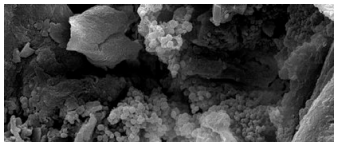
Community Associated MRSA

Dr. Rachel Gorwitz, CDC

A Webber Training Teleclass

Community-Associated MRSA: What's Up and What's Next?



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Division of Healthcare Quality Promotion
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Learning Objectives

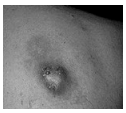
- Describe the changing epidemiology of MRSA in community settings
- Discuss important findings from recent studies of CA-MRSA prevalence, incidence, risk factors, and virulence factors
- Describe emerging antimicrobial resistance in CA-MRSA and discuss implications for clinical management of skin infections
- Identify current and future strategies to prevent CA-MRSA infections

Staphylococcus aureus

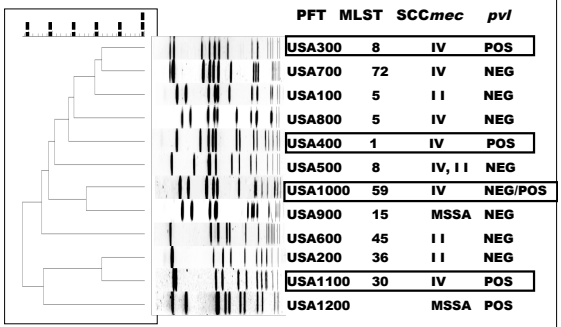
- Common human colonizer and pathogen throughout history
- Transmitted by direct or indirect contact
- MRSA:
  - 1st described 1960s
  - Resistant to all currently available β-lactam agents (penicillins, cephalosporins)
  - Historically linked to healthcare settings
  - 1990s: Distinct MRSA strains emerged in the community as cause of infection in otherwise healthy people

Community-Associated MRSA

- Defined epidemiologically as MRSA infections with community onset in persons that lack significant healthcare exposure
- Predominantly skin infections
- Transmission associated with:
  - Frequent skin-to-skin contact
  - Compromised skin
  - Sharing contaminated objects / surfaces
  - Crowding
  - Lack of cleanliness
  - Prior antibiotic use
  - Lack of access to healthcare



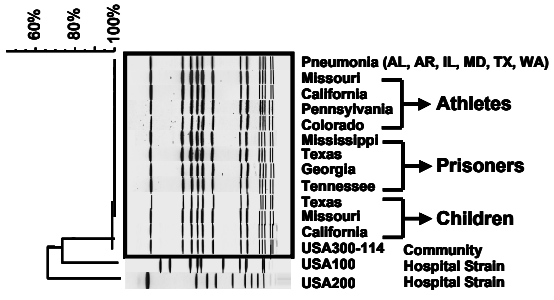
National Database of MRSA Pulsed-Field Types (Highlighted PFTs: historically community-associated)



PFT	MLST	SCC*mec*	*pvl*
USA300	8	IV	POS
USA700	72	IV	NEG
USA100	5	I I	NEG
USA800	5	IV	NEG
USA400	1	IV	POS
USA500	8	IV, I I	NEG
USA1000	59	IV	NEG/POS
USA900	15	MSSA	NEG
USA600	45	I I	NEG
USA200	36	I I	NEG
USA1100	30	IV	POS
USA1200		MSSA	POS

McDougal et al J Clin Micro 2003;41:5113-5120

A Single Pulsed-Field Type (USA300) has Accounted for Most Community-Associated MRSA Infections in the U.S.



