MRSA: We Don't Want It, But Can We Eradicate It?

Senior talk: Graham Snyder

February 6th, 2008

OBJECTIVE:

Should we adopt a “search and destroy” strategy to eradicate MRSA?

MRSA: We Don’t Want It, But Can We Eradicate It?

OBJECTIVE:

Should we adopt a “search and destroy” strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA problems worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVE:

Should we adopt a "search and destroy" strategy to eradicate MRSA?

AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

* Colonization vs. infection:	Should we attempt to eradicate one or both?
* Prevention of acquisition:	There are choices better than eradication…
* Risk factors for acquisition:	Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA:	What are the tools for eradication?
* Eradication regimens:	What works?

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVE:

Should we adopt a "search and destroy" strategy to eradicate MRSA?

A SPECTRE IS HAUNTING EUROPE

* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVES:

1) Should we adopt a "search and destroy" strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA a problem worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

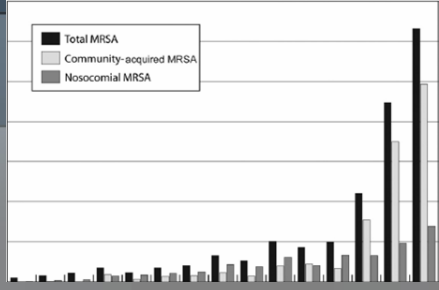
AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

* Colonization vs. infection: Should we attempt to eradicate one or both?
* Prevention of acquisition: There are choices better than eradication…
* Risk factors for acquisition: Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA: What are the tools for eradication?
* Eradication regimens: What works?

A SPECTRE IS HAUNTING EUROPE

* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

PREVALENCE AND SEVERITY



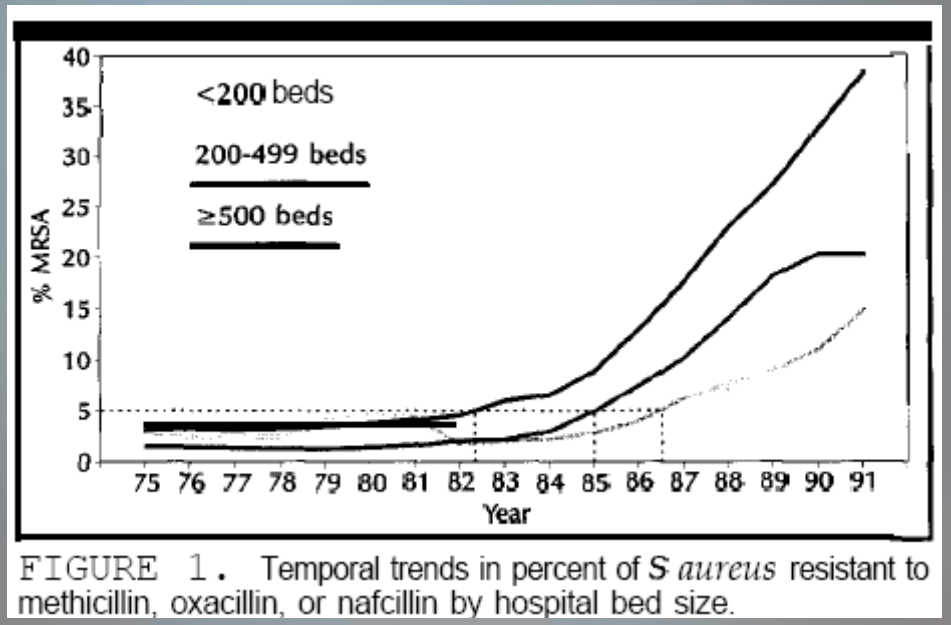
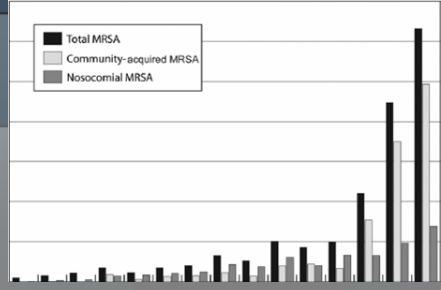


