**Overview**

Methicillin Resistant Staph Aureus

- Epidemiology
- State Laws
- Prevalence in obstetric population
- Vulvar abscess
- Genital tract colonization
- Perinatal Transmission
- Chorioamnionitis
- Mastitis/Breast Abscess
- Neonatal infections
- Economic considerations in obstetrics
- Summary

**Epidemiology**

- 1-3% of population MRSA colonized
  - Nares > intact skin, vagina
- MRSA infections classified as epidemic
- 19,000 deaths per year attributed to MRSA
- 2X increase in infection treatment in hospitals
- 8X increase in rate of patients entering hospital with MRSA between 1999 and 2006
- MRSA transmission
  - Contact with colonized individual or fomite

CDC 2007, RM Kleven 2007, MW Ellis 2004
Epidemiology
- Community-associated MRSA (CA-MRSA)
- Healthcare-associated MRSA (HA-MRSA)
- Common mecA gene
- Difference based on 5 SCCmec types
- CA-MRSA
  - Lacks multiple antibiotic resistance genes
  - Potential virulence factors
- CA-MRSA/HA-MRSA clinical setting classifications
  - No longer distinct!!!
  - HA-MRSA increasing in community settings
  - CA-MRSA increasing in hospital settings/nosocomial infections
  - Annual incidence in San Francisco in mid 2000’s
  - CA-MRSA surpassed HA-MRSA

CA-MRSA vs. HA-MRSA
- Skin, soft tissue infections
- "Closed populations"
- Multiple clonal origins
- Dermatologic condition
- Younger age group
- Non-white ethnicity
- Susceptible to multiple Abx
- Susceptible to multiple Abx
- SCCmec type-type IV, V
- CX time 24-72 hr after admn
- PVL toxin present >80% (virulent CA-MRSA strains)
- Resp tract, urinary tract, pulm, wound, bloodstream infections
- Healthcare-associated
- Few disseminated clones
- Healthcare-associated RF
- Older age group
- White ethnicity
- Resistant to multiple Abx
- SCCmec type-type I, II, III
- CX time >72 time after admn
- PVL toxin absent
- Higher mortality risk
- BMW Diederen 2006, RA Herman 2008, CDC 2007

Laboratory Detection
- PCR
  - Most accurate method of MRSA detection
  - MecA gene and latex agglutination for protein products
  - Real-time PCR (mecA) detection within 2 hours
  - Limited commercial availability/use
- Culture
  - Oxacillin-salt agar screening plates and cefoxitin disk diffusion tests
  - Surveillance cultures of colonized sites (anterior nares)
  - Asymptomatic MRSA colonization anterior nares culture
    - Sensitivity 73-93%
  - Screening open lesions/multiple sites increases sensitivity
  - Traditional culture detection 48-72 hours
  - Chromogenic selective agar detection within 24 hours
- Laboratory Detection
  - PCR
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- Antimicrobial Susceptibility
  - CA-MRSA vs. HA-MRSA
    - Ciprofloxacin
    - Clindamycin
    - Erythromycin
    - Gentamicin
    - Rifampin
    - Tetracycline
    - TMP/SMX
    - Vancomycin
    - CA-MRSA
      - HA-MRSA
      - TS Naimi 2003 Minnesota DPH

Antimicrobial Susceptibility
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Risk Factors

- HIV infection
- Injection drug use
- Non-white ethnicity
- Sharing needles, razors, sharp objects, tattoos (skin trauma)
- Military service (closed communities)
- Incarceration, correctional facility, or shelters
- Residence in long term care facility
- Sharing sports equipment
- Men who have sex with men
- Recent or prolonged hospitalization (especially ICU)
- Recent antibiotic therapy
- MRSA colonization or proximity to MRSA-colonized or -infected
- Surgical site infection
- Hemodialysis

State Laws for MRSA Screening

- Laws
  - California
  - Illinois
  - New Jersey
  - Pennsylvania
- Bills filed
  - Washington
  - Kentucky

California State Law

- Nares screened for MRSA within 24 hr of admisn (active surveillance cultures)
- Scheduled for inpatient surgery and have medical condition considered susceptible to infection
- Discharged from acute care hospital within 30 days
- Admitted to an intensive care or burn unit
- Receives in-patient dialysis
- Transferred from skilled nursing facility