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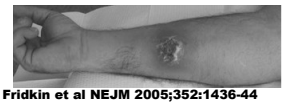
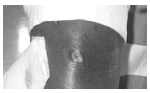
CA-MRSA Infections are Mainly Skin Infections

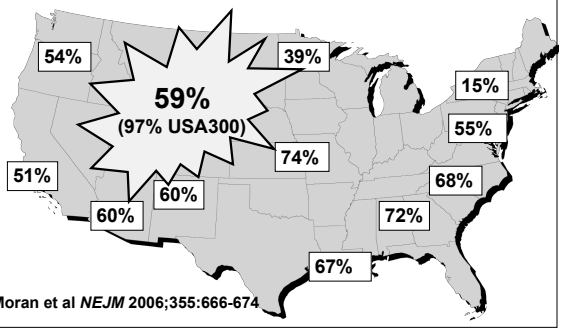
Disease Syndrome	(%)
Skin/soft tissue	1,266 (77%)
Wound (Traumatic)	157 (10%)
Urinary Tract Infection	64 (4%)
Sinusitis	61 (4%)
Bacteremia	43 (3%)
Pneumonia	31 (2%)





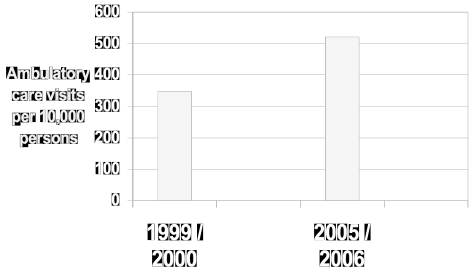
Fridkin et al NEJM 2005;352:1436-44

MRSA Was the Most Commonly Identified Cause of Purulent Skin Infections Among Adult ED Patients
(*EMERGE*ncy ID Net), August 2004



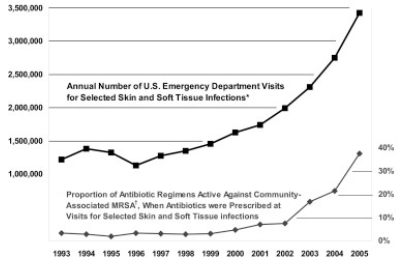
Moran et al *NEJM* 2006;355:666-674

Increase in Ambulatory Care Visits for Skin Infections Typical of *S. aureus*
LF McCaig et al, APHA 2008

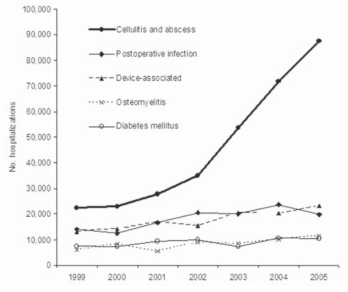


2005/06: 15.2 million visits annually in the United States

Increased Emergency Department Visits for Skin Infections Typical of *S. aureus*
DJ Pallin et al, *Ann Emerg Med* 2008;51:291-8



Hospitalizations for *S. aureus* Skin Infections Increasing Dramatically
E Klein et al. *Emerg Infect Dis* 2007;13:1840-6



RM Klevens, MA Morrison, J. Nadle, et al.
Invasive Methicillin-Resistant *Staphylococcus aureus* Infections in the United States
JAMA 2007;298:1763-71

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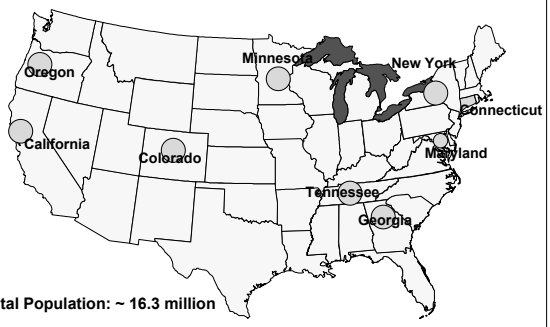
Active Bacterial Core Surveillance Areas (Invasive MRSA)



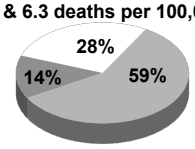
Total Population: ~ 16.3 million

MRSA Case Categorization (ABCs Population-Based Surveillance)

