Transferred from a skilled nursing facility

What is the Rationale for Active Surveillance Cultures (ASC)?

- Prevent patient-to-patient transmission?
  - Contact precautions/ isolation
  - Decolonization

- Prevent infection of colonized patients?
  - Decolonization
  - Modification of perioperative prophylaxis
Conflicting Evidence...

- Robicsek et al Ann Intern Med 2008: Prospective, observational study over 3 consecutive time periods
  - Compared to no ASC or ICU ASC only, universal ASC for all hospital admissions ↓ MRSA infections and bacteremia

- Harbarth et al JAMA 2008: Prospective, crossover design of surgical pts to receive no ASC or ASC on admit
  - No difference between control or intervention: HA-MRSA infection or MRSA surgical site infections

The CDC, Society for Healthcare Epidemiology of America, and Associations for Professionals in Infection Control currently state that there is insufficient evidence to warrant routine or mandated use of active surveillance testing for detection of MRSA and recommend against implementation of such procedures at this time...It must also be recognized that ‘one size does not fit all’ with regard to optimal practices for individual health care settings.”

Stanley Deresinski, M.D.
Clinical Infectious Diseases 2008; 47 (1 September)
What to do with the results?

- Contact precautions/isolation?
- Decolonization?
- Modification of perioperative prophylaxis?
- Patient education?

Contact Isolation: Does it Work?

- Cooper et al BMJ ‘04: Systematic review of 46 studies
  - Most retrospective, interrupted time series, no RCTs
    - ↓ in MRSA
    - Major methodological weaknesses (no studies impact of isolation alone) – alternative explanations for ↓ in MRSA possible

- Cepeda et al Lancet ‘05: Prospective 2-center study
  - No ↓ in MRSA transmission when patients placed in single room or cohort isolation vs. no use of isolation measures
Potential Adverse Events Associated with Contact Precautions

- Examined less frequently and for shorter periods, compared to those who are not in isolation
- More likely to experience preventable adverse events (pressure ulcers, falls, electrolyte imbalances)
- Increased rates of depression and anxiety


Strategies to Reduce Transmission of Antimicrobial Resistant Bacteria in ICUs (STAR-ICU) Trial

- Ongoing multicenter, randomized, open-labeled trial
  - Intensive infection control strategy + standard care
    - Active surveillance cultures for MRSA or VRE
    - Universal gloving until surveillance cx show they are not colonized
    - Contact precautions during care of colonized or infected patients
    - Program to promote hand hygiene and standard precautions
  - Standard infection control strategy
    - Program to promote hand hygiene and standard precautions
    - Collection of surveillance cultures (but results not reported)

Clinicaltrials.gov NCT00342745
Legislation and contact isolation assumes the traditional model of MRSA epidemiology – that the hospital is the primary source of infection.

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

History of methicillin-resistant *Staphylococcus aureus* (MRSA)

- **'59**: Introduction of methicillin
- 1st MRSA isolate identified
- **'98**: Report of MRSA infxn in children w/o “classic” risk factors
- **'99**: MMWR report of 4 deaths due to MRSA in previously healthy children
- **'06**: CA-MRSA predominant cause of SSTI
- Outbreaks of CA-MRSA reported in multiple diverse populations
Origins of CA-MRSA

2 hypotheses:
1) Hospital strains were carried out into the community

2) De novo acquisition of resistance by a methicillin-susceptible strain
   - Horizontal transfer of meca gene into a community strain

CA-MRSA is genetically distinct from HA-MRSA

- Novel SCC mec element (type IV)
- Lack of multiple antibiotic resistance genes
- Presence of additional genetic elements, potential virulence factors (Panton-Valentine leukocidin, ACME, phenol-soluble modulins etc.)
CA-MRSA: Spectrum of Disease
Active Bacterial Core Surveillance, 2001-2002

- Population, laboratory-based surveillance study in Baltimore, Atlanta, Minnesota, 2001-2002

Antimicrobial Susceptibility Patterns of CA vs. HA-MRSA

Fridkin NEJM 2005

Naimi JAMA 2003
Epidemiology of MRSA Infection In San Francisco 1996-2004

Is There a Role for Decolonization?

