Methicillin Resistant
Staphylococcus aureus

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Methicillin Resistant *Staph aureus*

Community-acquired MRSA
Community-associated MRSA
Skin and soft tissue infections: focus
Invasive disease: briefly
Epidemiology: general, Louisiana
Management of recurrent infections
Prevention of recurrent infections
Staph aureus

First recognized > 100 yrs ago
MRSA first found in 1961
CDC estimates: 1.5% colonized with MRSA
MRSA

Case:
Pt is X yr old male/female, generally healthy. Has had Y number of skin infections (furuncles). During the Zth episode culture was obtained and grew MRSA. Has responded each time to TMP/SMX – minocycline – clindamycin. Recurs when off abx.
MRSA

Case questions:
What do you do for the acute episodes?
What can you do to try to prevent recurrences?
What do you tell the family that is worried about invasive infections (they have read the newspaper reports of children dying of MRSA)?
Definitions

Health care associated
Community onset
Hospital onset
Community–associated
Community onset
MRSA

Clinical presentations
Skin and soft tissue infections
boil, abscess, furuncle
erythema, swelling, pain, drainage
Invasive infections
osteomyelitis, pneumonia, blood
stream infxn, CNS infxn
MRSA
Skin and Soft Tissue Infections

Furuncles
  abscessed hair follicles (boils)
Carbuncles
  coalesced furuncles
Abscesses
MRSA
Invasive Disease

Childhood deaths—invasive disease

October 2007

4 children in NH, MS, NY, VA (4–17 yrs)

December 2006 – January 2007

3 children in GA, LA; pneumonia
MRSA

Some Epidemiology
Figure 1: Number of MRSA invasive diseases – Louisiana, 1999-2007
Figure 2: Age group distribution of cases – Louisiana and United States, 2003-2007
Figure 3: Proportion of MRSA among Staphylococci isolated in hospitals
Louisiana, 1999-2006

Year & Percent MRSA

<table>
<thead>
<tr>
<th>Year</th>
<th>Percent Staphylococci</th>
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</thead>
<tbody>
<tr>
<td>1999</td>
<td>33%</td>
</tr>
<tr>
<td>2000</td>
<td>38%</td>
</tr>
<tr>
<td>2001</td>
<td>45%</td>
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<tr>
<td>2002</td>
<td>54%</td>
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<tr>
<td>2003</td>
<td>57%</td>
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<td>2004</td>
<td>61%</td>
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<tr>
<td>2005</td>
<td>65%</td>
</tr>
<tr>
<td>2006</td>
<td>62%</td>
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</table>
Table 2: Crude mortality rates /100,000 resulting from staphylococcal infection as the main cause of death or as secondary cause of death - Louisiana, 1999-2006

<table>
<thead>
<tr>
<th>Year</th>
<th>Main</th>
<th>Secondary</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>27.2</td>
<td>24.7</td>
<td>51.9</td>
</tr>
<tr>
<td>2000</td>
<td>20.9</td>
<td>24.5</td>
<td>45.4</td>
</tr>
<tr>
<td>2001</td>
<td>17.4</td>
<td>24.6</td>
<td>42.0</td>
</tr>
<tr>
<td>2002</td>
<td>17.1</td>
<td>18.0</td>
<td>35.2</td>
</tr>
<tr>
<td>2003</td>
<td>22.2</td>
<td>27.8</td>
<td>50.0</td>
</tr>
<tr>
<td>2004</td>
<td>15.9</td>
<td>24.3</td>
<td>40.3</td>
</tr>
<tr>
<td>2005</td>
<td>13.9</td>
<td>16.8</td>
<td>30.7</td>
</tr>
<tr>
<td>2006</td>
<td>16.6</td>
<td>18.8</td>
<td>35.4</td>
</tr>
</tbody>
</table>
Figure 5: Rate of Staphylococcal infection at discharge as main diagnosis per 1,000 hospitalizations – Louisiana, 1999-2004

\[ y = 1.9314x + 9.04 \]
In Louisiana, it is estimated that
- 30% of the general population is a carrier of Staphylococci.
- 1% of the low risk population is a carrier of MRSA.
- 5-20% of high risk population is a carrier of MRSA (patients with multiple hospitalization, residents of long term facilities, chronically ill patients, inmates in detention facilities...)
- This means that out of a 4,500,000 population, 1,500,000 are carriers of S. aureus and 45,000 are carriers of MRSA.

