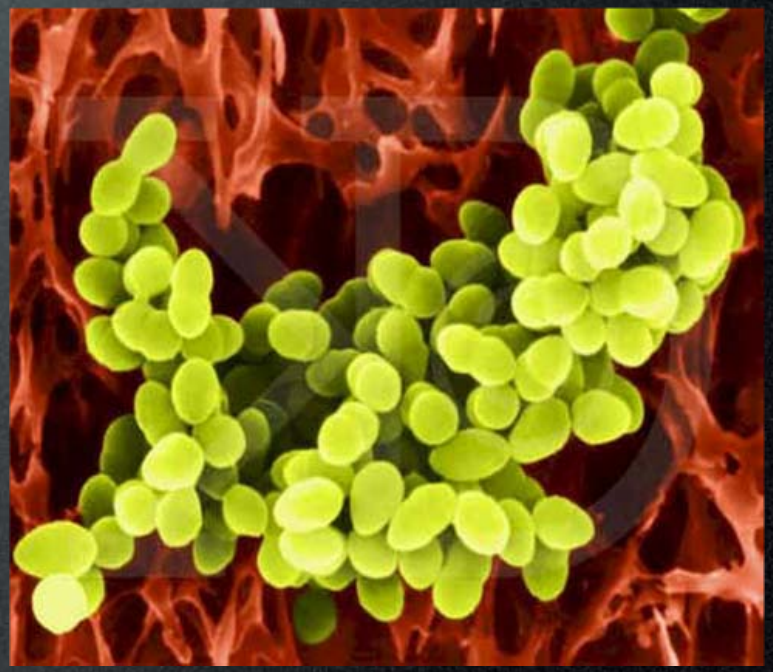
MRSA Screening

University of Colorado
Grand Rounds
November 1, 2010
Kaitlyn Gilman

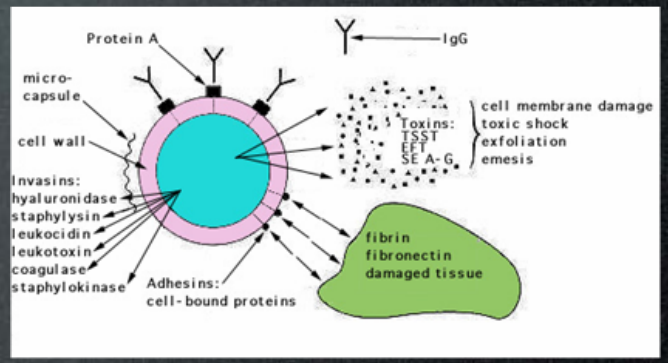
Staphylococcus Aureus: Golden Grapes

- Gram positive coccus in clusters
- Catalase positive
- Beta hemolytic
- Facultatively anaerobic



Protein Arsenal

- **Protein A**: Protects against opsonization and phagocytosis by binding Fc portion of IgG
- **Coagulase:** Protects from phagocytosis by fibrin formation
- **Hemolysins-alpha, beta, gamma, delta:** Destroys RBCs, neutrophils, platelets, macrophages

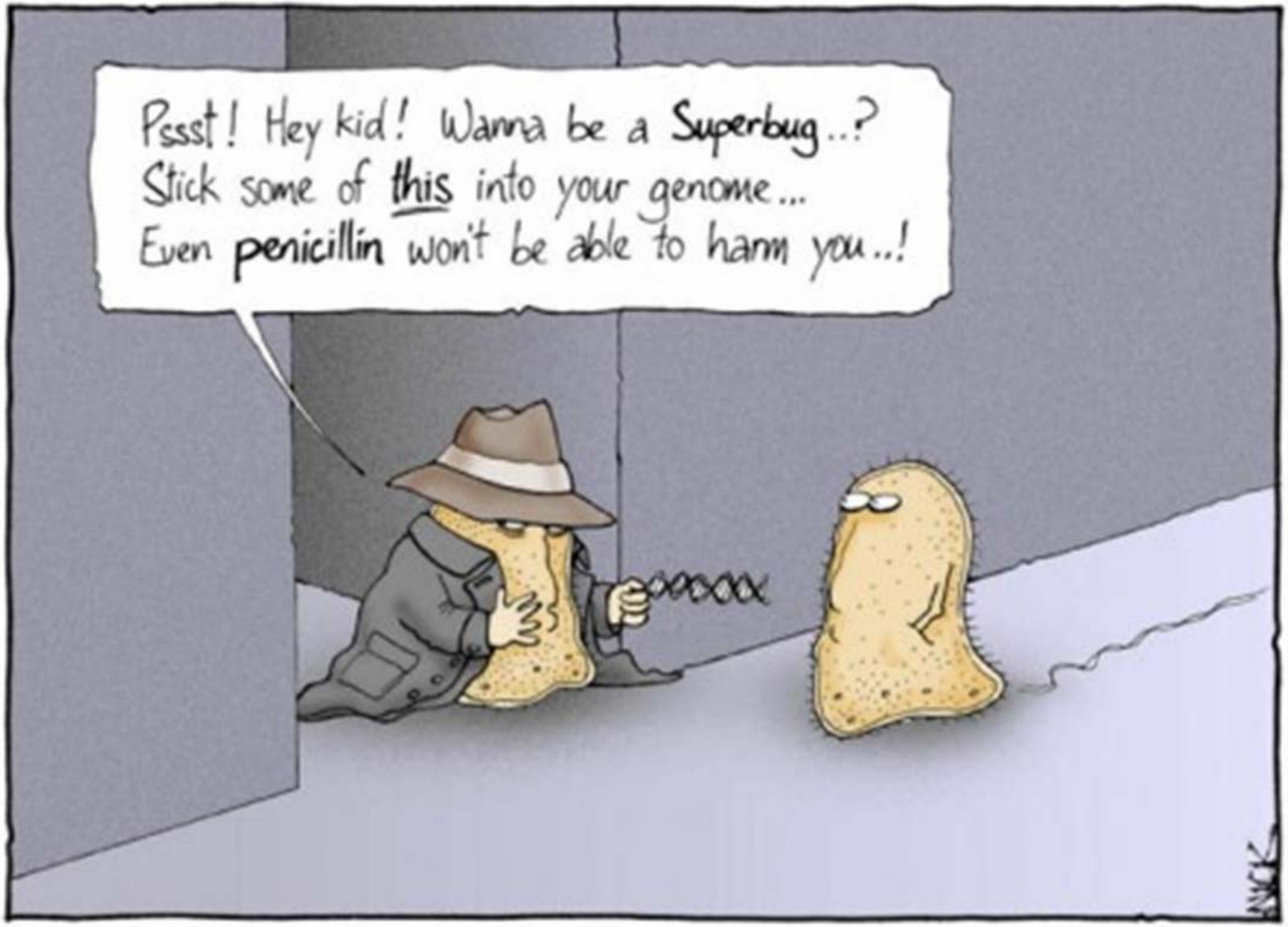


- **Leukocidins:** Destroys leukocytes
- **Penicillinase:** Secreted form of beta-lactamase that inactivates antibiotics by disrupting the beta-lactam portion of PCN
- **Novel PCN Binding Protein:** Transpeptidase necessary for cell wall peptidoglycan formation. Inhibited by PCN
- **Hyaluronidase, staphylokinase, lipase, protease:** Lyse proteoglycans, fibrin clots, fats, and proteins to facilitate bacterial spread