Senate Bill 1058
Effective January 1, 2009
Most studies support ASC in setting of hospital outbreaks or in high-prevalence, high-risk populations

Evidence limited
- Lack of control groups, confounding variables
- Most studies not designed to assess the primary outcome
  - MRSA transmission/colonization vs. MRSA infection

CDC, Society for Healthcare Epi of America, Assoc’n for Professionals in Infection Control and Epi
- “Insufficient evidence to warrant routine or mandated use of active surveillance testing for detection of MRSA”

IDSA and SHEA: ASC as “special approach”

63% required inpatient treatment

Topical antimicrobial or antiseptic agents
- To decrease/prevent recurrent infections of high-risk patients
- To eradicate/suppress the carrier state in colonized patients
- Mupirocin intranasal x 5-14 days
- +/- chlorhexidine baths daily
- +/- systemic antimicrobials

Routine decolonization not supported
- Cochrane Review 2003
  - “Insufficient evidence to support use of topical or systemic antimicrobial therapy for eradicating nasal or extra-nasal MRSA”

Decolonization in subpopulations?
- Cochrane Review 2008
  - “Intranasal mupirocin should be considered for use in proven nasal carriers of S. aureus in hospitalized surgical, dialysis, and non-surgical patient groups at risk of infection”

- Retrospective chart review
  - 57 pregnant women with MRSA infections between 2000-2004
  - Increasing MRSA infection incidence
  - RF for MRSA infection: multiparity, CD, repeat CD
  - Gestational age diagnosed
    - 2nd trim (45%) > 1st trim > Postpartum > 3rd trim
  - Lesion sites
    - Extremities (44%) > buttocks > breast/mastitis > vulva/groin > abdomen
  - Postpartum lesions
    - Breast (40%) > incision (30%) > other soft tissue (30%)
  - 96% skin or soft tissue infections
  - 58% recurrent episodes
  - 63% required in-patient treatment

VR Labi 2005
Vulvar Abscess

- 162 women with vulvar abscesses
- 16% (26) patients pregnant
- 64% of cultured abscesses were MRSA
- 40% required inpatient management
- In-patient treatment more common with comorbidities, larger abscess, systemic illness
- No difference in inpatient admission or treatment complications in MRSA group
- Treatment
  - I&D plus TMP/SMX, vancomycin, or clindamycin

AR Thurman 2008

Genital Tract Colonization

- 2,963 pregnant women recto-vaginal screening
  - 17% (507) Staph aureus (MSSA and MRSA)
  - Staph aureus isolates
    - 2.8% (14) MRSA positive
  - 0.5% (14) MRSA colonization
    - Majority (13 of 14) specimens CA-MRSA
  - GBS associated with Staph aureus colonization
    - OR 2.1 (CI 1.7-2.5)
  - No neonatal data

Case control study

- 13 CA-MRSA, 52 MSSA, 52 Staph
- CA-MRSA colonization associated with lack of GBS carriage
- MSSA more likely to be associated with GBS colonization

KT Chen 2006, KT Chen 2007

Genital Colonization in Pregnancy and Perinatal Transmission?

- 5732 pregnant women (5804 infant deliveries)
- Recto-vaginal cultures at 35-37 weeks
- Overall MRSA colonization rate 3.5%
- MRSA colonization
  - More common among GBS-pos women (RR 1.6%)
- No cases of MRSA early-onset invasive neonatal infection among 200+ infants born to MRSA colonized women

WW Andrews 2008
Genital Colonization in Pregnancy and Perinatal Transmission?
- 304 pregnant women
- Nares and vagina cultured in labor
- Overall MRSA colonization rate 3.0%
- 3.6% (9 of 252) infants MRSA colonization
- ONLY 0.4% (1 of 252) concordant mother-infant organism pair
- Transmission to newborns from VD unlikely
- Neonatal colonization in first 4 weeks of life likely occurred after discharge

Chorioamnionitis
- Very rare organism in chorioamnionitis
- Geisler 1998
  - 25 weeks PPROM, chorio, endometritis due to MRSA
  - Unit clerk on pediatric pulmonary unit
- Fowler 2002
  - 36 week PPROM, chorio, IUFD due to MRSA

