Staphylococcus aureus: Epidemiology and Prevention

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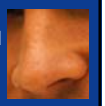
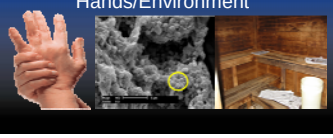
Staphylococcus aureus "*Staph aureus*"

- Bacteria commonly found in the nose and on the skin of healthy people
- Common cause of infection in community and healthcare settings
  - Associated with breach in normal immune defense
  - Skin infection most common
  - Severe, invasive syndromes also occur

How is *Staph aureus* spread?





Methicillin-Resistant *Staphylococcus aureus* (MRSA)

- Resistant to beta-lactam antibiotics (penicillins, cephalosporins)
  - Conferred by *mec*A gene carried on mobile genetic element (SCC*mec*)
  - Altered penicillin-binding protein (PBP 2a)
- Historically linked to healthcare settings
- More recently, emerged in the community
- Relatively small number of lineages transmitted widely
- Antimicrobial treatment options more limited

MRSA Strain Characteristics Were *Initially* Distinct

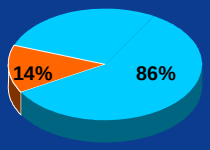
	MRSA in Healthcare	MRSA in the Community
Prevalent genotypes (U.S.)	USA100, USA200	USA300, USA400
Antimicrobial resistance	Multiple agents	Few agents
SCC*mec* (genetic element carrying *mec*A resistance gene)	Types I-III	Types IV, V
PVL toxin genes	Rare	Common

National Estimates of Invasive MRSA Infections: United States, 2005

- **Invasive MRSA infections:**
  - **94,360 (31.8 cases per 100,000 persons)**
- **Deaths (In-hospital mortality in persons with invasive MRSA infections):**
  - **18,650 (6.3 deaths per 100,000 persons)**

Klevens et al JAMA 2007;298:1763-71

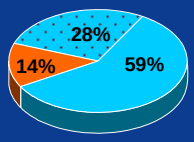
Most Invasive MRSA Infections are Healthcare-Associated



Community-Associated (CA-MRSA)
Healthcare-Associated

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

Most Healthcare-Associated MRSA Infections Have Their Onset Outside of the Hospital



Community-Associated
Healthcare-Associated (community-onset)
Healthcare-Associated (hospital-onset)

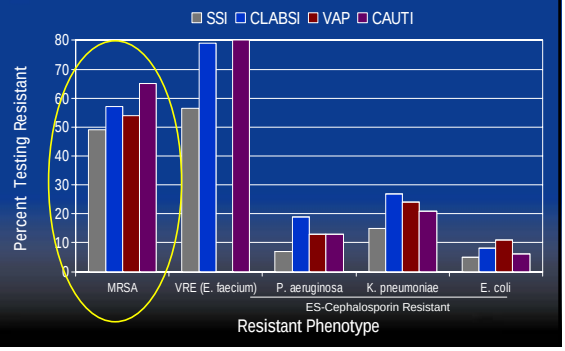
Klevens et al *JAMA* 2007;298:1763-71

Distribution and Rank Order of 9 Most Common Pathogens Reported for 28,502 HAIs, NHSN 2006-2007

	Column %				
	CLABSI	CAUTI	VAP	SSI	Total*
Pathogen	11,428	9,377	5,960	7,025	33,848
CoNS	**34**	3	1	**14**	**15**
S. aureus	**10**	2	**24**	**30**	**14**
Enterococcus spp.	**15**	**15**	1	**11**	**12**
Candida spp.	12	**21**	<1	2	11
E. coli	3	**22**	5	10	10
P. aeruginosa	3	10	**16**	5	8
K. pneumoniae	5	8	7	3	6
Enterobacter spp.	4	4	**8**	4	5
A. baumannni	2	1	**8**	1	3

* **15.6% of HAIs had >1 pathogen (polymicrobial)**

Pooled Mean (%) Resistance by HAI Type, NHSN 2006-2007



There is a growing body of evidence suggesting that endemic healthcare-associated MRSA infection and colonization can be prevented

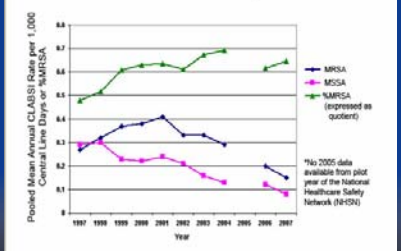
Campaign to Prevent Antimicrobial Resistance in Healthcare Settings

Key Prevention Strategies

- Prevent infection
- Diagnose and treat infection effectively
- Use antimicrobials wisely
- Prevent transmission

Clinicians hold the solution!