Exotoxin Arsenal

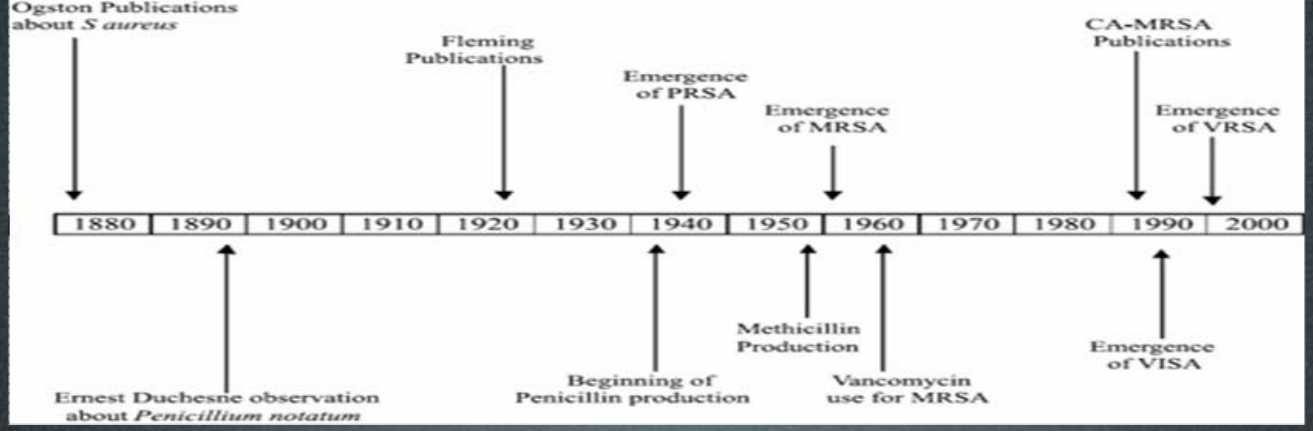

langetextbooks.com

- Toxic Shock Syndrome Toxin (TSST-1)
  - Pyrogenic toxins binds to MHC class II molecules on antigen presenting cells.
  - Leads to non-specific, polyclonal T-cell activation with resultin massive cytokine release
- Exfoliative Toxins (Scalded Skin Syndrome)-Sloughing of skin
- Enterotoxin Heat Stable Toxins (Food Poisoning)-Vomiting, diarrhea



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

History 101

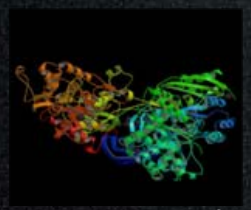


- 1928 Alexander Fleming discovered PCN, the super drug! Used for any type of minor infection.
- 1943 PCN used for *S. aureus* infections
- 1947 First strains of PCN resistant *S. aureus*
- 1950s resistance rendered PCN ineffective for *S. aureus*
- 1959 Methicillin developed by Beecham
- 1961 UK hospital reported first strain of MRSA

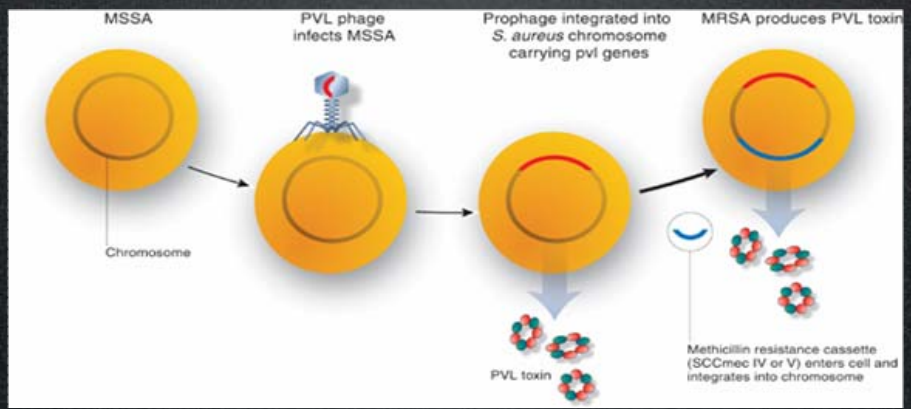
- 1968 First US case of MRSA in a Boston man. However, MRSA remained isolated to those immunocompromised and recently hospitalized
- 1970’s First major MRSA outbreak in Eastern Australia. MRSA spread throughout Europe, with many health cares centers affected
- 1980s resistance in the US spread from mainly IVDU and immunocompromised to healthcare workers, prisoners