Hospital acquired MRSA (HA-MRSA) shows multi-resistance to other antibiotics while community acquired MRSA (CA-MRSA) remains multi-sensitive

<table>
<thead>
<tr>
<th>Resistant to:</th>
<th>CA-MRSA</th>
<th>HA-MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin</td>
<td>2-8 %</td>
<td>50-60%</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>2-5 %</td>
<td>30-40%</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>10-20 %</td>
<td>70-80%</td>
</tr>
<tr>
<td>Tmp-sxt*</td>
<td>2-10 %</td>
<td>20-40%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>1-5 %</td>
<td>27.4 %</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0 %</td>
<td>0 %</td>
</tr>
</tbody>
</table>

*Tmp-sxt = Trimethoprim-sulfamethoxazole
HA-MRSA strains show much more resistance to all other antibiotics.
CA–MRSA
Molecular Epidemiology

Pulse–field types
USA300, USA400
Multilocus sequence types
8, 1
Panton–Valentine leukocidin toxin
controversial role in virulence
Arginine catabolic mobile element
?enhances ability to survive at low pH
Phenol–soluble modulin peptides
SCCmec IV
CA–MRSA Resistance

mecA gene confers R to beta-lactams carried on gene complex SCCmec

CA = SCCmec IV, V
HA = SCCmec I, II, III
CA–MRSA Resistance

Increasing R to clindamycin
D zone test
erythromycin R, clindamycin S
induced to express clindamycin R
CA–MRSA

1993–2005 ED visits for SSTIs tripled
1995–2005 hospitalizations quadrupled
78% Staph SSTIs = MRSA
59% purulent SSTIs
97% USA300
CA–MRSA

Incidence 2005

Invasive infections
4.5/100,000

Deaths
0.5/100,000
MRSA

Children

*Staph aureus* colonizes ~ 50% of children
Skin, anterior nares, other sites
Invasive 3.5/100,000 age < 12 mos
Osteoarticular–most common
Complications–venous thrombosis, disseminated infection
MRSA

High risk groups

Most community-acquired infections in persons with no identifiable risk factors
CA–MRSA
Risk Factors

- Children, young adults
- Racial/ethnic minorities
- Low SES
- Crowding
- Skin–skin contact
- Compromised skin
- Sharing items
- Challenges maintaining hygiene
- Frequent or recent antibiotic use
CA–MRSA Clusters

- Inmates
- Competitive sports participants
- Military recruits
- Childcare center attendees
- MSM
- Evacuation shelters
- Full term infants
- Tattoo recipients
CA–MRSA

Colonization

Nasal:

2001–02 0.8% age > 1 yr
2003–04 1.5%

(Peds TN = 9.2% 2004)

19.7% carry USA300 or USA400

Other sites:

vaginal–rectal swabs in pregnancy, pharynx, axilla, perineum
CA–MRSA Management

I & D may be enough (trials in ‘70’s–’80’s)
Supplemental antibiotics
severity of local symptoms, systemic inxn, co morbidities,
immunosuppression, extremes of age
Antimicrobial Treatment

Clindamycin
  FDA approved (for \textit{S. aureus} serious infxn)
  D – test
  CDAD ?

Tetracyclines – doxycycline, minocycline
  Doxy FDA approved (skin infxn)
  Pregnancy, children under 8 yrs
  ? activity against GABHS

http://www.cdc.gov/mrsa/mrsa_initiative/skin_infection/mrsa_algorithm.html
Antimicrobial Treatment

TMP/SMX – not FDA approved for *Staph* 3rd trimester pregnancy, infants < 2 mos  
May not cover GABHS

Rifampin  
Only in combination  
Drug–drug interactions

Linezolid – FDA approved complicated skin infxn  
Consult ID  
Myelosuppression, neuropathy

http://www.cdc.gov/mrsa/mrsa_initiative/skin_infection/mrsa_algorithm.html
Antimicrobial Treatment

Vancomycin
- Mainstay of therapy
- Concern over slow bactericidal activity
- Emergence of resistance
- MIC creep
- Variable tissue penetration
Antimicrobial Treatment

Daptomycin
- FDA approved for adults with *S aureus* bacteremia, R side IE, cSSTI
- NOT for pneumonia
- Ongoing trials in children

Quinupristin–Dalfopristin
- FDA approved for cSSTI in age > 16 yrs
- Limited by toxicity

Telavancin
- FDA approved cSSTI in adults
- Monitor creatinine clearance
Management SSTIs

Signs/symptoms of infxn
Redness, swelling, warmth, tenderness

Purulent?
Drain, send for culture/susceptibility

Not purulent? >> Cellulitis without abscess
Antibiotic with coverage for *Strep*
Add MRSA coverage if no response

http://www.cdc.gov/mrsa/mrsa_initiative/skin_infection/mrsa_algorithm.html
Recent Study

Randomized Controlled Trial of Cephalexin Versus Clindamycin for Uncomplicated Pediatric Skin Infections

Aaron E. Chen, MDa, Karen C. Carroll, MDb, Marie Diener-West, PhDc, Tracy Ross, MSb, Joyce Ordun, MS, CRNPa, Mitchell A. Goldstein, MDa, Gaurav Kulkarni, MDa, J. B. Cantey, MDa, George K. Siberry, MD, MPHd