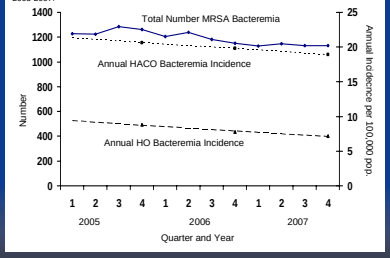
Figure. Trends in %MRSA and Incidences of MRSA and MSSA Central Line-Associated Bloodstream Infections (CLABSIs) in Intensive Care Units—United States, 1997–2007*



Source: Burton et al., abstract presentation, SHEA 2008

Healthcare-Associated MRSA Bacteremia Decreasing, 2005-2007

Figure. Quarterly reports of all MRSA bacteremia at ABCs sites and estimated annual incidence of hospital-onset and healthcare-associated community-onset bacteremia per 100,000 population, 2005-2007.



AJ Kallen, Y Mu, S. Bulens, R Cochran, Talbot T, A Reingold, S Petit, K Gershman, L Harrison, R Lynfield, G Dumyati, J Townes, W. Schaffner,

S Ray, J Edwards, J Jernigan, S Fridkin, for the Active Bacterial Core surveillance of the Emerging Infections Program Network

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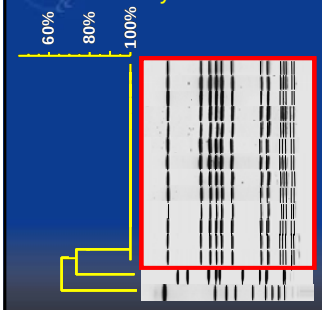
Community MRSA Outbreaks

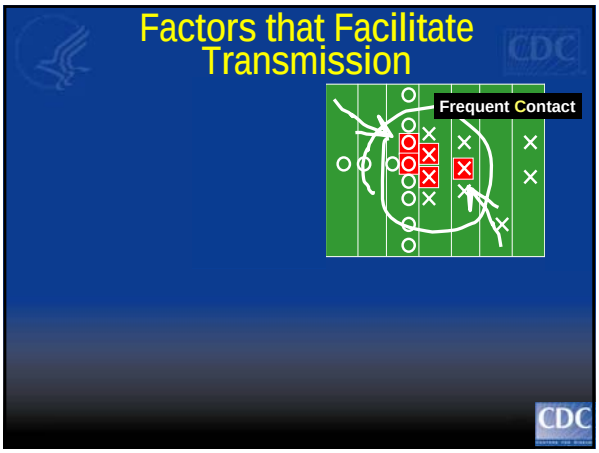
Courtesy of Indian Health Service, DHHS

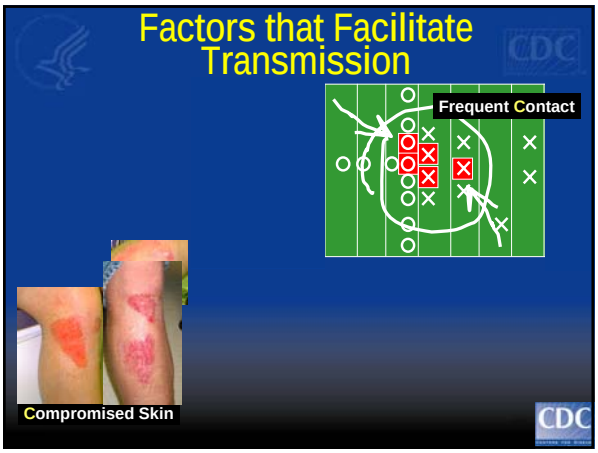
A Single Pulsed-Field Type (USA300) has Accounted for Most Community-Associated MRSA Infections in the U.S.