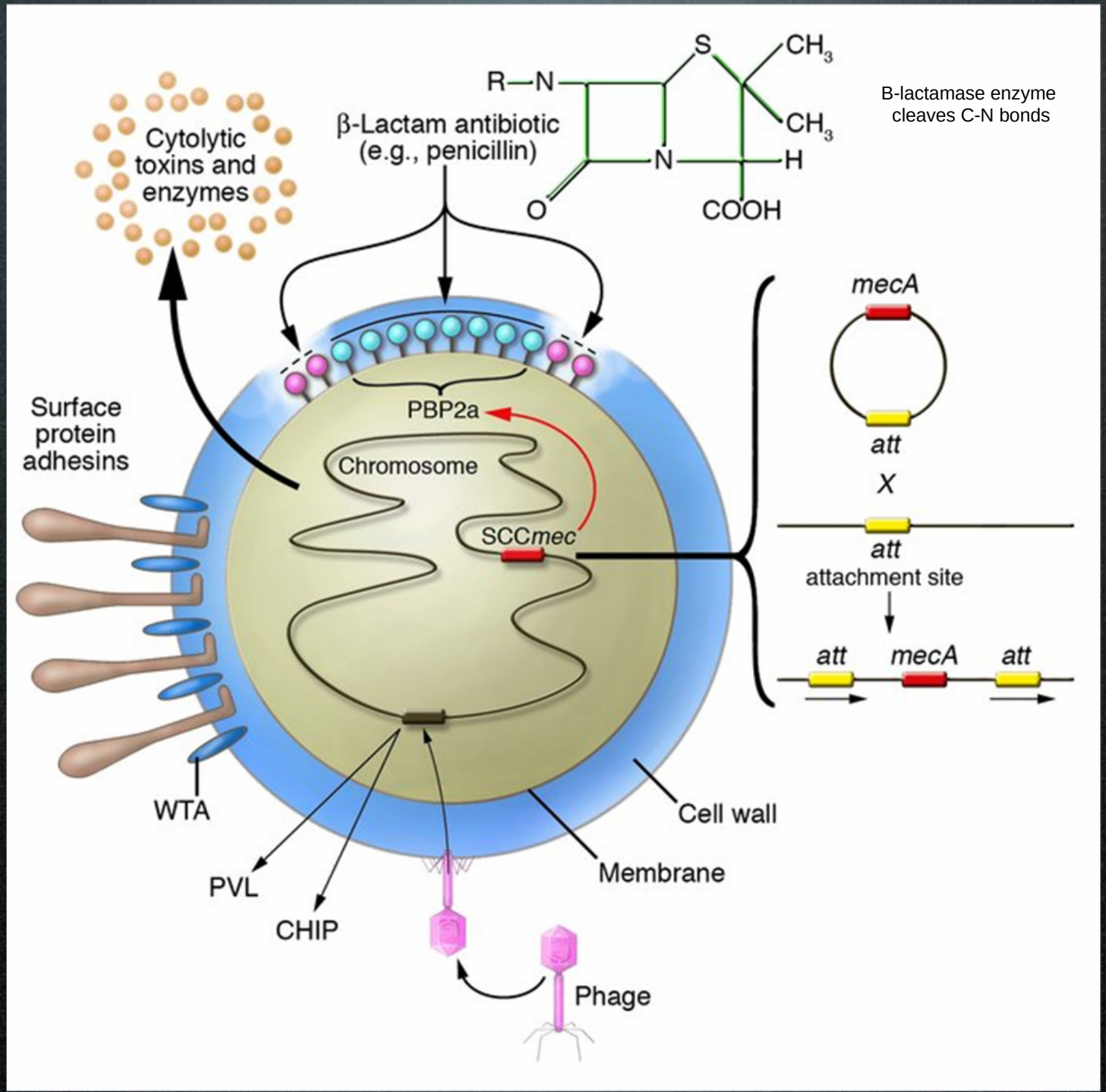
Methicillin-Resistant *Staphylococcus Aureus*

- MRSA-Strain of *S. aureus* with acquired multiple drug resistance
- Resistance-Conferred through mobile genetic elements such as bacteriophages, plasmids, and pathogenicity islands which transform commensal organisms into pathogenic organisms
- *Staphyloccocal* Cassette Chromosome Mec (*SCCmec*)- mobile genetic element coding for the chromosomal segment *MecA*
- *MecA*-encodes for an altered PCN binding protein 2A (PBP2a)



- PBP2a: Altered component of the cell wall that lowers the affinity for binding B-lactams (PCN, oxacillin, cephalosporins, carbapenems)
- Penicillinase: Cleaves B-Lactam ring of PCN





Foster, TJ, The *Staphylococcus aureus* "superbug" *J Clin Invest.* 2004; 114(12):1693

The Problem

- 20% of the population are persistently colonized by *S. aureus*. 30% acquire it intermittently [1,4]
- 1.5% of the US population are colonized with MRSA [1]
- MRSA accounts for 40-60% of the *S. aureus* isolates in some healthcare institutions [3]
- The prevalence of MRSA colonization in US adult ICUs is approximately 8% (ranges 5-20%) [4]
- The risk of MRSA infection among MRSA-colonized patients varies from 10% to 25% [4]
- Compared to MSSA, MRSA infections carry a 40% higher mortality [4]

A Very Expensive Problem

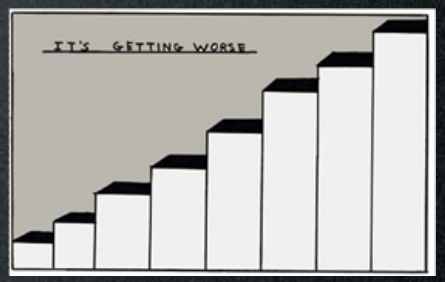
- Compared to MSSA, an infection with MRSA increase cost $3,000-$35,000 [3]
- Excluding indirect costs, MRSA infections cost the healthcare system an extra $830 million to $9.7 billion [3]

MRSA Statistical References

- 1. Gorwitz RJ et al. Journal of Infectious *Diseases*. 2008;197:1226-34
- 2. Klevens RM et al. *Clinical Infectious Diseases* 2006;42:389-91 Invasive Methicillin-Resistant Staphylococcus aureus Infections in the United States Journal of the AMA 2007;298(15):1763-1771
- 3. Klein E, Smith D, Laxminarayan R. Emerging infectious diseases. 2007 Dec; 13(12). www.cdc.gov/eid
- 4. Lin MY, Hayden MK. Methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *enterococcus*: recognition and prevention in intensive care units. Crit Care Med. 2010 Aug;38(8 Suppl):S335-44

A Growing Problem

- Increasing prevalence: 2% of USA ICU *S. aureus* infections were MRSA in 1974, 22% in 1995, 64% in 2004 [2]



- In 2005...
  - 278,000 MRSA related hospitalizations [2]
  - 94,360 people developed invasive MRSA infections [2]
  - 85% of invasive MRSA infections were healthcare associated [2]
  - 18,650 MRSA related deaths during hospitalization [2]
    - Approximately equal to deaths from AIDS, TB, and hepatitis combined


"The patient in the next bed is highly infectious. Thank God for these curtains."


Surfaces commonly contaminated by MRSA
(Methicillin-resistant *staphylococcus aureus*)
R.S. Ulrich with P.A. Wilson

Strategies Overseas: Search and Destroy

- Netherlands: <1% prevalence of MRSA
- Finland: 0.5% prevalence of MRSA
- Denmark : <1% prevalence of MRSA
- Sweden and Norway <2% prevalence of MRSA
- Belgium 28%, France 33%, Germany 19%

- Wertheim HF, Vos MC, Boelens HA, et al. Low prevalence of methicillin - resistant *Staphylococcus aureus* (MRSA) at hospital admission in The Netherlands: the value of search and destroy and restrictive antibiotic use. *J Hosp Infect* 2004;56:321 - 325
- Rosdahl VT, Knudsen AM. The decline of methicillin resistance among Danish *Staphylococcus aureus* strains. *Infect Control Hosp Epidemiol* 1991;12:83 - 88.

MRSA Prevalence Is High Globally

Lowy FD. *New Engl J Med*. 1998;339:520-532; CDC. *MMWR*. 1997;46:624-628, 635; NNIS Antimicrobial Resistance Surveillance Report. 1999; Wertheim HF et al. *J Hosp Infect*. 2004;56:321-325; Canada Communicable Disease Report. Public Health Agency of Canada (PHAC). 1997;23-06.