PEDIATRICS (doi:10.1542/peds.2010–2053)
New Guidelines

Infectious Diseases Society of America
Published in CID Feb 1, 2011
Available online: www.idsociety.org
Management of patients with MRSA

SSTI
Bacteremia/endocarditis
Pneumonia
Bone/joint infections
CNS infections
New Guidelines

First MRSA guidelines from IDSA

Objective

  Provide recommendations on management of most common clinical syndromes

Address vancomycin dosing and monitoring

Pediatric considerations for each topic

Research gaps identified
New Guidelines

SSTIs

Minor skin infections and secondarily infected lesions
  mupirocin 2%
Hospitalized cSSTI
  vancomycin
  clindamycin if resistance rate low
  linezolid
New Guidelines

Recurrent SSTIs
Prevention education on hygiene
Environmental hygiene
Decolonization in selected cases
  nasal decolonization
  topical body decolonization
New Guidelines

Vancomycin

15 mg/kg/dose q 6 hrs for serious or invasive infection

Consider trough 15–20 μg/ml for serious infections; efficacy and safety not well studied

MIC > 2 μg/ml, use alternative agent
New Guidelines

Neonates

- Neonatal pustulosis
  - mild cases, full-term -> topical
  - extensive disease or pre-term -> vanc

Sepsis

- vancomycin
- clindamycin or linezolid (non-endovascular)
Research Gaps

Optimal management of nonpurulent cellulitis
Is initial empiric coverage for MRSA necessary

Optimal management of abscesses
Is there additional benefit of antibiotics; impact on recurrent infections and transmission

Optimal management for recurrent SSTIs
Is decolonization effective; environmental hygiene
Decolonization?
Hypochlorite Solutions
‘Bleach Baths’

Hypochlorite killing of community–associated methicillin–resistant *Staphylococcus aureus* Laboratory strain and clinical isolates

Dose–dependent killing
- 2.5 ul/ml >>> 3 log decrease

Time dependent killing
- 5 min >>> 3 log decrease
- 15 min >>> 4 log decrease

Pediatr Infect Dis J 2008;27: 934–5
Variability among pediatric infectious disease specialists in the treatment and prevention of methicillin-resistant *Staphylococcus aureus* skin and soft tissue infections
Treatment and Prevention

114 ID consultants (58% response)
30.9% many more, 46.4% somewhat more in prior 12 mos
95.5% many/somewhat more compared to prior 3 yrs
19.7% ‘curbsides’
67% buttock/perineum
Treatment and Prevention

Antibiotic treatment
56% clindamycin
38% TMP/SMX

Recurrence
20% different antibiotic
48% same antibiotic, same duration
31.7% same antibiotic, longer duration

Pediatr Infect Dis J 2008;27: 270-3
Treatment and Prevention

98% labs perform D test
95% modify treatment based on result
Treatment and Prevention

Decolonization
- 11% never
- 8% after first episode
- 40% after second episode

Evidence of severe disease or spread

Family/household
- 49% whole family
- 47% no family members
- 4% culture and treat if positive

Pediatr Infect Dis J 2008;27: 270-3
Resources


http://www.doh.wa.gov/Topics/Antibiotics/MRSA.htm

http://here.doh.wa.gov/materials/living-with-mrsa
Resources

National MRSA Education Initiative: Preventing MRSA Skin Infections

http://www.cdc.gov/mrsa/mrsa_initiative/skin_infection/index.html
Resources

http://new.dhh.louisiana.gov/

http://www.dhh.louisiana.gov/offices/page.asp?id=249&detail=8022

Selected References


http://www.idsociety.org/content.asp?x?id=4432#mrsa
Selected References

http://www.cdc.gov/ncidod/dhqp/ar_mrsa.ca.html
Selected References


The Staphylococc—A Poem
(with apologies to Lewis Carroll\(^1\))

*Frank E. Berkowitz, MBBCh, MPH*

A restless infant, and febrile
Did sweat and tremble on the way.
Leg swollen, red, and immobile,
No longer could he play.

"Beware the Staphylococc, my son!
The pyrogens as hot as hell.
Beware coagulase, and watch for
Toxic PVL”

He took the mighty Pen in hand:
But Staphylococc a laugh did raise,
For many years it could withstand
With beta-lactamase.

So striding forth, this time with Meth
He thought that he could end the fray.
But all the Staphylococces were left
With PBP 2A.

What could he do? the Staphylcoce
Was multiplying as he slept.
With years of antibiotic use
He didn’t have much left.

So took he clind and vancomyce
Long time to quell the cocci’s fun.
And depended he on imagery
To show the damage done.

“And hast thou slain the Staphylococc?
Come to my arms my beamish boy!”
“No! Woe the days, For Staph always
Devises a new ploy.”