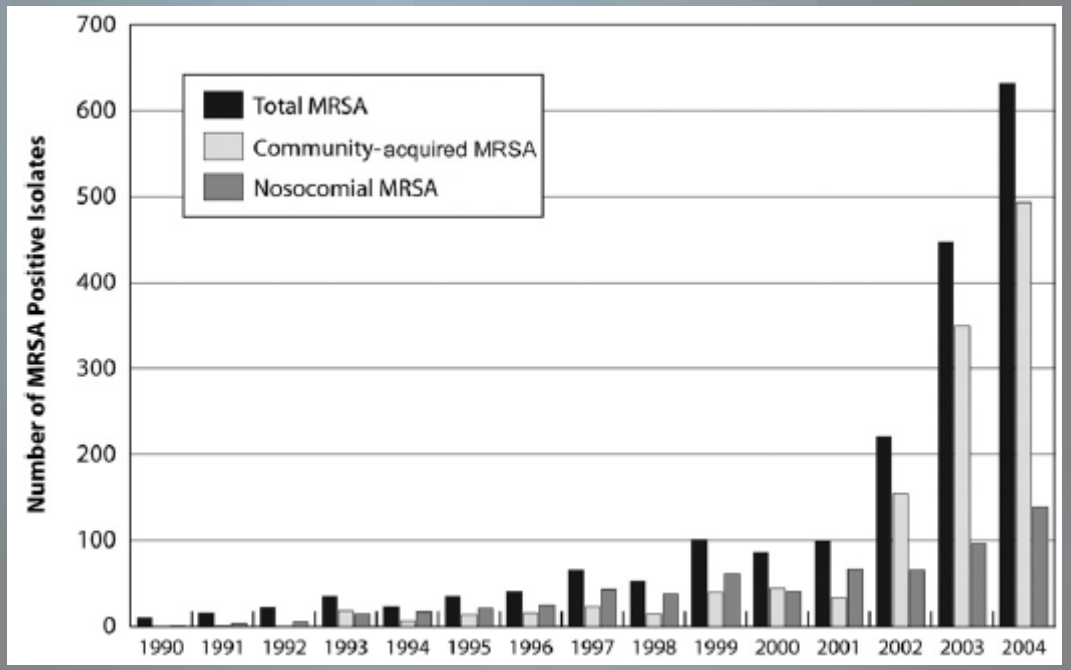
FIGURE 1. Temporal trends in percent of *S aureus* resistant to methicillin, oxacillin, or nafcillin by hospital bed size.