- **Cochrane Database of Systematic Reviews 2008**
  - Mupirocin reduces nosocomial *S. aureus* infections in surgical and dialysis patients, most with MSSA
  - No benefit in 2 studies that included non-surgical pts and MRSA carriers
- **Cochrane Database of Systematic Reviews 2003**
  - Topical and systemic antimicrobial therapy not effective in eradicating nasal or extra-nasal MRSA
  - Adverse events and development of resistance observed with therapy
**MRSA carriage in pregnancy**

- 60/209 (29%) women were staphylococcal carriers (only 1% MRSA)
- 11/205 (5%) infants were carriers (<1% MRSA)
- No evidence of maternal-infant transmission

**MRSA Vaginal-Rectal Colonization**

- Prevalence appears to be low
  - 0.4%-3.5%\(^1,2\)
  - Conflicting data re: association with GBS carriage\(^2,3\)
- Colonization and risk of vertical transmission in pregnant women
  - No cases of early-onset invasive neonatal infections by MRSA occurred among 202 anovaginal colonized women\(^2\)

\(^1\)Chen et al Obstet Gynecol 2006; \(^2\)Andrews et al Obstet Gynecol 2008; \(^3\)Chen et al Am J Perinatol 2007
Is MRSA Screening and Decolonization Cost-Effective in Obstetric Patients?

- Cost-effectiveness decision model:
  - Estimated 14,294 of peripartum women with invasive MRSA infection annually (mostly mastitis)
  - Estimated economic impact ~ $8 million

### Incremental Cost-Effectiveness Ratios* for Variable Levels of Decolonization Success

<table>
<thead>
<tr>
<th>Rates of successful decol (%)</th>
<th>ICER* ($)</th>
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<tbody>
<tr>
<td>10</td>
<td>$4,352,894</td>
</tr>
<tr>
<td>30</td>
<td>$2,006,311</td>
</tr>
<tr>
<td>50</td>
<td>$929,316</td>
</tr>
<tr>
<td>70</td>
<td>$689,218</td>
</tr>
<tr>
<td>90</td>
<td>$426,686</td>
</tr>
</tbody>
</table>

*Failed to meet benchmark goal of $50,000/ QALY

Beigi RH et al Obstet Gynec 2009

Vancomycin Perioperative Prophylaxis: What does the data show?

- Bolon et al: Meta-analysis cardiac surgery patients

Risk Ratio

Glycopeptides ↓ SSI due to methicillin-resistant gram positives (RR 0.54; 95% CI 0.33-0.90)

- No threshold prevalence of MRSA infections defined

Bolon et al CID 2004; Updated info courtesy of Maureen Bolon, M.D.
“A fundamental principle of any screening program is often overlooked in discussions of active surveillance cultures: although we can identify asymptomatic carriers and place them in isolation, there is poor evidence that our interventions prevent infections.”

UCSF Response to the Legislation

- Perform active surveillance cultures on selected patient groups

- Patient education
  (http://infectioncontrol.ucsfmedicalcenter.org/MRSA/MRSA_Infx_PtInfo_Adult.pdf)

- Education of physicians, RNs and other healthcare workers to reinforce standard precautions and hand hygiene
MRSA in the Ob/gyn Patient

Clinical Presentations of CA-MRSA in Pregnancy

- Laibl et al 2005: Retrospective chart review ’00-’04 (n=57)
  - Majority multiparous (70%)
  - Gestational age at clinical infection
    - 2° trimester (46%) > 1° trimester (19%) > postpartum (18%) > 3° trimester (14%)
  - Postpartum infections
    - Breast (40%), surgical site (30%), other soft tissue infection (30%)
  - Skin and soft tissue infections predominant clinical presentation
    - Extremity (44%), buttock (25%), breast (23%), vulva/ groin (21%), abdomen (21%)
  - Multiple sites of infection reported in 58% of pts

Laibl et al Obstet Gynec 2005
Obstetric Outcomes in Women with CA-MRSA

Table 3. Obstetric Outcomes in Women With Community-Acquired Methicillin-Resistant Staphylococcus aureus Compared With the General Obstetric Population