- Healthcare-associated:
  - Hospital-onset: Cases with positive culture obtained >48 hrs after hospital admission (may also have risk factors)
  - Community-onset: Cases with at least 1 of the following risk factors:
    - Invasive device at time of admission; h/o MRSA infection or colonization; h/o surgery, hospitalization, dialysis, or residence in a LTC facility in 12 mos preceding culture
- Community-associated: Cases with community-onset and none of above risk factors documented

Most Invasive MRSA Infections are Healthcare-Associated

National estimates:
94,360 infections; 18,650 deaths
31.8 cases & 6.3 deaths per 100,000 persons

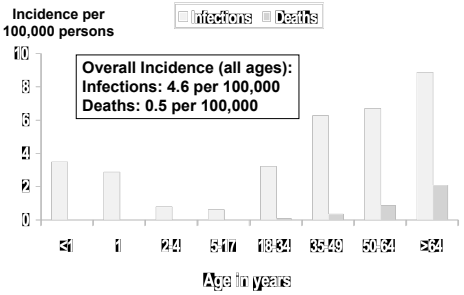


- Community-Associated (CA-MRSA)
- Healthcare-Associated, Community-Onset (HACO-MRSA)
- Healthcare-Associated, Hospital-Onset (HAHO-MRSA)

Klevens et al *JAMA* 2007;298:1763-71

Incidence of Invasive CA-MRSA Infections and Deaths by Age

Active Bacterial Core surveillance (ABCS), 2005



Klevens et al JAMA 2007;298:1763-71

Distribution of Clinical Syndromes: Invasive CA-MRSA

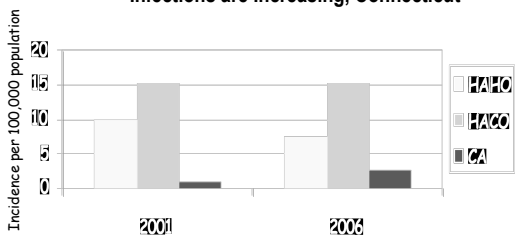
ABCs 2005-06

Infectious Syndrome*	%
Bacteremia +/- other syndromes	77%
Pneumonia (mostly bacteremic)	16%
SSTI (mostly bacteremic)	26%
Endocarditis (metastatic complication)	13%
Osteomyelitis	10%
Bacteremia without other syndrome	24%

*Categories not mutually exclusive

Fridkin SHEA 2008

Invasive Hospital-Onset MRSA Infections are Decreasing while Community-Associated Infections are Increasing, Connecticut



Petit S et al. Presented March 17, 2008 at the International Conference on Emerging Infectious Diseases, Atlanta, GA

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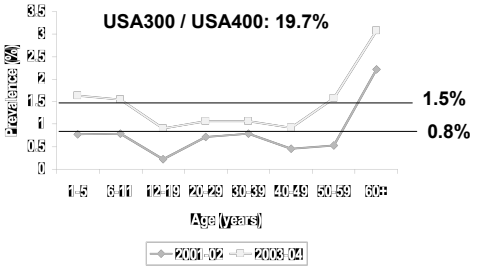
Community-Acquired Pneumonia (CAP)

- *S. aureus* is a recognized cause of CAP (~3% of cases with pathogen identified)
  - Associated with preceding influenza infection
  - Rapid progression; Case-fatality 29-60%
- Several recent case series of severe MRSA CAP[1]
  - Median age: late teens
  - ~50% with antecedent or concurrent viral illness
  - 43% empirically treated with antimicrobial agents recommended for MRSA CAP (vancomycin, linezolid)
  - Replacing MSSA or adding to overall burden?

[1]Hageman et al. *Emerg Infect Dis* 2006:12:894-9; *MMWR* 2007 56:325-9; Kallen et al. *Annals Emerg Med* 2008 (in press)

Prevalence of MRSA Nasal Colonization by Age and Survey Cycle (N=18,626)

National Health and Nutrition Examination Survey, 2001-04



Gorwitz et al; JID 2008;197:1226-34

Prevalence of MRSA Nasal Colonization Low, Proportion MRSA in *S. aureus* Infections High

- Transmission via direct inoculation from exogenous source?
- Limited subset of population affected?
- High attack rate?
- Intermittent or low-level colonization?
- Predilection of USA300 for non-nasal colonization?

