Understanding and Fighting Methicillin-Resistant Staphylococcus Aureus "MRSA"

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Understanding and Fighting MRSA

1. What is MRSA?
2. Why is it such a problem today?
3. What is Community-associated MRSA?
4. Is it really that serious?
5. How is it treated?
6. How can we prevent it?
What is MRSA?

Methicillin-resistant Staphylococcus aureus
Staph aureus

- Transient skin flora
- Most common cause of skin infections
- Various strains with variety of virulence factors
  - Encoded by phages, plasmids, pathogenicity islands and SCC
- Virulence factors
  - Leukocidin (kills WBC)
  - Exfoliatins (scalded skin syndrome)
  - Toxic shock toxin TSS T1 (Toxic shock syndrome)
  - Enterotoxins (food borne illness)
History of S. aureus Resistance

- 1941 - Introduction of Penicillin into treatment of infectious disease
- 1944 - S. aureus becomes Pen resistant
- 1959 - Methicillin introduced
- 1960’s - MRSA strains emerge
- 1968 - First case found USA
- 1970/80’s - Problem in hospitals (ICU, burn units)
History of S. aureus Resistance

- 1988 2% MRSA
- 1991 29% MRSA
- Today ~ 70% of S. aureus in USA is MRSA
Prevalence of MRSA Colonization

- Carriage rates in the general population range from 2 to 10%
- Recent pediatric study: 36% s. aureus in nares (9% were MRSA)
- Higher rates among certain populations
  - Old (nursing home residents)
  - Sick (hospitalized, dialysis)
  - Health care workers (ICU, surgical wards)
    - One study showed up to 70% colonized
Prevalence of MRSA Infection

- 18-25 cases/100,000 noted in 2001/02 study from CA, GA, and MN
  - Majority SSTIs (77%)
  - 73% resistant to initial antibiotics

- Proportion of Post-op infections with MRSA from 1992 to 2002 increased from 9.2% to 49.3% (NNSI/CDC)
Invasive MRSA Infection Incidence

- For every 100,000 people living in the U.S. there were 32 cases of invasive MRSA in 2005

- MRSA was responsible for an estimated 94,000 life-threatening infections and 18,650 deaths in 2005

(CDC report; Oct 17, 2007 *The Journal of the American Medical Association*)
What happened?

Community-associated MRSA
CA vs. HA MRSA

- **CDC definitions**
  - “Community-associated”
    - In prior year no hospitalizations, NH, dialysis, surgery, or permanent indwelling devices
  - “associated” vs. “acquired/onset”
    - Community-acquired = diagnosed in outpatient setting or w/in 48hrs of stay
CA MRSA

- Responsible for dramatic increase in incidence of MRSA
  - Increased rates of invasive MRSA infections
  - Increased skin and soft tissue infections in Emergency Departments
  - Increased mortality among MRSA-related infections
CA MRSA

“Four Pediatric Deaths from Community-Acquired Methicillin-Resistant *Staphylococcus aureus* -- Minnesota and North Dakota, 1997-1999”
The Culprit!

USA300
CA MRSA Outbreaks

- Saint Louis Rams in 2003
- Fencers in Colorado
- Prison inmates (MS, GA, TX)
- Children in Tennessee
- Gay men in California
USA 300 MRSA Strain

- Originated in the community
- “A single clone of CA MRSA accounts for the majority of infections”

CA vs. HA MRSA Genetics

- **Community Associated**
  - USA300 and USA400 PF-types
  - Carry SCCmec IV gene

- **Healthcare Associated**
  - USA100 and USA200 PF-types
  - Carry the SCCmec types II and III

CA vs. HA Characteristics

- **CA MRSA**
  - “multi-drug susceptible”
  - Produce super-antigens (SEB, SEC, and TSST-1)

- **HA MRSA**
  - “multi-drug resistant”
  - Fewer toxins produced
CA MRSA in the hospital

USA300 accounted for 34% of MRSA BSI over a 7 mo period in 2004 at Grady Memorial Hospital in Atlanta

Methicillin-resistant S. Aureus

- More frequent development of symptomatic infections
- Skin and STI are most common
  - Furuncles, impetigo
  - Large, painful skin abscesses
MRSA in the ED

- MRSA the most common cause of SSTI among ED patients (76%)
- USA300 accounted for 97% of MRSA isolates and 31% of MSSA isolates

Methicillin-Resistant S. aureus Infections among Patients in the Emergency Department
MRSA in the ED

- SSTI
  - 1993 1.2 million visits
  - 2005 3.5 million visits
  - After 2001 increasing use of antibiotics effective against MRSA
    - 51% TMP/SMX in 2005


“Increased US Emergency Department Visits for Skin and Soft Tissue Infections, and Changes in Antibiotic Choices, During the Emergence of Community-Associated MRSA”
How bad can it get?