National Nosocomial Infections Surveillance

Panlilio et al, Infect Control Hosp Epi 1992

PREVALENCE AND SEVERITY

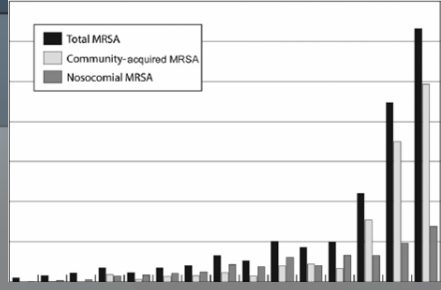




San Diego: 15-year varied setting longitudinal study

Crum et al,
Amer J Med 2006

PREVALENCE AND SEVERITY



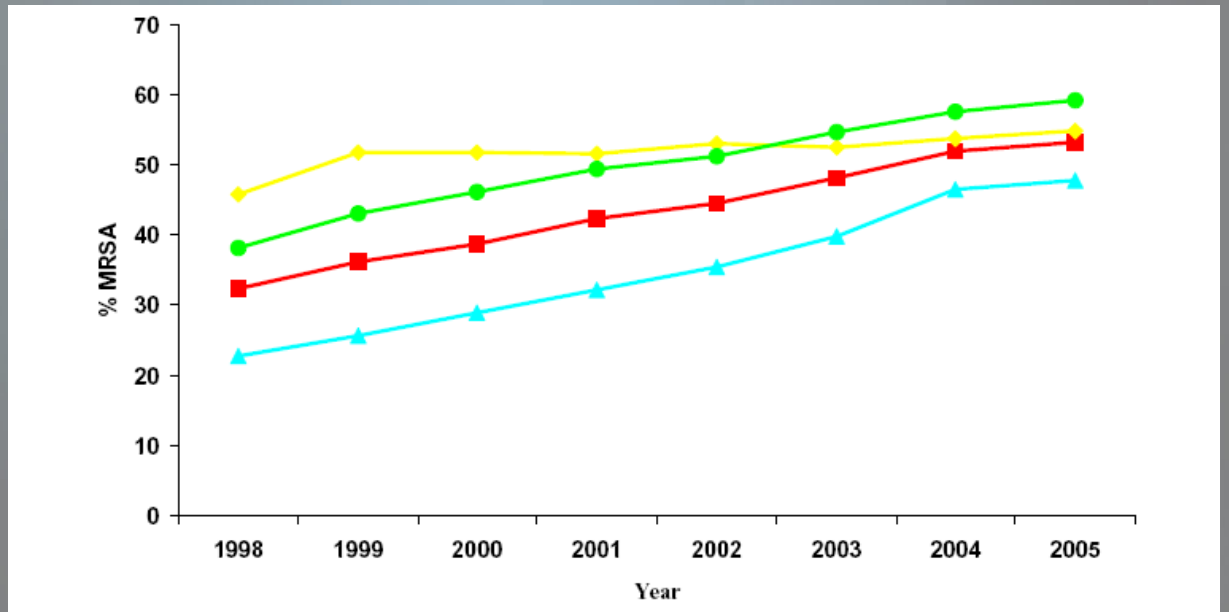
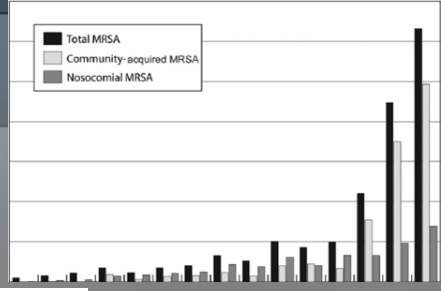


Figure 3