<table>
<thead>
<tr>
<th></th>
<th>Women with MRSA (N = 43)</th>
<th>General Obstetric Population (N = 57,214)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuliparous</td>
<td>10 (23)</td>
<td>23,175 (40)</td>
<td>.025</td>
</tr>
<tr>
<td>Gestational age at delivery (wk)</td>
<td>38.9 ± 2.1</td>
<td>39.3 ± 2.2</td>
<td>.452</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3186 ± 698</td>
<td>3294 ± 616</td>
<td>.243</td>
</tr>
<tr>
<td>Preterm delivery (≤ 36 wk)</td>
<td>4 (9)</td>
<td>4,434 (8)</td>
<td>.701</td>
</tr>
<tr>
<td>Preterm delivery (≤ 34 wk)</td>
<td>3 (7)</td>
<td>1,978 (3)</td>
<td>.206</td>
</tr>
<tr>
<td>Preterm premature rupture of membranes</td>
<td>1 (2)</td>
<td>1,630 (2)</td>
<td>.877</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>20 (47)</td>
<td>41,208 (72)</td>
<td>.182</td>
</tr>
<tr>
<td>Repeat cesarean delivery</td>
<td>15 (35)</td>
<td>3,092 (4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cesarean delivery for dystocia</td>
<td>4 (9)</td>
<td>2,113 (3)</td>
<td>.183</td>
</tr>
<tr>
<td>Cesarean delivery for nonmeasuring fetal status</td>
<td>4 (9)</td>
<td>2,475 (4)</td>
<td>.108</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>2 (5)</td>
<td>5,369 (9)</td>
<td>.289</td>
</tr>
<tr>
<td>Culture-proven neonatal sepsis</td>
<td>0 (0)</td>
<td>63 (1.1)</td>
<td>.827</td>
</tr>
<tr>
<td>Multiple gestations</td>
<td>1 (2)</td>
<td>713 (1)</td>
<td>.553</td>
</tr>
</tbody>
</table>

MRSA, methicillin-resistant Staphylococcus aureus.
Values are n (%) or mean ± standard deviation.

CA-MRSA and Postpartum Mastitis

*Northwestern
Clinical Features of CA-MRSA vs. MSSA Postpartum Mastitis

Case control study: 21 MRSA, 27 MSSA
- No differences in:
  - Age, pregnancy history, clinical presentation
  - Prenatal or intrapartum risk factors
- More likely to be multiparous (57% vs. 33%)
  - May reflect ↑ prevalence of MRSA among children
- Less likely to receive adequate and timely antimicrobial therapy
- No significant differences in clinical outcomes

Microbiology of Puerperal Mastitis

No Abscess
- MSSA, 44%
- S. epidermidis, 35%
- Other, 6%
- MRSA, 2%
- No growth, 13%
N=54

Abscess
- MSSA, 19%
- MRSA, 67%
- Other, 7%
- No growth, 7%
N=35

*UT Southwestern
Stafford Obstet Gynecol 2008
**Microbiology of Nonpuerperal Breast Abscess**

- MRSA, 19%
- MSSA, 14%
- Coag neg staph, 16%
- Diphtheroids, 16%
- Streptococcus, 10%
- Pseudomonas, 8%
- Proteus, 5%
- Anaerobes, 5%
- Other, 7%

*Moazzez Arch Surg 2007*

**Management of Uncomplicated Skin and Soft Tissue Infections: Abscess**

- **Abscess: Primary Rx - incision & drainage (AII)**
  - No difference in outcomes whether an active antibiotic is used\(^1\)
  - Randomized trial of patients with skin abscesses (mostly MRSA), high cure rates in all: cephalexin (84.1%); placebo (90.5%)\(^2\)
  - Additional benefit of MRSA active oral antibiotic beyond I&D is unknown; clinical trials underway.
  - Consider empiric Rx for CA-MRSA if: systemic symptoms, severe local symptoms, immunosuppression, extremes of patient age, critical location, failure to respond to I&D

\(^1\)Lee MC PIDJ '04; Young DM Arch Surg '04; Fridkin SK NEJM '05; Moran G NEJM '06  
\(^2\)Rajendran PM AAC'07
Management of Breast Abscesses Due to MRSA

- Incision and drainage
  - Stafford 2008: 56% of women with MRSA received surgical drainage + an inactive antibiotic
    - All discharged without complication, no treatment failures

- Ultrasound-guided aspiration or catheter drainage
  - Antibiotics may play a more important role in patients treated with minimally invasive techniques

Empiric therapy for mastitis?