- Higher fatality rates
  - 2X more likely to die from MRSA than MSSA

- Pyomyositis, necrotizing fasciitis, septic thrombophlebitis

- Necrotizing pneumonia
  - Lung necrosis, empyema
  - Rapid progression to death within 48 to 72 hours
MRSA Pneumonia

- Severe necrotizing pneumonia
  - Hemoptysis
  - Necrotic appearance on CXR
  - Recent influenza
MRSA Pneumonia

- S. aureus is most common cause of Hospital-acquired pneumonia
- MRSA nosocomial pneumonia has been associated with significantly poorer outcomes than MSSA pneumonia
Treatment of MRSA Pneumonia

Antibiotic Options
- vancomycin
- quinupristin/dalfopristin
- linezolid
- daptomycin
- tigecycline
Treatment of MRSA Pneumonia

- **Vancomycin**
  - 2g/day (15mg/kg q12hr)
    - Goal is trough concentration 15-20 mcg/mL
  - Poor lung perfusion
  - Failure rates up to 40% reported
Treatment of MRSA Pneumonia

- **Linezolid (Zyvox)**
  - Oxazolidinone
  - 100% bioavailability
  - Epithelial lining fluid levels exceed plasma concentrations
    - May benefit those with empyema/loculations/abscess
  - Aerobic gram positive organisms
Treatment of MRSA Pneumonia

- No definite superiority to vancomycin in studies to date

- Side effects
  - Serotonin syndrome (weak MOA inhibitor)
  - thrombocytopenia
  - neuropathies
Management of MRSA Infections

- Consider in all cases of skin and soft tissue infections
  - esp. abscesses and “spider bites”
- Consider in sepsis, osteomyelitis, septic arthritis, severe pneumonia, necrotizing fasciitis
- Culture all pus!
- Blood cultures?
  - Severe disease (sepsis, lymphangitis)
Management of SSTI Infections

**Recommendations:**

- Culture all wounds!
- I&D alone may be adequate. Consider antibiotics on individual basis:
  - severity and rapidity of progression
  - surrounding cellulitis (>5cm diam)
  - signs/symptoms of systemic illness
  - Co-morbidities (DM, malignancy, HIV)
  - extremes of age
  - unable to drain completely
Antibiotic Options

- **Bactrim**
  - Not FDA approved for use in staph but it works.
  - GAS commonly resistant (consider adding Beta-lactam if cellulitis)

- **Tetracycline/minocycline/doxycycline**
  - Limited studies to support efficacy in invasive infections
  - Not in children/pregnancy
  - Also need double coverage for Strep
Antibiotic Options

- **Clindamycin**
  - High level of resistance in HA strain
  - Increased incidence of C. diff colitis

- **Levaquinn**
  - High prevalence of resistance
  - Not recommended first line
Vancomycin

- For severe infections requiring hospitalization
- Must be given IV
- “Red man syndrome”
- Ototoxic
- Thrombophlebitis
Newer Agents

- **Linezolid (Zyvox)**
  - VERY effective, but VERY expensive
  - Available orally
  - Resistance has been reported
  - Myelosuppression with prolonged use

- **Tigecycline (Tygacil)**
  - glycylcycline
  - FDA approved for complicated SSTI and intraabdominal infections (not pneumonia)
  - Active against MRSA and VRE
Newer Agents

- **Quinupristin-dalfopristin (Synercid)**
  - Not approved for MRSA infections
  - Poor tolerability profile (arthralgias, myalgias, thrombophlebitis)
  - Need central line

- **Daptomycin (Cubicin)**
  - FDA approved in 2003 for MRSA – bactericidal
  - Dose dependant myopathy
  - Not for pneumonia, CNS or bone
Newer Agents

- Ceftobiprole
  - “fifth generation”
  - Phase III trials for treatment of nosocomial pneumonia
  - Phase II trials for complicated STTI
  - Bacteriocidal

The Problem

CA MRSA is spreading fast!
Controlling the Spread of MRSA
CA MRSA Risk Factors

- Crowding
- Person to person contact (athletes)
- Contact with wounds
- Poor hygiene
- Low socioeconomic status
- IVDA
- Homosexuals
- Prisoners
HA MRSA Risk Factors

- Previous antibiotic use
- >8.4 days in hospital
- Indwelling catheters/IVs
- Surgical procedures
- Dialysis
- Diabetes
- Nursing Home Residents
The Solution

Hygiene!

Antibiotic stewardship!

Education!
Questions?