MRSA trends (1998 – YTD 2005) according to patient location. Data is cumulative data: 1998 – March 2005. Red line, all patients; yellow line, ICU patients; green line, inpatients; blue line, outpatients.

The Surveillance Network-USA

Styers et al, Ann Clin Microbiol Antimicrob 2006

PREVALENCE AND SEVERITY



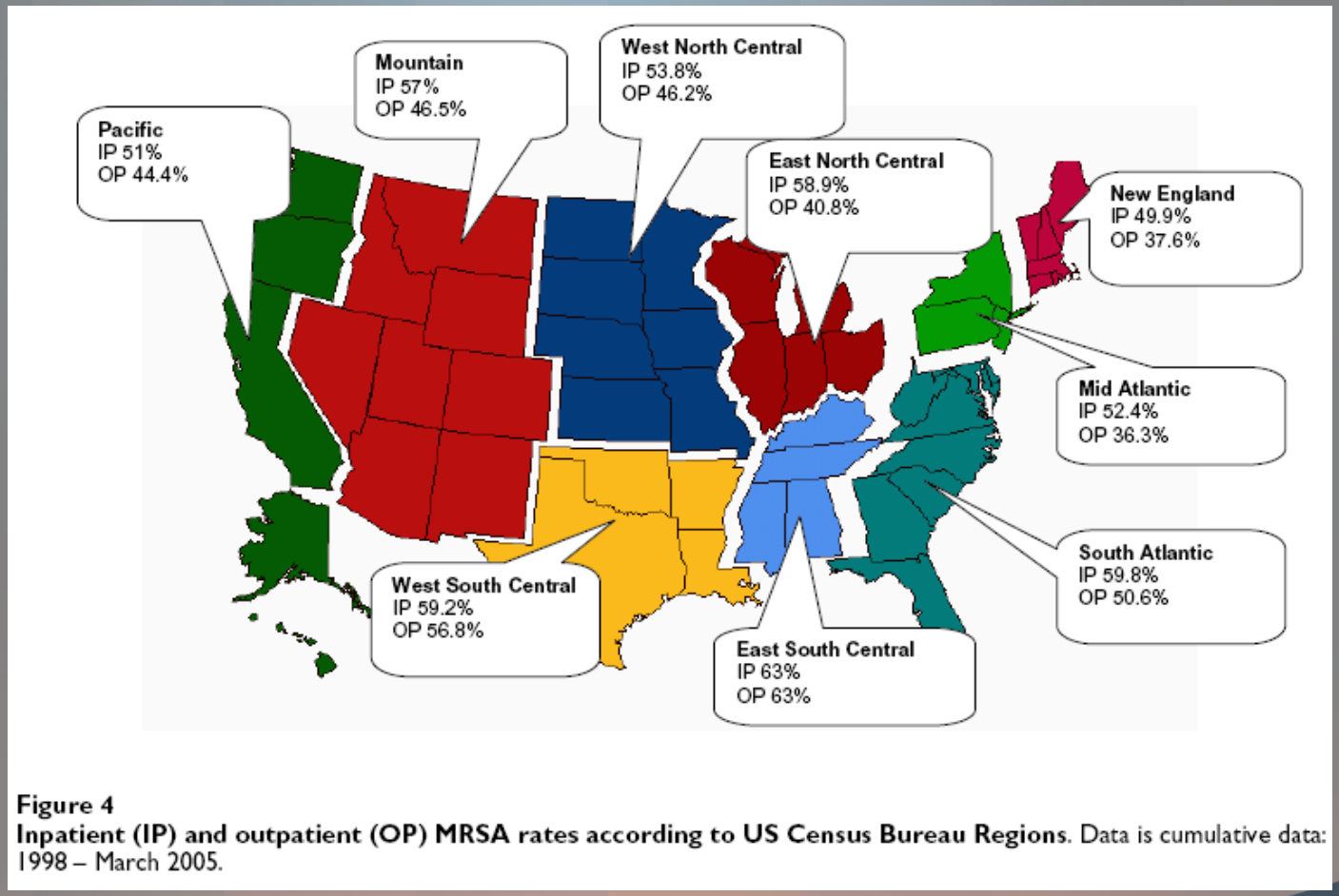
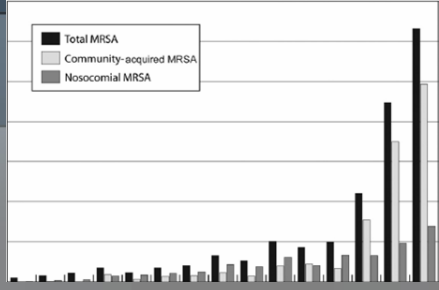