- **Abscess**: if antibiotic therapy indicated, consider coverage for CA-MRSA pending culture data
  - Moran G NEJM 2006: MRSA isolated from 61% of abscesses in patients with SSTI presenting to 11 EDs

- **Mastitis without abscess**: relative contribution of CA-MRSA compared to MSSA, strep unclear
  - Consider coverage for CA-MRSA if fails to respond to β-lactam therapy
  - Our own local epidemiology?
## Oral Antimicrobial Therapy for MRSA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dose</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Pregnancy Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP/SMX</td>
<td>1-2 DS BID</td>
<td>- Extremely low rate of resistance - MRSA &amp; MSSA</td>
<td>- Unreliable for group A strep</td>
<td>C/D in 3rd trimester</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>300-450 TID</td>
<td>- MRSA, MSSA, &amp; group A strep - Excellent tissue &amp; abscess penetration</td>
<td>- Potential for resistance - C. difficile risk</td>
<td>B</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 BID</td>
<td>- Low resistance - MRSA, MSSA</td>
<td>- Unreliable for group A strep</td>
<td>D</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 BID</td>
<td>- Complicated SSTI</td>
<td>- Adverse events with long-term use - Expensive</td>
<td>C</td>
</tr>
</tbody>
</table>

### Inducible clindamycin resistance?

- Not detected by standard broth microdilution testing
- When to consider
  - Erythromycin resistant, clindamycin susceptible
  - Frequency – 0-7%
  - How to test - D-test
- What to do if D-test + but clindamycin being used?
  - Improving – continue
  - Failing/mod-severe infxn - change

A positive D-test
Management of Complicated Skin and Soft Tissue Infections

- Management of cSSTI and necrotizing fasciitis
  - Surgical evaluation and debridement (AIII)
  - Empiric Rx for MRSA is recommended¹ (AII)

- Rx for MRSA cSSTI and necrotizing fasciitis
  - Vancomycin (C), daptomycin (B)², linezolid (C)³, tigecycline (D)⁴ (AI)
    - No significant difference in primary outcome of clinical cure


MRSA and Breastfeeding

- Transmission of MRSA via breastmilk in asymptomatic mother
  - Behari 2004: 2/3 preterm triplets with MRSA infection
    - Infant A: MRSA sepsis, pneumonia, conjunctivitis
    - Infant B: MRSA conjunctivitis

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FIGURE. Pulse-field gel electrophoresis of methicillin-resistant Staphylococcus aureus isolates: lane 1 = blood of infant A; lane 2 = breast milk for infant A; lane 3 = breast milk for infant B; and lane 4 = surveillance swab of infant B.

Behari Inf Control Hosp Epi 2004
Should a Woman with Postpartum MRSA Mastitis Continue Breastfeeding?

- No clear data
- Breast emptying is a mainstay of therapy
- Various expert opinions:
  - Continue breastfeeding if mom is on antibiotics unless draining wound or cellulitis in the area where the baby may have skin to skin contact
  - Consider breastfeeding on the contra-lateral side and expressing on the infected side.

CA-MRSA and Vulvar Abscesses

- Thurman et al: Review of 162 women Rx for vulvar abscess 2006-08 (Texas)
  - Microbiology:
    - MRSA dominant pathogen (64%)
    - Others: group B strep, enterococcus, proteus, E. coli (36%)
  - MRSA vulvar abscesses:
    - No distinguishing clinical signs or symptoms
    - No difference in clinical outcomes
  - Therapy:
    - Incision and drainage
    - TMP/SMX (covers MRSA and majority of other pathogens)

Thurman et al Obstetrics and Gynecology 2008
**Summary**

- The data to support active surveillance testing for MRSA are controversial; risk of vertical transmission appears to be low
- Emphasize infection control measures: hand hygiene and wound care
- Additional benefit of contact precautions, decolonization, modification of perioperative prophylaxis unclear ➔ tailor to individual institution, “one size does not fit all”

**Summary**

- CA-MRSA has emerged as a significant pathogen distinct from HA-MRSA
- Incision and drainage is the primary Rx of abscesses; if antibiotic therapy is clinically indicated, empiric coverage for CA-MRSA should be considered in women presenting with a breast abscess
- No significant difference in obstetric or clinical outcomes in women with CA-MRSA infections
- More research needed in the obstetrics population, to characterize risk to neonate
Thank you!