Non-Nasal MRSA Colonization?

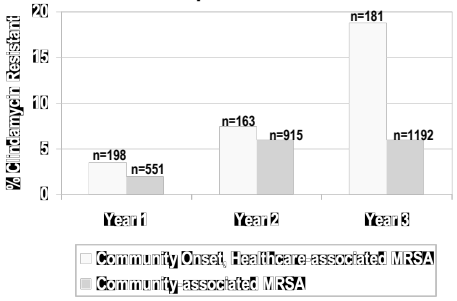
- LA inpatients & outpatients with CA-MRSA infection[1]:
  - 40% colonized with MRSA in any of 4 sites
  - 26% nares, 8% axilla, 20% inguinal, 15% rectum
- Boston community clinic[2]:
  - 4.7% of 532 MRSA+ nares; 2.0% of 508 peri-anal & nares
- Atlanta VA HIV Clinic (preliminary)[3]:
  - 70 (12%) of 578 patients MRSA+ in nose or groin
    - 33 (47%) both, 26 (37%) nose only, 11 (16%) groin only
- Similar studies in healthcare settings (USA300 not prevalent) describe increases in sensitivity when adding rectal or peri-anal cultures to nasal cultures[4,5]

[1]Yang et al. *IDSA* 2007 #285. [2]Wener et al. *IDSA* 2006 #380. [3]CDC Unpublished. [4]Currie et al SHEA 2008 #359. [5]Williams et al SHEA 2008 #360.

Vaginal MRSA Colonization

- *S. aureus* vaginal colonization in 5-20% of women of child-bearing age
- Recent studies have detected MRSA in vaginal-rectal swabs obtained for group B strep screening
  - Chen et al. *Ob & Gyn* 2006;108:482-7: 0.5% of 2963 cultures ("community" strains)
  - Andrews et al. Ob & Gyn 2008;111:113-8: 3.5% of 5732 cultures (no strain typing done)
- No increased incidence of vertically transmitted early-onset neonatal infections due to MRSA

Clindamycin Resistance Among MRSA Isolates, Texas Children's Hospital, Houston Texas,2001-2004



Source: Hulten et al. PIDJ 2006;25:349-53, and Kaplan et al. Clin Infect Dis 2005;40:1785-91

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Multi-Drug Resistant USA300

- Resistance to multiple classes of antimicrobial agents described in MRSA USA300 isolates containing a conjugative plasmid[1,2]
  - *erm*C (erythro / clinda), *mup*A (mupirocin) – conjugative plasmid
  - +/- tetracycline resistance (*tet*K) - separate plasmid
  - +/- fluoroquinolone resistance - chromosomal
  - Susceptible to TMP/SMX
- Initially described in isolates from adult clinic patients in Boston and San Francisco[1,2]
  - Association with self-identifications as a man-who-has-sex-with-men
- CDC isolate database (N>2000): 10 isolates from 5 states; 3/10 in women
- Sexually-transmitted infection?[3]
  - Can be transmitted by skin-skin contact during sex, but does not meet classical criteria for an STI

[1]Han et al. *J Clin Micro* 2007;45:1350-2. [2]Diep et al. *Ann Int Med* 2008;148:249-57. [3]Gorwitz et al. *Ann Int Med* 2008;148:310-12.