The Policy

- Screening of high-risk patients (those with a previous h/o MRSA, from a hospital with a high MRSA prevalence, hospitals in other countries, job working with pigs and calves)
- Screening of other patients and personal in contact with MRSA carriers
- Isolation of MRSA positive patients and staff
- Disinfection of skin, hair, and nasal passages of MRSA carriers (personnel must screen negative before working with MRSA free patients)
- “Outbreak” (2 or more MRSA infections) disaster plan

Catching on…

- In mid 2000 numerous European countries with endemic MRSA initiated or intensified infection control measures including
  - Screening for MRSA, isolation, decontamination
  - Hand hygiene
  - Antibiotic stewardship

• Struelens MJ, Monnet DL. Prevention of methicillin-resistant *Staphylococcus aureus* infections: is Europe winning the fight? *Infect Control Hosp Epidemiol* 2010;31:S42–S44

Percentage of MRSA Bacteremia

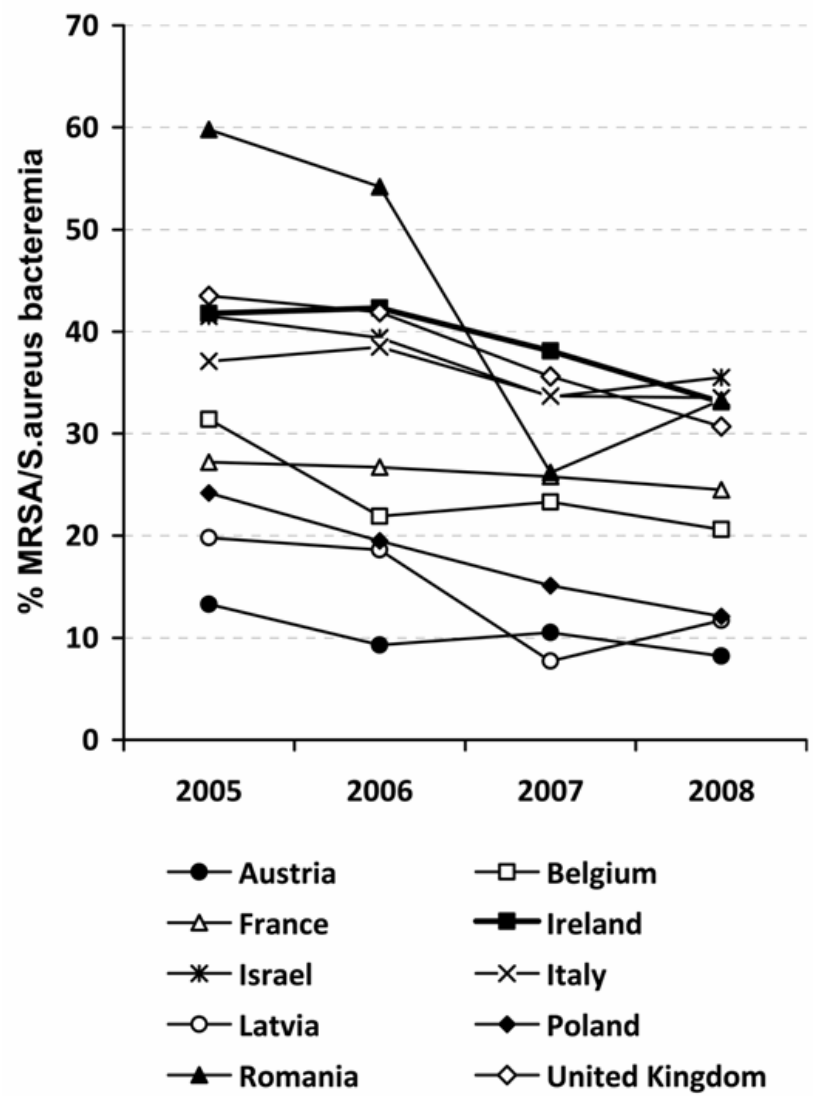


Figure 1. Trends of decreases in the percentage of S. aureus bacteremia cases caused by methicillin‐resistant S. aureus (MRSA) in 10 countries reporting to the European Antibiotic Resistance Surveillance System, 2005–2008. Adapted with permission from the European Antimicrobial Resistance Surveillance System 2008 annual report.1

Struelens MJ, Monnet DL. Prevention of methicillin-resistant *Staphylococcus aureus* infections: is Europe winning the fight? *Infect Control Hosp Epidemiol* 2010;31:S42–S44

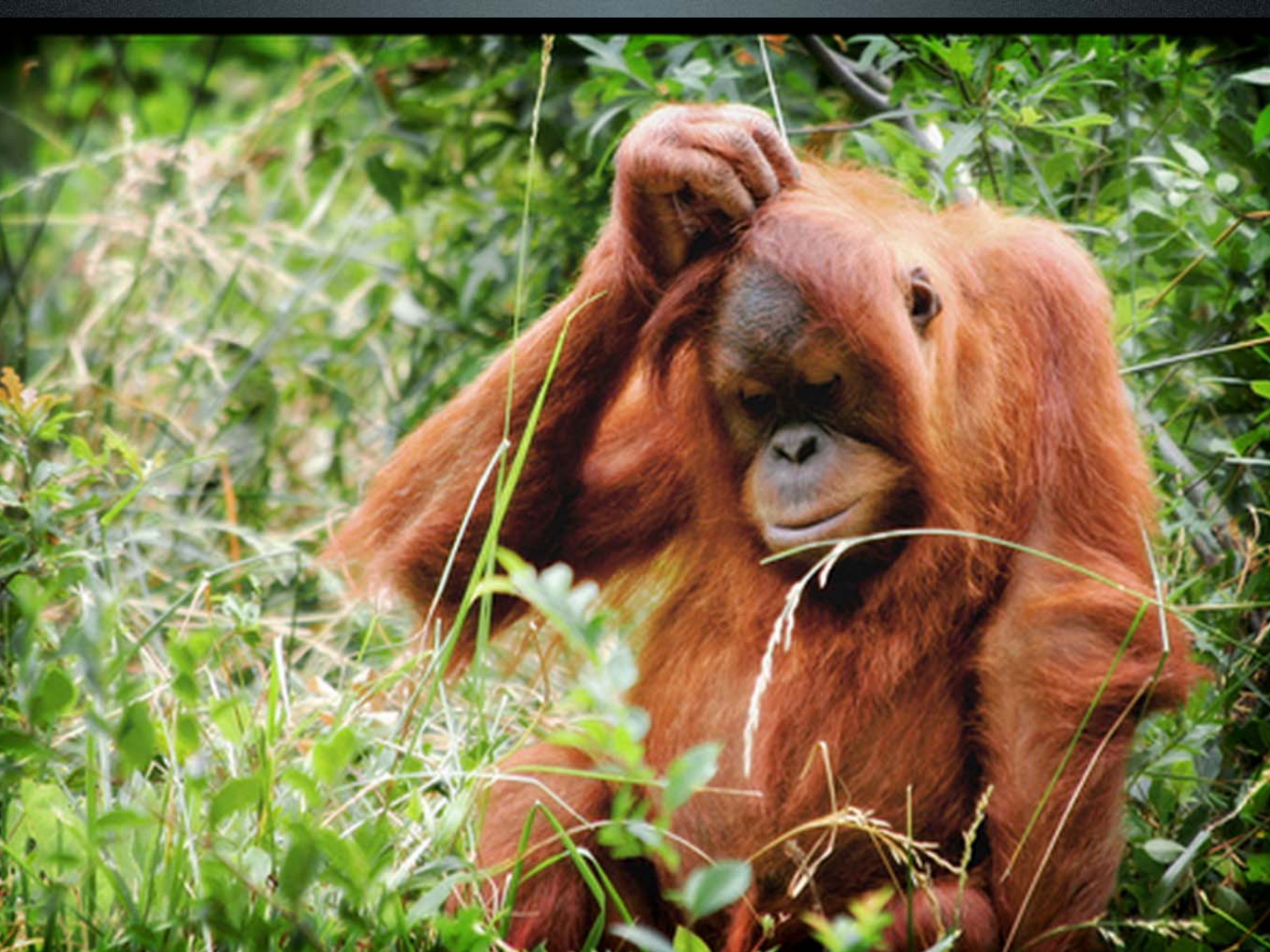
SHEA Guideline for Preventing Nosocomial Transmission of Multidrug-Resistant Strains of Staphylococcus aureus and Enterococcus