Figure 4
Inpatient (IP) and outpatient (OP) MRSA rates according to US Census Bureau Regions. Data is cumulative data: 1998 – March 2005.

The Surveillance Network-USA

Styers et al, Ann Clin MIcrobiol Antimicrob 2006

PREVALENCE AND SEVERITY



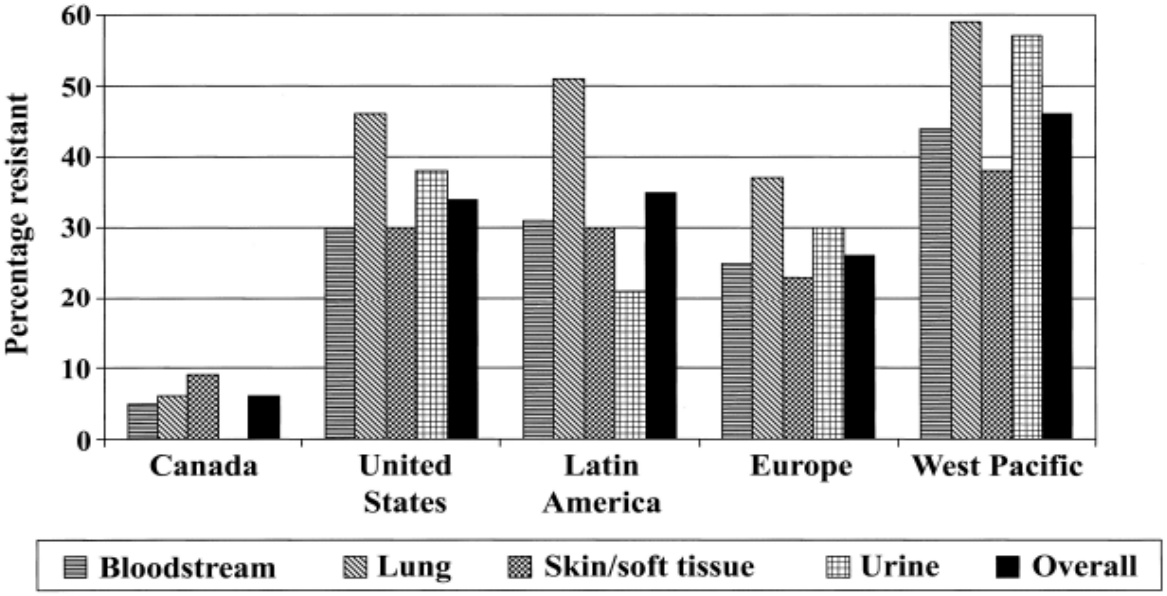


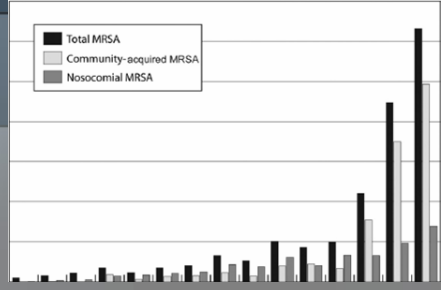
Figure 1. Methicillin resistance rates among *Staphylococcus aureus* isolates, by region and by site of infection, in the SENTRY program, 1997–1999

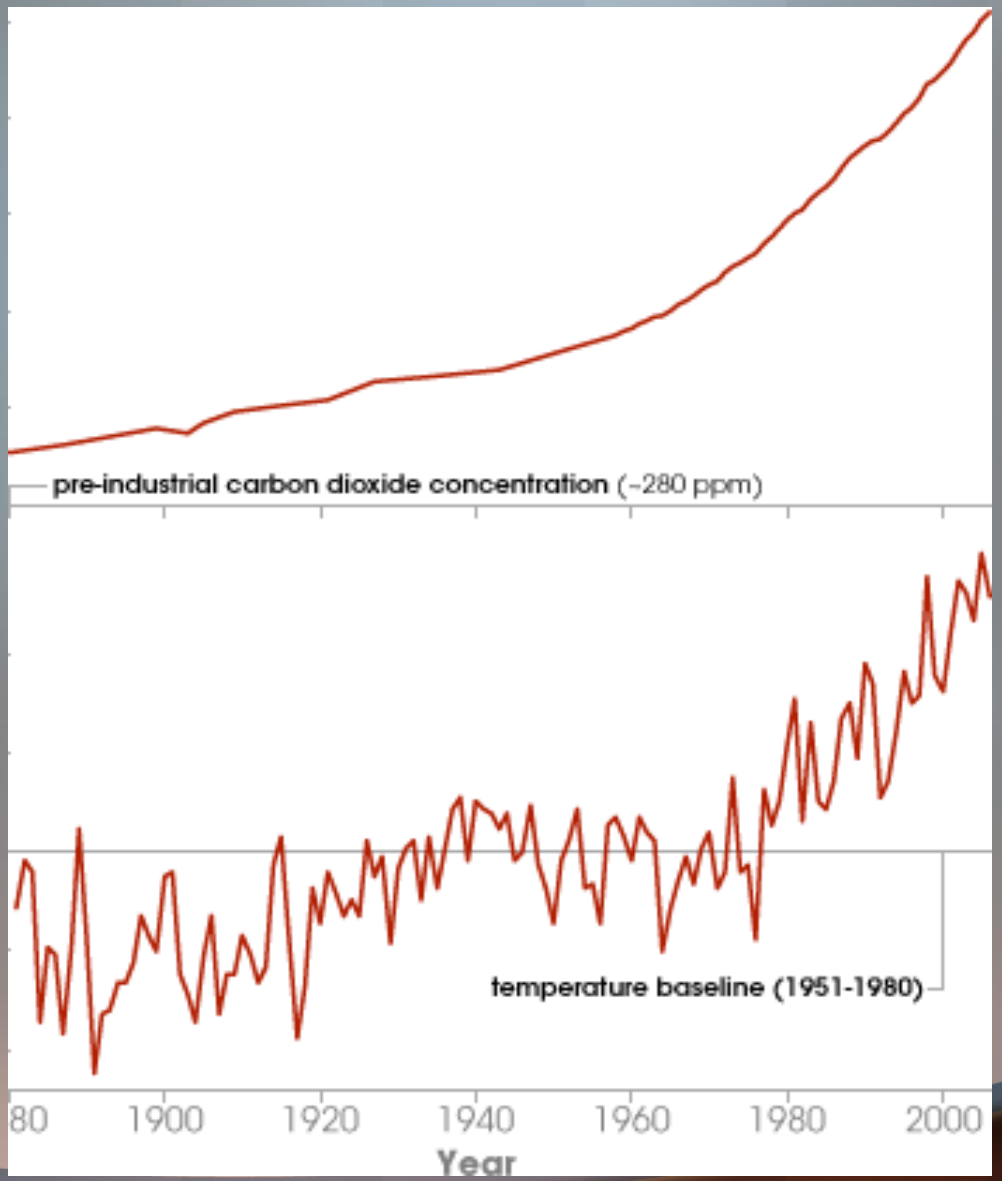
SENTRY Antimicrobial Surveillance Program