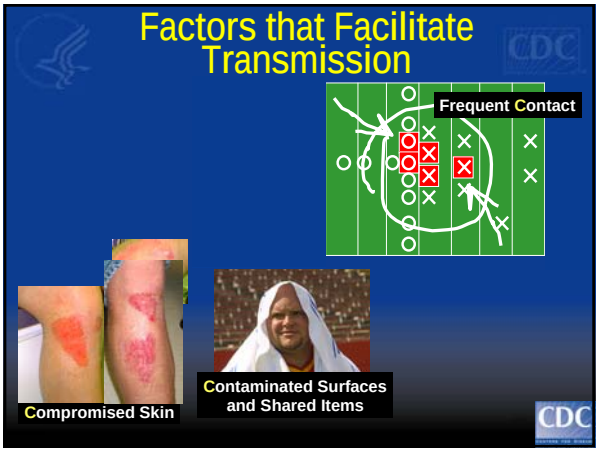


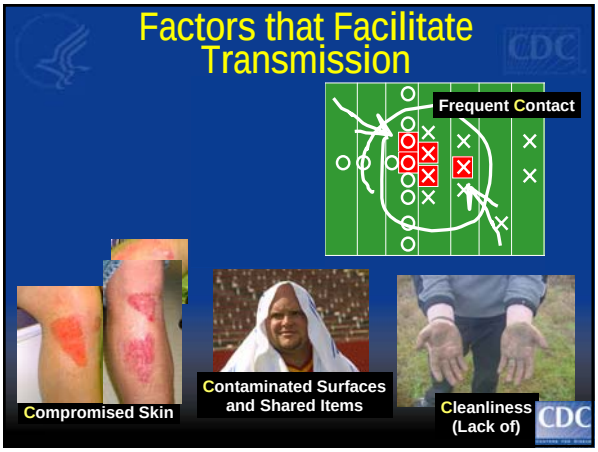
Pneumonia (AL, AR, IL, MD, TX, WA)	
Missouri	Athletes
California	
Pennsylvania	
Colorado	
Mississippi	Prisoners
Texas	
Georgia	
Tennessee	
Texas	Children
Missouri	
California	
USA300-114	Community
USA100	Hospital Strain
USA200	Hospital Strain

Factors that Facilitate Transmission

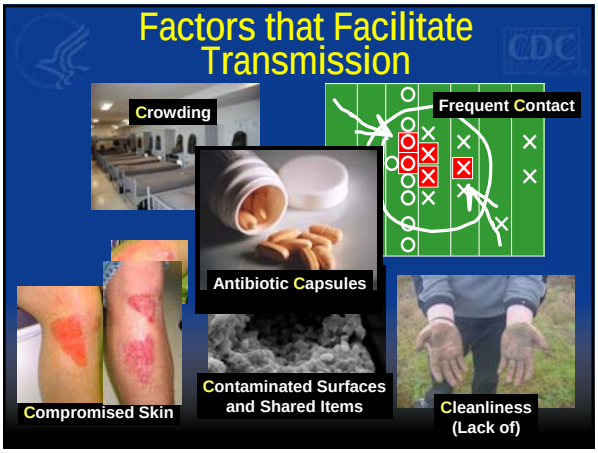

Factors that Facilitate Transmission
Frequent Contact
CDC


Factors that Facilitate Transmission
Frequent Contact
Compromised Skin
CDC


Factors that Facilitate Transmission
Frequent Contact
Compromised Skin
Contaminated Surfaces and Shared Items
CDC


Factors that Facilitate Transmission
Frequent Contact
Compromised Skin
Contaminated Surfaces and Shared Items
Cleanliness (Lack of)
CDC


Factors that Facilitate Transmission
Crowding
Frequent Contact
Compromised Skin
Contaminated Surfaces and Shared Items
Cleanliness (Lack of)
CDC

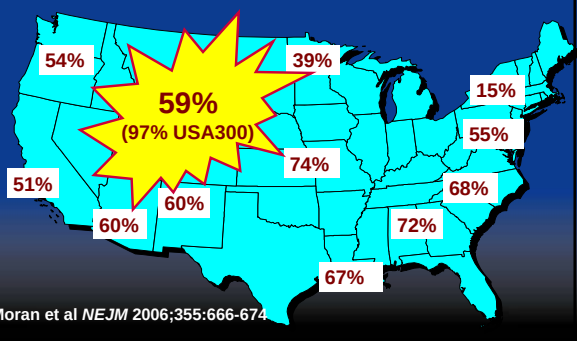

Factors that Facilitate Transmission
Crowding
Frequent Contact
Antibiotic Capsules
Compromised Skin
Contaminated Surfaces and Shared Items
Cleanliness (Lack of)

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

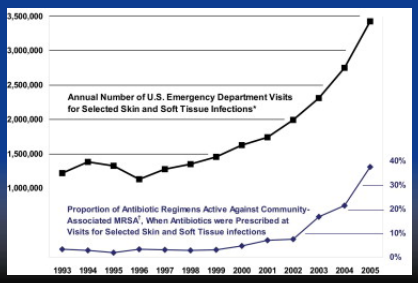
MRSA Was the Most Commonly Identified Cause of Purulent Skin Infections Among Adult ED Patients (*EMERGE*ncy ID Net), August 2004