Carlene A. Muto, MD, MS; John A. Jernigan, MD, MS; Belinda E. Ostrowsky, MD, MPH; Hervé M. Richet, MD; William R. Jarvis, MD; John M. Boyce, MD; Barry M. Farr, MD, MSc

- May 2003, the Society for Healthcare Epidemiology of America (SHEA) published guidelines for preventing nosocomial transmission of MRSA and vancomycin-resistant enterococci.
- CONCLUSION:

  "Active surveillance cultures are essential to identify the reservoir for spread of MRSA and VRE infections and make control possible using the CDC's long-recommended contact precautions."

Infect Control Hosp Epidemiol 2003;24:362-386



Controversies

- Efficacy?
- Cost?
- Patient satisfaction?

Contact Precautions: Not Just for Style Points

Detection of Methicillin-Resistant *Staphylococcus aureus* and Vancomycin-Resistant Enterococci on the Gowns and Gloves of Healthcare Workers

Snyder, Graham M. MD; Thom, Kerri A. MD; Furuno, Jon P. PhD; Perencevich, Eli N. MD, MS; Roghmann, Mary-Claire MD, MS; Strauss, Sandra M. BS MT(ASCP); Netzer, Giora MD, MSCE; Harris, Anthony D. MD, MPH

- Healthcare workers providing routine care in a 29-bed ICU at University of Maryland Medical Center
  - Urban tertiary care academic hospital
- Cultures from hands prior and after entering a patient room, gloves and gowns

- *Infect Control Hosp Epidemiol*. July 2008 29(7): 583-9

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TABLE 1. Rates of Detection of Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Vancomycin-Resistant Enterococci (VRE) on the Gowns and Gloves Worn by Healthcare Workers Caring for Patients with MRSA and VRE Carriage

	Patients with MRSA carriage		Patients with VRE carriage	
Sample cultured	Proportion of observations	Percentage of observations (95% CI)	Proportion of observations	Percentage of observations (95% CI)
Gloves	14/79	17.7 (9.3–26.1)	7/91	7.7 (2.2–13.2)
Gown	5/81	6.2 (1–11.4)	4/94	4.3 (0.2–8.4)
Gloves and/or gown	15/81	18.5 (10–27)	8/94	8.5 (2.9–14.1)
Hands after removing gloves and gown	2/78	2.6 (−0.9 to 6.1)	0/94	0

NOTE. For some interactions, gown or glove samples could not be obtained, so the total number of observations varies. CI, confidence interval.

- *Infect Control Hosp Epidemiol* 2008 July; 29(7): 583-9

Active Surveillance for Methicillin-Resistant *Staphylococcus aureus* (MRSA) Decreases the Incidence of MRSA Bacteremia

Pnina Shitrit, MD; Bat - Sheva Gottesman, MD; Michal Katzir, MD; Avi Kilman, MSc; Yona Ben - Nissan, BSc; Michal Chowers, MD

- 700 bed hospital
- Compared MRSA Bacteremia 13 months before and 15 months after intervention
- Intervention:
  - Surveillance of high risk patients
  - Contact precautions and isolation
  - Eradication

Infect Control Hosp Epidemiol 2006;27:1004–100

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- Surveillance cultures at admission and once/month

  Hospitalized in the previous month
  Transfered from another hospital, ward, LTCF
  Receiving long term HD
  Known history of MRSA
  All patients admitted to SICU or Geriatric ward

- Contact precautions and isolation

  Single room when available
  Gown and gloves for all patents
  Mask for ventilated patients

- Eradication treatment

  Mupirocin ointment to anterior nares TID
  Chlorhexidine showers daily X 5 days

Infect Control Hosp Epidemiol 2006;27:1004–100

Episodes of MRSA Bacteremia Per Month

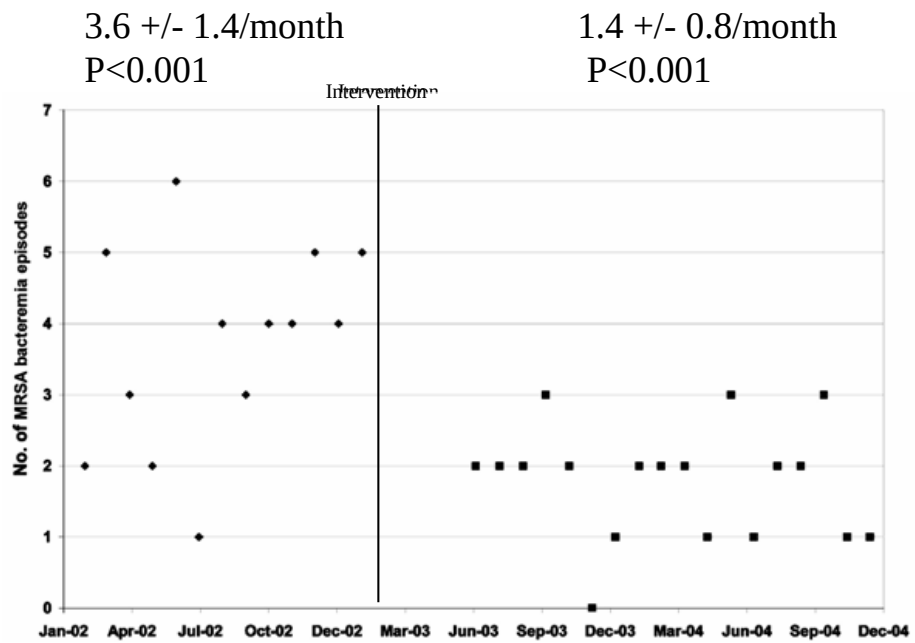


Figure. Number of episodes of methicillin‐resistant Staphylococcus aureus (MRSA) bacteremia per month before (from January 2002 through February 2003) and after (from July 2003 through October 2004) initiation of active surveillance for MRSA.