Postpartum Considerations
- Postpartum Infections (n=10)
  - Breast (40%) > incision (30%) > soft tissue (30%)
- Postpartum Infections (n=8)
  - Breast (50%), wound infxn, cellulitis, pustulosis, UTI
  - 3 of 4 mastitis progressed to abscess
  - Mean time to infection 23 days PP (4-73 days)
- Most postpartum cases soft tissue/mastitis
- Mastitis commonly leads to abscess

Mastitis/Breast Abscess

Journal of Midwifery and Womens Health 2007

DM Pinter 2008, M Reusch 2008

Chorioamnionitis

VR Laibl 2005, L Saiman 2003
Mastitis/Breast Abscess

Rise CA-MRSA mastitis/breast abscesses
CA-MRSA >10% of community isolates
Retrospective case series nonpuerperal breast abscess
– 44 women
– 19% MRSA > Coag neg Staph 16% > MSSA 14%
Case control postpartum mastitis
– 27 MSSA and 21 MRSA
– Increasing incidence of MRSA mastitis infections
– 95% CA-MRSA of 21 MRSA cases
– MRSA cases more often multiparous (57%) vs. MSSA (33%)
– Higher temperature with MRSA vs. MSSA (p=0.05)
– No significant difference in clinical outcome

A Moazzez 2007, P Reddy 2007

Mastitis/Breast Abscess

127 women hospitalized with puerperal mastitis
Mastitis only cultures (n=54)
– MSSA (44%) > S. epi (35%) > MRSA (2%)
Mastitis + breast abscess cultures (n=35)
– CA-MRSA most common breast abscess organism
– MRSA (67%) vs. MSSA (19%)
Women with CA-MRSA inappropriately treated
– 56% did NOT receive appropriate antibiotic
Empiric use of ineffective antibiotic DID NOT adversely affect outcomes

I Stafford 2008

Mastitis/Breast Abscess

SFGH Experience: Mastitis

<table>
<thead>
<tr>
<th></th>
<th>MSSA</th>
<th>MRSA</th>
<th>Coag Neg Staph</th>
<th>Neg Cx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastitis:</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>6</td>
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<tr>
<td>breast milk cx</td>
<td></td>
<td></td>
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<tr>
<td>(n=15)</td>
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<tr>
<td>Breast abscess:</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
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<tr>
<td>culture (n=3)</td>
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</table>

August 2004-March 2005
J Vargas 2005
Mastitis/Breast Abscess Management

- CA-MRSA increasingly more common in puerperal mastitis and especially abscesses
- Continue first line mastitis treatment in routine cases
- Consider cultures if tx failure, recurrence, high prevalence, RF’s
- Consider CA-MRSA therapy
  - Recurrence, tx (beta lactam) failure, abscess, severe infection until cultures obtained
  - Local epidemiology
  - Adjunct drainage or aspiration may be warranted
- Treatment/Management for MRSA mastitis
  - Continue breastfeeding/pumping
  - TMP/SMX = first line (efficacy, cost, compliance)
  - Clindamycin and Linezolid 2nd line alternatives
  - I&D or aspiration/catheter drainage for abscess


Neonatal MRSA Transmission via Breastmilk

- MRSA transmitted between mother-infant pairs
  - 8 lactating mother-infant pairs
  - 2 of 4 Staph species isolated MRSA
  - No evidence of mastitis
  - No active infection in term infants
- 2 of 3 preterm triplets with MRSA infection
  - Triplet pregnancy delivered at 26 weeks
  - Infant A: MRSA sepsis, pneumonia, conjunctivitis
  - Infant B: MRSA conjunctivitis
  - All isolated identical susceptibility and banding

M Kawada 2003, P Behari 2004

Neonatal MRSA Transmission via Breastmilk

Pulsed-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.

P Behari 2004

MRSA Colonization Breastfeeding Considerations

- Limited data in MRSA cases
- Hand hygiene
- Mastitis education
- If colonized with MRSA encourage precautions
- CONTINUE breastfeeding term, healthy infants while mother being treated
- Consider deferring breastfeeding if infant significantly premature or severely ill
  - Maternal colonization
  - Mastitis until infection treated

M Bianuzzo 2002
**Neonatal CA-MRSA Considerations**

- Case reports of CA-MRSA transmission from mother to neonate 48 hours after birth
- CA-MRSA from mother to 3 of 4 premies
  - Maternal RF: 2 recent hospitalizations
- CA-MRSA and neonatal cellulitis, pustulosis c/w peripartum transmission in nursery setting
- Neonatal RF for infection
  - Maternal colonization
  - Breastfeeding
  - Number of siblings