Potential Virulence Factors

- Panton-Valentine leukocidin (PVL) toxin
  - Associated with more severe clinical manifestations in some reports (osteomyelitis[1], invasive infections[2], CAP[3])
  - Conflicting results from animal model studies using isogenic PVL+ and PVL- MRSA strains[4,5]
- Arginine catabolic mobile element (ACME)
  - Identified in USA300-0114[6], some isolates of USA100 (US)[7], ST97 & ST1 (UK)[8]
  - Products of this gene cluster may enhance survival at low pH on human skin and within phagocytic cells
- Phenol-soluble modulin (PSM) peptides[9]
  - Described in MRSA USA300, USA400
  - Recruit, activate, & lyse human neutrophils
  - In mouse model, PSM+ strains of USA300/400 had increased ability to produce skin lesions and increased mortality compared to isogenic PSM- strains

[1]Bocchini Pediatrics 2006; [2]Gonzalez CID 2005; [3]Gillet Lancet 2002; [4]Labandeira-Rey Science 2007; [5]Voyich JID 2006; [6]Diep Lancet 2006; [7]Ellington JAC 2007; [8]Goering JCM 2007; [9]Wang Nat Med 2007

MRSA in Animals

- Food Animals[1-4]
  - MRSA ST398 in pigs (Europe, Canada, U.S.), pig farmers (Europe, Canada), retail pork (Europe)
  - Health risks of MRSA in food products unknown
- Non-Food Animals[5-6]
  - Strains reflect predominant human strains
  - Transmission between humans and animals (both directions) described – small % of human infections
  - Pets may play role in sustained household transmission
  - Little evidence to support antimicrobial decolonization in animals, but colonization is typically short-lived

[1]Van Loo et al. *Emerg Infect Dis* 2007;13:1834-9. [2]Van Loo et al. *Emerg Infect Dis* 2007;13:1753-5. [3]Khanna et al. *Vet Microbiol* 2007. [4]Smith TC et al. *ICEID* 2008. [5]Van Duijkeren et al. *J Clin Micro* 2005;43:6209-11. [6]Weese et al. *Vet Microbiol* 2006;115:148-55.

Primary Prevention

- *S. aureus* vaccine?
  - Most extensively tested vaccine (Nabi StaphVAX) showed promise initially but was found ineffective in confirmatory trial
  - A number of novel antigens being tested for potential inclusion in vaccine
  - Development of a vaccine with levels of protection similar to other commonly administered vaccines unlikely to occur in near future
  - Target population?

Primary Prevention

- Hygiene and wound care remain cornerstones of primary prevention
  - Keep cuts / scrapes clean and covered
  - Avoid direct and indirect contact with wound drainage
  - Clean hands and shower regularly, particularly after skin-skin contact and contact with shared environmental surfaces

Controlling Transmission

- Promptly identify & manage new infections
- Use local data to guide empiric therapy
- Educate on wound care / containment
- Promote enhanced personal hygiene and limit sharing of personal items
- Exclude patients from direct-contact activities if unable to contain wound drainage
- Achieve and maintain a clean environment
- Use standard precautions in ambulatory care
- Use antibiotics appropriately

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Environmental Management

- Role of environment in spread of MRSA is unclear
  - Not naturally found in the environment
  - Can survive on surfaces for months, depending on conditions
- Cover infected skin to avoid contaminating surfaces
- Focus cleaning on surfaces frequently touched by people's bare skin and surfaces that could come in contact with infected skin (e.g., benches in weight room)
- Use barriers between skin and shared surfaces, and clean skin after use
- Protect difficult to clean surfaces such as keyboards with covers that can be removed and cleaned

Cleaning & Disinfecting Environmental Surfaces

- Cleaners: Lift soil, organic matter, microorganisms, etc from surface so they can be rinsed away with water
- Disinfectants: Chemical products that destroy or inactivate microorganisms
  - Can use after cleaning for surfaces that have visible drainage from infected skin
- Read label instructions for how to apply, contact time, safety for the surface, precautions to protect skin, etc
- More information:
  http://www.cdc.gov/ncidod/dhqp/ar_mrsa_Enviro_Manage.html#3

Colonization Screening and Decolonization

- In general, colonization cultures of infected or exposed persons in community settings are not recommended.
- "Decolonization" = Use of antimicrobial regimens to suppress or eliminate *S. aureus* colonization
  - Goal is to prevent infection in high-risk patient or to prevent transmission
  - Effectiveness in community settings not established