Infect Control Hosp Epidemiol 2006;27:1004–100

Rapid Screening Tests for Methicillin-Resistant *Saphylococcus aureus* at Hospital Admission: Systematic Review and Meta-Analysis.

Tacconelli E, De Angelis G, de Waure C, Cataldo MA, La Torre G, Cauda R

- Meta-analysis of 10 studies comparing active screening of MRSA (rapid or culture) versus no screening
- Screening for MRSA significantly decreased MRSA bacteremia by 46%

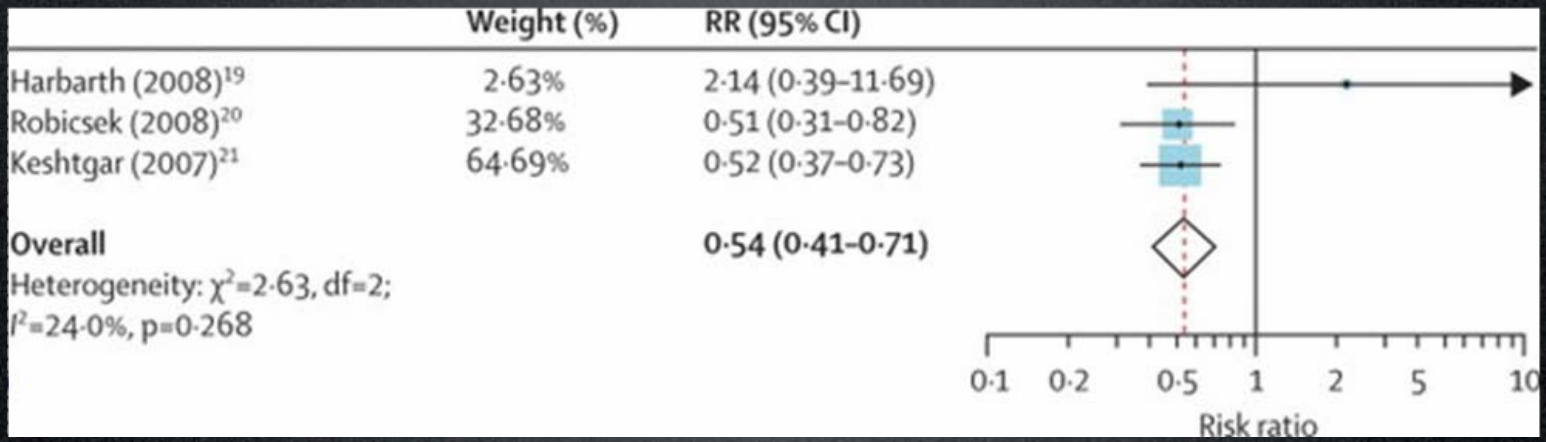


Figure: Effect of rapid molecular tests for meticillin-resistant *Staphylococcus aureus* (MRSA) at hospital admission on the incidence of MRSA bloodstream infections per 1000 patient-daysComparison is between units in which screening was done by molecular tests and units in which screening was not done at all. Risk ratios (RR) and their 95% CIs are shown (fixed effects). Dotted line indicates combined RR. Squares indicate point estimates and the size of the square indicates the weight of each study in the meta-analysis.

- Lancet Infect Dis. 2009 Sep;9(9):546-54.

On the Home Front

ROCKY MOUNTAIN REGIONAL TRAUMA CENTER
DENVER HEALTH
Level One Care for ALL



Clancy M, Graepler A, Wilson M, Ivor D, Johnson J, et al. Active screening in high-risk units is an effective and cost-avoidant method to reduce the rate of methicillin-resistant *Staphylococcus aureus* infection in hospital. *Infect Control Hosp Epidemiol* 2006;27:1009-17

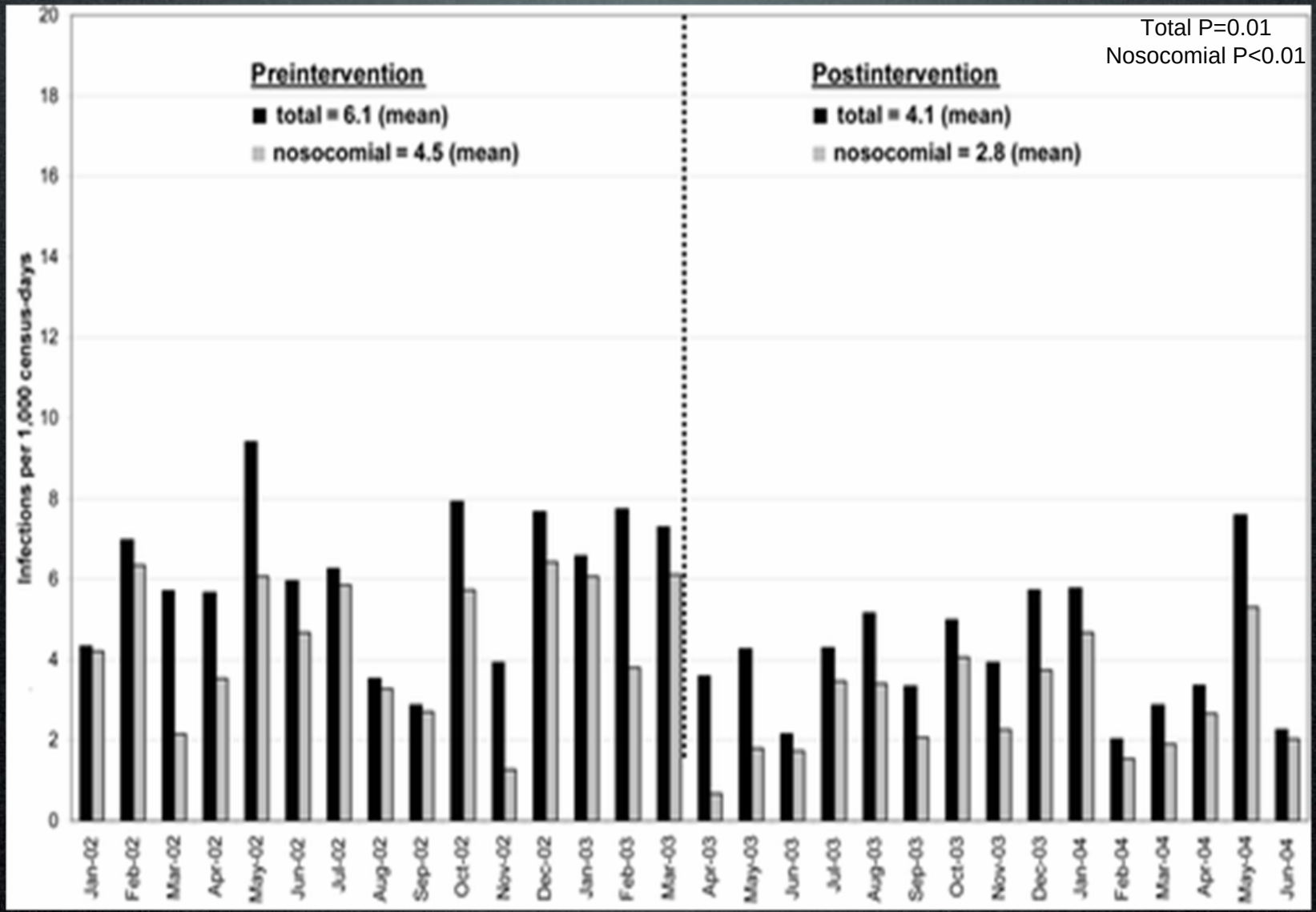
Active Screening in High-Risk Units Is an Effective and Cost-Avoidant Method to Reduce the Rate of Methicillin-Resistant *Staphylococcus aureus* Infection in the Hospital