Diekema et al, Clin Infect Dis 2001

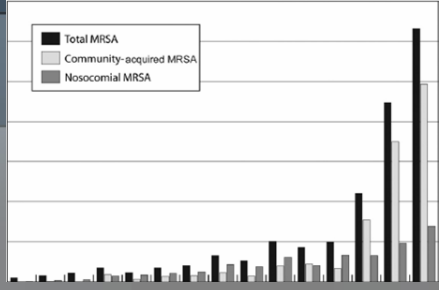
PREVALENCE AND SEVERITY

COST





PREVALENCE AND SEVERITY



ORIGINAL CONTRIBUTION

Invasive Methicillin-Resistant *Staphylococcus aureus* Infections in the United States

R. Monina Klevens, DDS, MPH
Melissa A. Morrison, MPH
Joelle Nadle, MPH
Susan Petit, MPH
Ken Gershman, MD, MPH
Susan Ray, MD
Lee H. Harrison, MD
Ruth Lynfield, MD
Ghinwa Dumyati, MD
John M. Townes, MD
Allen S. Craig, MD
Elizabeth R. Zell, MSTAT
Gregory E. Fosheim, MPH
Linda K. McDougal, MS
Roberta B. Carey, PhD
Scott K. Fridkin, MD
for the Active Bacterial Core surveillance (ABCs) MRSA Investigators

Context As the epidemiology of infections with methicillin-resistant *Staphylococcus aureus* (MRSA) changes, accurate information on the scope and magnitude of MRSA infections in the US population is needed.

Objectives To describe the incidence and distribution of invasive MRSA disease in 9 US communities and to estimate the burden of invasive MRSA infections in the United States in 2005.

Design and Setting Active, population-based surveillance for invasive MRSA in 9 sites participating in the Active Bacterial Core surveillance (ABCs)/Emerging Infections Program Network from July 2004 through December 2005. Reports of MRSA were investigated and classified as either health care–associated (either hospital-onset or community-onset) or community-associated (patients without established health care risk factors for MRSA).

Main Outcome Measures Incidence rates and estimated number of invasive MRSA infections and in-hospital deaths among patients with MRSA in the United States in 2005; interval estimates of incidence excluding 1 site that appeared to be an outlier with the highest incidence; molecular characterization of infecting strains.

Results There were 8987 observed cases of invasive MRSA reported during the surveillance period. Most MRSA infections were health care–associated: 5250 (58.4%) were community-onset infections, 2389 (26.6%) were hospital-onset infections; 1234 (13.7%) were community-associated infections, and 114 (1.3%) could not be classified. In 2005, the standardized incidence rate of invasive MRSA was 31.8 per 100 000 (interval estimate, 24.4-35.2). Incidence rates were highest among persons 65 years and older (127.7 per 100 000; interval estimate, 92.6-156.9), blacks (66.5 per 100 000; interval estimate, 43.5-63.1), and males (37.5 per 100 000; interval estimate, 26.8-39.5). There were 1598 in-hospital deaths among patients with MRSA infection during the surveillance period. In 2005, the standardized mortality rate was 6.3 per 100 000 (interval estimate, 3.3-7.5). Molecular testing identified strains historically associated with community-associated disease outbreaks recovered from cultures in both hospital-onset and community-onset health care–associated infections in all surveillance areas.

Conclusions Invasive MRSA infection affects certain populations disproportionately. It is a major public health problem primarily related to health care but no longer confined to intensive care units, acute care hospitals, or any health care institution.

JAMA. 2007;298(15):1763-1771 www.jama.com

After being initially reported among injecting drug users in Detroit in 1981[1] and then associated with the deaths of 4 children in Minnesota and North Dakota in 1997,[2] community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) has become the most frequent cause of skin and soft tissue infections presenting to emergency departments in the United States.[3] Although community outbreaks of MRSA in diverse populations, including American Indian and Alaska Natives,[4] sports

See also p 1803 and Patient Page.