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

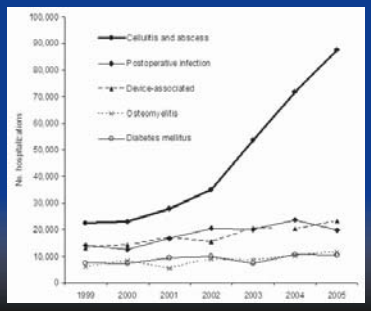
Increased Emergency Department Visits for Skin Infections Typical of *S. aureus*

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

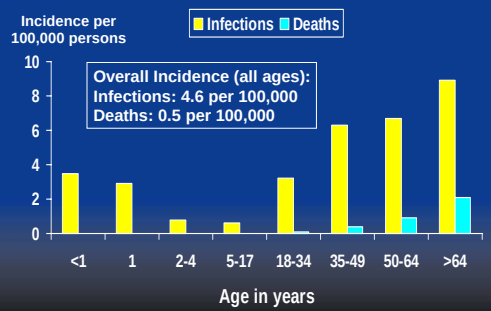


Community *Staph aureus* / MRSA Infections Can Be Severe

- Osteomyelitis
- Septic arthritis
- Bloodstream infection
- Septic shock
- Pneumonia
- Endocarditis
- Necrotizing fasciitis
- Purpura fulminans
- Bacteremia + Triad: osteomyelitis, venous thrombosis, septic pulmonary emboli

Incidence of Invasive CA-MRSA Infections and Deaths by Age

Active Bacterial Core surveillance (ABCS), 2005



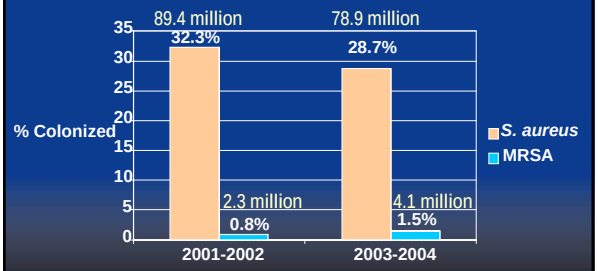
Klevens et al *JAMA* 2007;298:1763-71

Community-Acquired Pneumonia (CAP)

- Historically, *S. aureus* ~3% of cases with pathogen identified
  - Association with influenza epidemics
  - Severe, high case-fatality rate (29-60%)
- Recent *S. aureus* CAP case series[1]:
  - MRSA in ~half (frequently USA300) – many did not receive empiric coverage for MRSA
  - Median age mid-teens
  - Rapid progression and high case-fatality rate
  - Preceding or concurrent ILI documented in ~50%, but documented influenza infection uncommon
  - Is MRSA simply replacing MSSA as a cause of CAP or is overall burden increasing?

[1]Hageman et al. *Emerg Infect Dis* 2006, 12:894-9; *MMWR* 2007, 56:325-9; Kallen et al. *Annals Emerg Med* 2009; 53:358-65

Nationwide Study of Nasal Colonization with *S. aureus*



Kuhnert M, JID. 2006; 193:169-71
Gorwitz R, JID. 2008; 197:1226-34

USA Strain Types for MRSA from U.S. Nasal Colonization Study

2001-2002 n=75	2003-2004 n=134
USA100; 36 (48.0)	USA100; 60 (44.8)
USA800; 17 (22.7)	USA800; 23 (17.2)
USA700; 7 (9.3)	USA300; 23 (17.2)
USA300; 6 (8.0)	USA400; 8 (6.0)
USA1000; 2 (2.7)	USA200; 6 (4.5)
USA400; 1(1.3)	USA700; 3 (2.2)
Others; 6 (8%)	Others; 11 (8.1%)

USA300 increased (P=0.031; Fisher's exact test)
Increase in USA300-0114 (P=0.0017, Fisher's exact test)


Annals of Internal Medicine | ARTICLE

Emergence of Multidrug-Resistant, Community-Associated, Methicillin-Resistant *Staphylococcus aureus* Clone USA300 in Men Who Have Sex with Men

Binh An Diep, PhD; Henry F. Chambers, MD; Christopher J. Graber, MD, MPH; John D. Szumowski, MD, MPH; Loren G. Miller, MD, MPH; Linda L. Han, MD; Jason H. Chen, BA; Felice Lin, BA; Jessica Lin, BA; Tiffany HaiVan Phan, BA; Heather A. Carleton, MPH; Linda K. McDougal, MS; Fred C. Tenover, PhD; Daniel E. Cohen, MD; Kenneth H. Mayer, MD; George F. Sensabaugh, DCrim; and Françoise Perdreau-Remington, PhD