Megan Clancy, MD; Amy Graepler, MT; Michael Wilson, MD; Ivor Douglas, MD, MRCP(UK); Jeff Johnson, MD; Connie Savor Price, MD

- Patients over 18 years of age admitted to the Denver Health SICU and MICU were screened by nasal swab on admission and weekly for 15 months
- MRSA positive patients were considered infected and placed under contact precautions
  - Private room, gown, gloves
  - Warning attached to the patient record.
- MRSA rates were compared with the 15 months prior to screening intervention

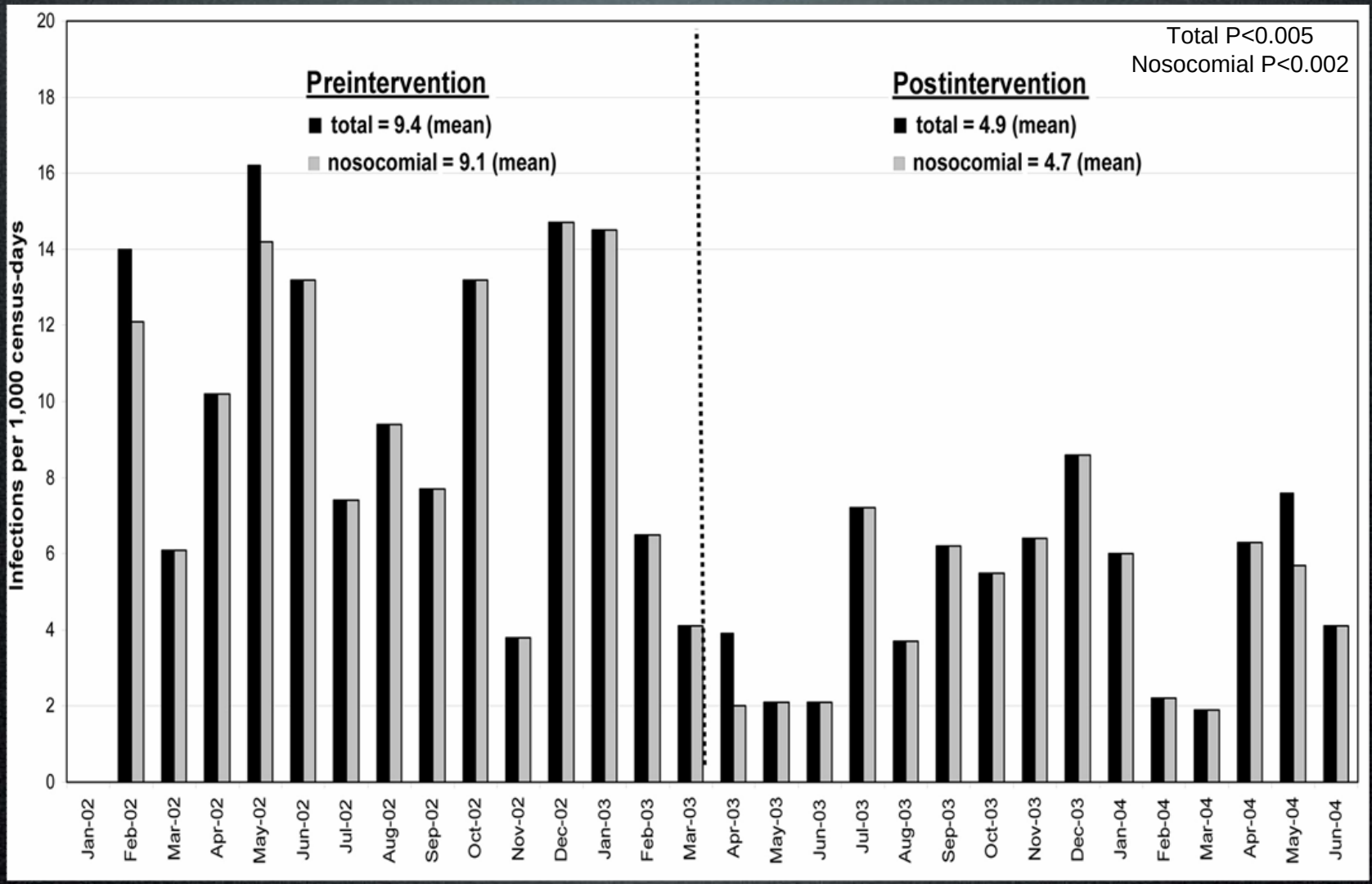
Infect Control Hosp Epidemiol 2006;27:1009-17