Author Affiliations: Centers for Disease Control and Prevention, Atlanta, Georgia (Drs Klevens, Carey, and Fridkin and Mss Morrison, Zell, and McDougal and Mr Fosheim); California Emerging Infections Program, Oakland (Ms Nadle); Connecticut Department of Health, Hartford (Ms Petit); Colorado Emerging Infections Program, Denver (Dr Gershman); Grady Memorial Hospital, Atlanta (Dr Ray); Maryland Emerging Infections Program and Johns Hopkins Bloomberg School of Public Health, Baltimore (Dr Harrison); Minnesota Department of Health, Minneapolis (Dr Lynfield); University of Rochester, Rochester General Hospital, Rochester, New York (Dr Dumyati); Oregon Health & Science University, Portland (Dr Townes); and Tennessee Department of Health, Nashville (Dr Craig).
The ABCs MRSA Investigators are listed at the end of this article.
Corresponding Author: R. Monina Klevens, DDS, MPH, Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, 1600 Clifton Rd (A-24), Atlanta, GA 30333 (rmk2@cdc.gov).

Klevens et al, JAMA 2007

PREVALENCE AND SEVERITY

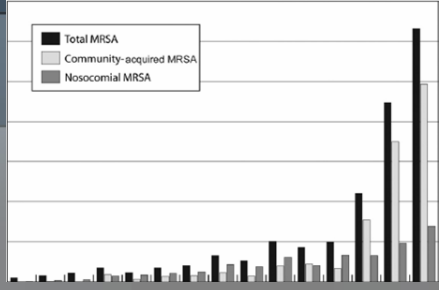


Table 2. Observed Incidence Rates of Invasive Methicillin-Resistant *Staphylococcus aureus* (MRSA) by Active Bacterial Core Surveillance Site and Epidemiologic Classification, United States, 2005[a]

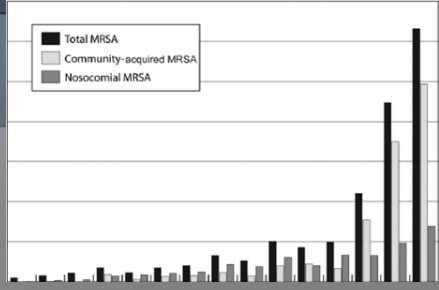
		Incidence per 100 000			
			Health Care–Associated		
Surveillance Site No. (Location)[b]	No. of Cases	Community-Associated	Community-Onset	Hospital-Onset	Total
1 (Connecticut)	952	2.7	15.6	8.4	27.1
2 (Atlanta, GA, metropolitan area)	1165	5.1	16.7	10.3	33.0
3 (San Francisco, CA, Bay Area)	936	4.5	15.9	7.7	29.2
4 (Denver, CO, metropolitan area)	480	2.8	12.3	6.0	21.2
5 (Portland, OR, metropolitan area)	305	4.7	11.4	3.6	19.8
6 (Monroe County, NY)	307	2.7	22.2	16.8	41.9
7 (Baltimore City, MD)	742	29.7	62.9	19.7	116.7
8 (Davidson County, TN)	305	6.8	30.4	13.9	53.0
9 (Ramsey County, MN)	95	1.6	11.5	6.1	19.2

[a] Epidemiologic classification of disease consisted of health care–associated (either hospital-onset cases with a culture collected >48 h after hospital admission or community-onset cases with health care risk factors but a culture collected ≤48 h after hospital admission) and community-associated cases (no health care risk factors).
[b] Site numbers were assigned in descending order of population size.

Klevens et al,
JAMA 2007

PREVALENCE AND SEVERITY

RECAP



Rates of MRSA are increasing

MRSA is an outpatient and inpatient problem

MRSA is a nationwide and global phenomenon

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVES:

1) Should we adopt a "search and destroy" strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA a problem worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

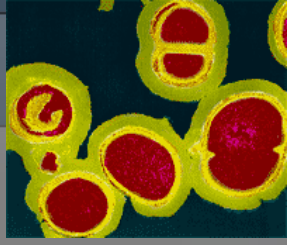
AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