Use of Decolonization in Community Settings

- R Raz et al. *Arch Int Med* 1996: Fewer recurrences of MSSA SSTIs in patients that received monthly mupirocin
- M Wiese-Posselt et al. *CID* 2007: Termination of MSSA furunculosis outbreak in German village following multi-component decolonization strategy of colonized or infected persons & family members
- MW Ellis et al. *Antimicrob Agents Chemo* 2007: RPCT of mupirocin decolonization of MRSA-colonized military trainees – no impact on MRSA infection or transmission

Decolonization: Current Guidance

- May be reasonable to administer, *after treating active infections and reinforcing hygiene and appropriate wound care*, when:
  - Individual patient has recurrent infections
  - Ongoing transmission in a closely-associated cohort (e.g., household)
- Appropriate regimens (agents and schedules) not established for community settings

Strategies for Clinical Management of MRSA in the Community

Strategies for Clinical Management of MRSA in the Community: Summary of an Experts' Meeting Convened by the Centers for Disease Control and Prevention

March 2006

Rachel J. Gorwitz[1], Daniel B. Jernigan[1], John H. Powers[2], John A. Jernigan[1], and Participants in the Centers for Disease Control and Prevention-Convened Experts' Meeting on Management of MRSA in the Community[3]

[1]Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention*
[2]Center for Drug Evaluation and Research, U.S. Food and Drug Administration*
[3]Appendix A

http:www.cdc.gov/ncidod/dhqp/ar_mrsa_ca.html

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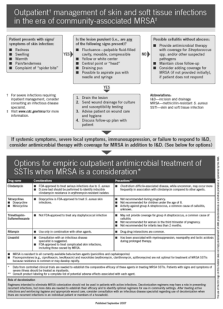
CDC / AMA/ IDSA Treatment Algorithm for Skin Infections



Management of Skin Infections in the Era of CA-MRSA

- Consider MRSA in differential diagnosis
- Drain purulent skin lesions*
- Obtain material for culture
  - Molecular typing, toxin testing not recommended to guide clinical management
- Consider antimicrobial therapy
  - Systemic symptoms, severe local symptoms, immune suppression, failure to respond to drainage
  - Variety of oral treatment options – use local data to inform empiric therapy
- Educate patients on wound management and hygiene
- Maintain adequate follow-up

*Fitch et al. Abscess incision and drainage. *NEJM 2007*;357:e20

Conclusions

- ***S. aureus*** **has long been a cause of localized and invasive infections in the community.**
- **MRSA has emerged as a cause of these infections, and may be contributing to increased burden and severity.**
- **Strains of MRSA identified in community and healthcare settings were initially distinct, but are becoming less so.**
- **Invasive infections are a minority of CA-MRSA infections, but risk factors are not well understood.**
- **While optimal prevention strategies have yet to be defined, strategies focusing on increased awareness, early detection and appropriate management, enhanced hygiene, and maintenance of a clean environment have been successful in controlling clusters / outbreaks of infection.**

Additional Resources

http://www.cdc.gov/mrsa

Additional Resources

- UNC Public Health Grand Rounds (April 2005)
  - www.publichealthgrandrounds.unc.edu
- Health Departments
  - www.lapublichealth.org
  - www.doh.wa.gov
  - www.tdh.state.tx.us
- NCAA
  - www.ncaa.org

CA-MRSA Working Group Meeting Participants, July 2004

Gordon L. Archer
Carol L. Baker
Elizabeth Bancroft
Henry F. Chambers
Robert S. Daum
Jeffrey S. Duchin
Monica Farley
James Hadler
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J. Kathryn MacDonald
Loren Miller
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L. Barth Reller
Nalini Singh
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Craig Zinderman
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John Jernigan*
Jay C. Butler
Denise Cardo
Roberta Carey
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Jeffrey C. Hageman
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James M. Hughes
Jean Patel
Fred Tenover
J. Todd Weber

*Meeting Co-Chair

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Thank-you!!

Questions?