Ann Intern Med. 2008;148:249-257

- Transferable plasmid that has capacity to incorporate multiple resistance elements
- Prevalence of plasmid among all MRSA USA300 isolates varies (approx. values):
  - 10% overall in San Francisco
  - 50% in Boston out-patient clinic population
  - 1% based on ER study
  - 3% of USA300 isolates from CDC invasive MRSA surveillance

Prevention of MRSA in the Community

- Hygiene and wound care remain cornerstones of prevention
  - Keep cuts / scrapes clean and covered
  - Keep infected skin covered
  - Clean hands and shower regularly, particularly after skin-skin contact and contact with shared environmental surfaces
  - Avoid sharing of personal items
  - Targeted environmental cleaning

Distribution of PFGE types among MRSA isolates recovered from nosocomial bloodstream infection cases, Grady Memorial Hospital, 2004

PFGE type	No. (%) of nosocomial cases (n = 49)
USA300	10 (20)
USA100	21 (43)
USA500	18 (37)
USA800	0 (0)

Seybold U, et al. Clin Infect Dis 2006;42:647-656

Conclusions

- *S. aureus* is an important public health problem in the U.S.
- An increasing proportion of *S. aureus* infections are MRSA
- Although most community-associated MRSA infections are non-life-threatening skin infections, serious and recurrent infections do occur
- Most of the severe MRSA infections and MRSA-associated deaths are healthcare-associated
- Epidemic strains of MRSA originally associated with the community have emerged as important causes of hospital-acquired infections
- MRSA infections in both healthcare and community settings are often preventable:
  - Healthcare: Multi-faceted tiered approach
  - Community: Increased awareness, wound care, and improved hygiene

THANK-YOU!

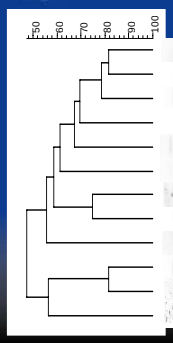
QUESTIONS?

Additional Resources:

http://www.cdc.gov/mrsa

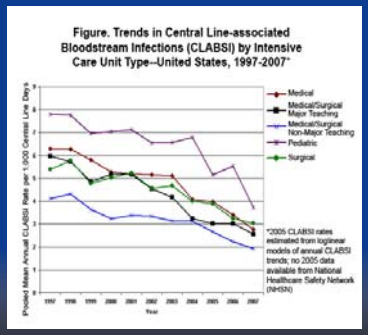
cdcinfo@cdc.gov

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



Source: Burton et al., abstract presentation, SHEA 2008

HICPAC Guidance On Management of Multidrug-Resistant Organisms (MDROs) in Healthcare Settings

First Tier: General Recommendations For All Acute Care Settings

If endemic rates not decreasing, or if first case of important organism

Second Tier: Intensified Interventions

HICPAC MDRO Guidance (acute care) First Tier: General Recommendations For All Acute Care Settings

- **Administrative engagement**
  - **Make MDRO prevention and control an organizational patient safety priority**
  - **Implement a multidisciplinary process to monitor and improve healthcare personnel (HCP) adherence to recommended practices**
  - **Feedback on facility and patient-care unit trends in MDRO incidence and adherence measure**
- **Education and training of personnel**
- **Judicious use of antimicrobial agents**
- **Standard precautions for all patients**
- **Contact Precautions for patients known to be infected or colonized (masks not routinely recommended)**
- **Monitoring of trends over time to determine whether additional interventions are needed**

HICPAC MDRO Guidance (acute care)

- **Indications for moving to second tier**
  - **First case or outbreak of an epidemiologically important MDRO**
  - **When endemic rates of a target MDRO *are not decreasing* despite implementation of and correct adherence to the first tier measures**

HICPAC MDRO Guidance (acute care) Second Tier: Intensified Interventions For Acute Care Settings

- **Active surveillance cultures from patients in populations at risk at the time of admission to high-risk area, and at periodic intervals as needed to asses transmission.**
  - **Contact Precautions until surveillance culture known to be negative**
- **Additional recommendations for intensifying:**
  - **administrative engagement/correction of systems failures**
  - **Education and training of personnel/adherence monitoring**
  - **Judicious use of antimicrobial agents**
  - **monitoring of trends**
- **Cohorting of staff to the care of MDRO patients only**
- **Enhanced environmental measures**
- **Consult with experts on case-by-case basis regarding use of decolonization therapy for patients or staff**
- **If transmission continues despite full implementation of above, stop new admissions to the unit.**

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