**Obstetric Economic Considerations**

- Cost-effectiveness decision analysis
- ~14,000 pregnant or postpartum women with invasive MRSA infection in US annually
- Mastitis = majority of invasive infections
  - ~8,800 (62%)
- Projected annual economic effect $8.7 M from societal and $8.0 M from payer perspective
- Sensitivity analyses key driving factors
  - MRSA prevalence, mastitis incidence, CD rate
- Universal screening and decolonization
  - Not cost effective

RH Beigi 2009

**General Summary MRSA in Obstetrics**

- CA-MRSA and HA-MRSA differ in clinical and molecular epidemiology
- CA-MRSA is emerging infection in obstetric population
- Increasing incidence
- Associated costs
- Recto-vaginal prevalence 0.5-3.5% pregnant women
- Conflicting data regarding association if genital colonization ass’d with GBS colonization

**General Summary MRSA in Obstetrics**

- Skin or soft tissue infections most common
- Commonly recurring skin abscesses
- Increasing vulvar and breast infections
- Common organism in breast abscess
- Low risk of perinatal transmission/colonization
- Very rare cause of chorioamnionitis
- No significant difference in adverse perinatal/PP outcomes
- No significant increase early-onset neonatal infections
<table>
<thead>
<tr>
<th>Management/Treatment Summary</th>
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<tbody>
<tr>
<td>- Consider aerobic/anaerobic cultures of vulvar abscess</td>
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<tr>
<td>- Culture if refractory/severe breast infection or abscess</td>
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<tr>
<td>- Universal screening in pregnancy NOT recommended</td>
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<tr>
<td>- Routine decolonization NOT recommended</td>
</tr>
<tr>
<td>- Contact isolation NOT routinely recommended/proven effective</td>
</tr>
<tr>
<td>- Colonized mothers do NOT need separation from infant</td>
</tr>
<tr>
<td>- Consider decolonization for recurrent infections or high-risk patients</td>
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<tr>
<td>- Careful consideration of antibiotic use/overuse</td>
</tr>
<tr>
<td>- Prevention</td>
</tr>
<tr>
<td>- Hand washing</td>
</tr>
<tr>
<td>- Use of gowns/gloves for contact of premature infants</td>
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Cepeda 2005

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<thead>
<tr>
<th>Management/Treatment Summary</th>
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<tbody>
<tr>
<td>- Oral therapy for mild or moderate infection</td>
</tr>
<tr>
<td>- Doxycycline 100 mg Q 12 hr</td>
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<tr>
<td>- Advantage: low resistance</td>
</tr>
<tr>
<td>- Disadvantage: Class D and unreliable GAS coverage</td>
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<tr>
<td>- But no human case reports of congenital anomaly association or teeth staining with doxycycline</td>
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<tr>
<td>- May consider use for short duration</td>
</tr>
<tr>
<td>- Rifampin 300 mg Q 12 hr used with 2nd agent</td>
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<tr>
<td>- No longer used as monotherapy- due to resistance!</td>
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<tr>
<td>- Linezolid 600 mg Q 12 hr</td>
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<td>- VRSA or intolerance</td>
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<tr>
<td>- Expensive and adverse events with long-term use!!!</td>
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<tr>
<td>- IV therapy for severe infection</td>
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<tr>
<td>- Vancomycin 1 g Q 12 hr = first line</td>
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<tr>
<td>- TMP-SMX 2.5 mg/kg Q 12 hr</td>
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<tr>
<td>- Clindamycin 600-900 mg Q 8 hr</td>
</tr>
<tr>
<td>- Linezolid 600 mg or Tigecycline 50 mg Q 12 hr</td>
</tr>
<tr>
<td>- VRSA or intolerance</td>
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<tr>
<td>- Expensive!!!</td>
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<td>- Tigecycline = class D</td>
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<td>- Decolonization</td>
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<td>- Mupirocin intranasal Q 12 hr x 5-14 days</td>
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<td>- +/- chlorhexidine baths daily</td>
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<tr>
<td>- +/- systemic antibiotics</td>
</tr>
<tr>
<td>- No standard recommendation for vancomycin use in perioperative prophylaxis (MRSA prevalence? Risks?)</td>
</tr>
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</table>
Resources

- http://www.cochrane.org/reviews

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