Overall Rates of Total and Nosocomial MRSA Infections in DH MICU, SICU & Wards



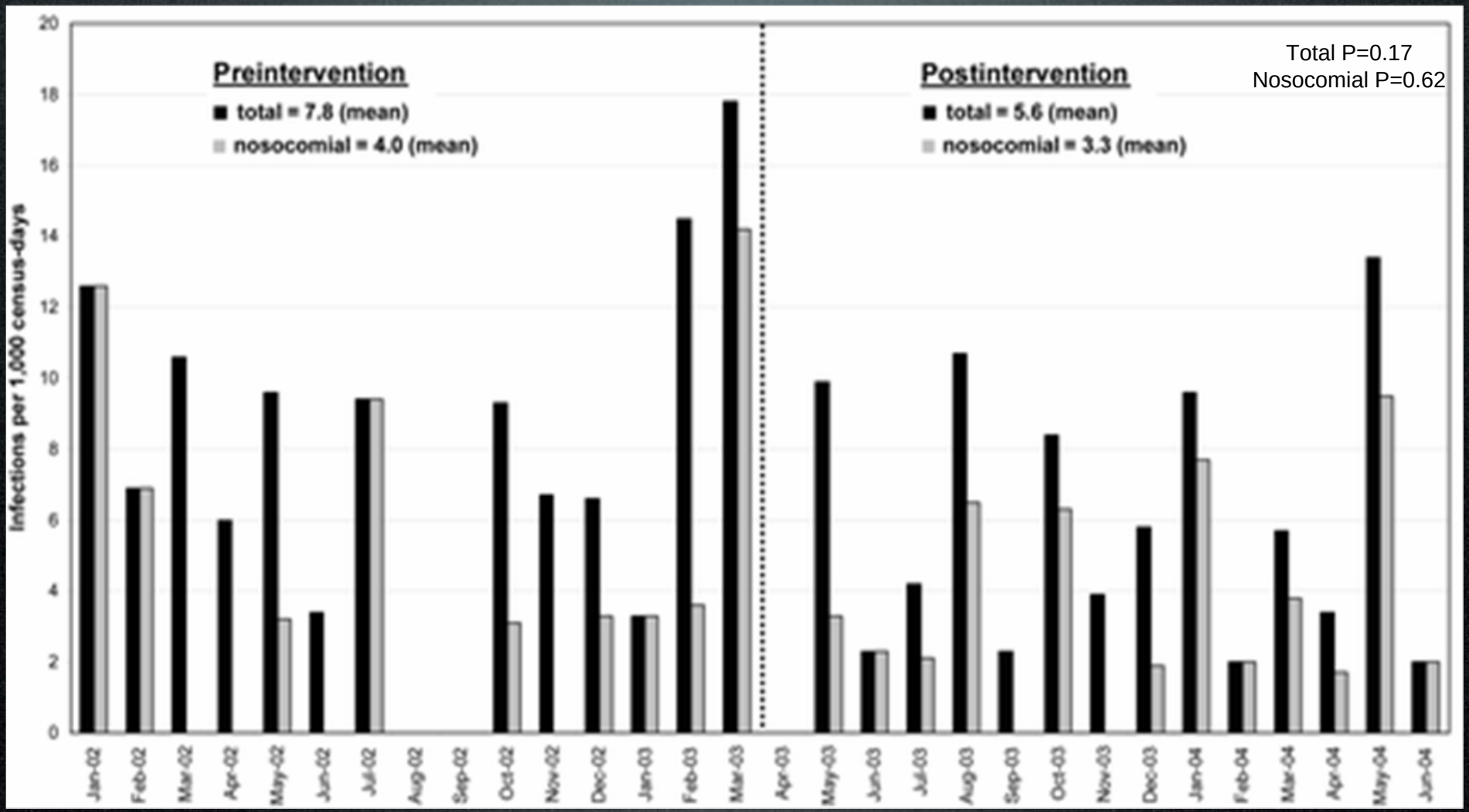
Infect Control Hosp Epidemiol 2006;27:1009-17

Rates of Total MRSA Infections Versus Nosocomial MRSA Infections in DH SICU



Infect Control Hosp Epidemiol 2006;27:1009-17

Rates of Total MRSA Infections Versus Nosocomial MRSA Infections in DH MICU



Infect Control Hosp Epidemiol 2006;27:1009-17

The Bottom Line

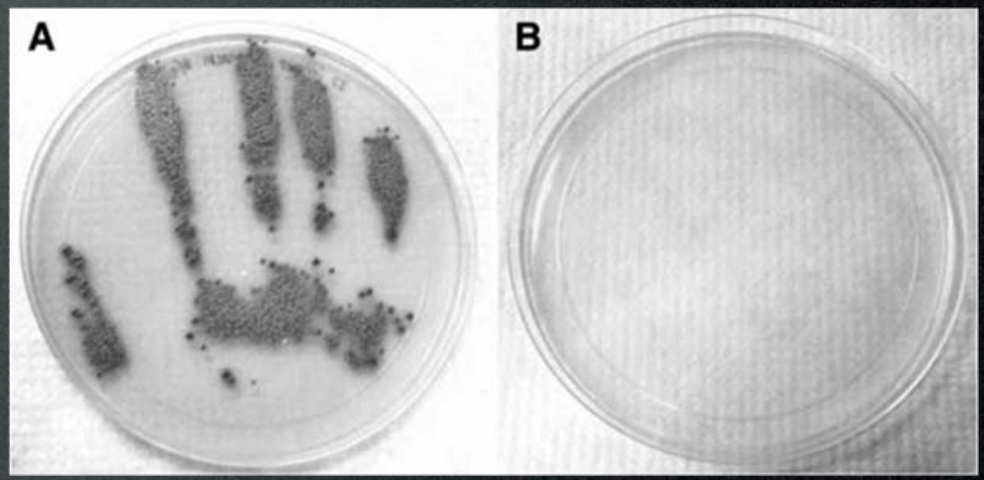
TABLE 2. Cost Analysis of the Methicillin-Resistant *Staphylococcus aureus* (MRSA) Screening Program at Denver Health Medical Center (Denver, CO)

Variable	Value
Cost of screening per month	
Swabs	
Cost per swab	$0.25
Mean number of patients swabbed	330
Total	$82.50
Microbiologic analysis	
Mean number MRSA-positive swabs	11
Cost per MRSA-positive swab	$5.50
Mean number MRSA-negative swabs	229
Cost for MRSA-negative swab	$1.24
Total	$337.36
Total screening cost	$419.86
Cost of isolation per month	
Cost of 1 pair of gloves	$0.08
Cost of 1 gown	$0.10
Cost of 60 s of nursing time	$0.47
Estimated no. of patient contacts per day	100
Estimated cost per patient per day	$65.00
Mean total excess isolation-days	47
Excess isolation cost	$3,055.00
Cost avoidance per month	
Averted no. of ICU infections	2.5
Excess cost of 1 MRSA infection	$9,275.00
Cost savings of averted cases	$23,188.00
Less excess isolation cost	$3,055.00
Less total screening cost	$419.86
Overall cost avoidance for ICUs	$19,714.00

Infect Control Hosp Epidemiol 2006;27:1009-17

Conclusion

- MRSA is a serious infection
- Effective abroad. Effective at home
  - Decreased MRSA infections and bacteremia
- Decreased cost



The Real Question?

- Should we be screening healthcare workers?
- Should we be eradicating MRSA once found on screening?

References

- Lin MY, Hayden MK. **Methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *enterococcus:* recognition and prevention in intensive care units.** Crit Care Med. 2010 Aug;38(8 Suppl):S335-44

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- **Hospital infection control strategies for vancomycin-resistant *Enterococcus*, methicillin-resistant *Staphylococcus aureus* and *Clostridium difficile*** CMAJ. 2009 Mar 17;180(6):627-31

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- Foster, TJ. The *Staphylococcus aureus* "superbug" *J Clin Invest.* 2004; 114(12):1693

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- McHugh CG, Riley LW. Risk factors and costs associated with methicillin-resistant *Staphylococcus aureus* bloodstream infections. Infect Control Hosp Epidemiol. 2004;25:425–30.

- Rubin RJ, Harrington CA, Poon A, Dietrich K, Greene JA, Moiduddin A. The economic impact of *Staphylococcus aureus* infection in New York City hospitals. Emerg Infect Dis. 1999;5:9–17.

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- Gorwitz RJ et al. *Journal of Infectious Diseases.* 2008;197;1226-34


Questions?