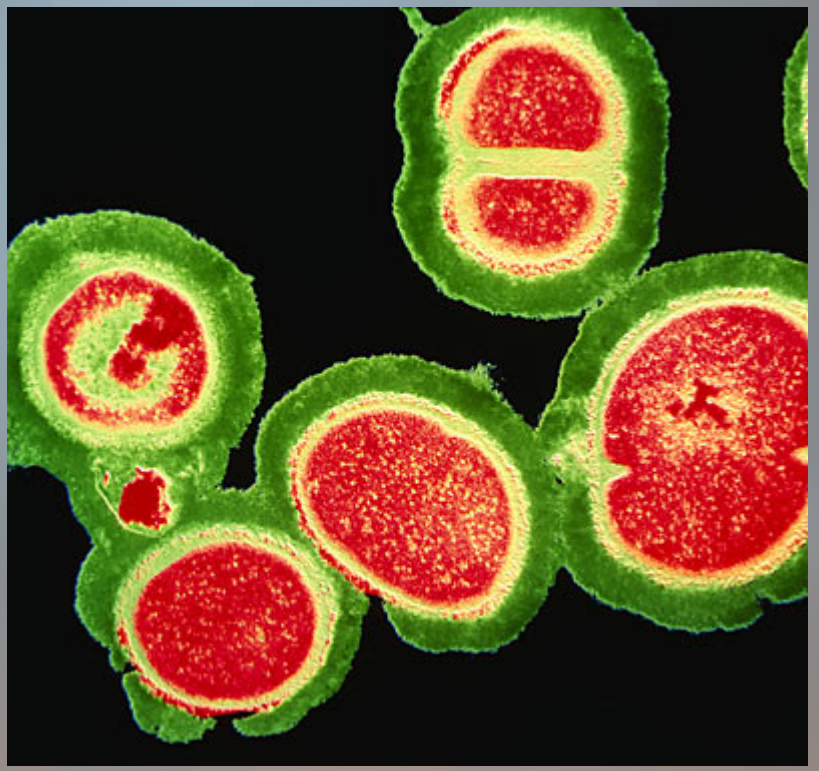
* Colonization vs. infection: Should we attempt to eradicate one or both?
* Prevention of acquisition: There are choices better than eradication…
* Risk factors for acquisition: Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA: What are the tools for eradication?
* Eradication regimens: What works?

A SPECTRE IS HAUNTING EUROPE

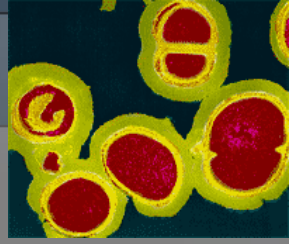
* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

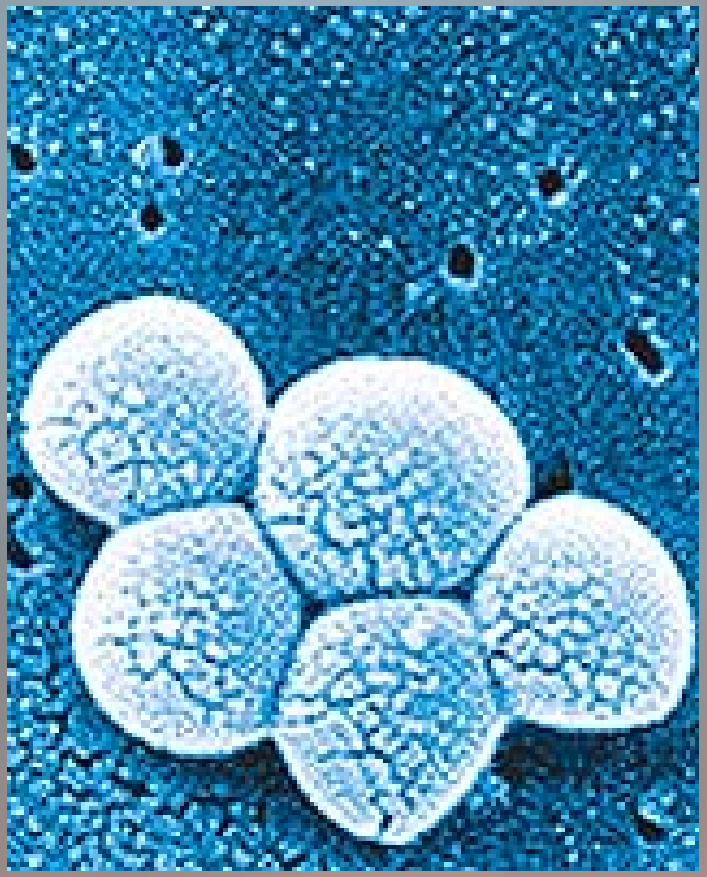
ESCAPE FROM THE INSTITUTION?



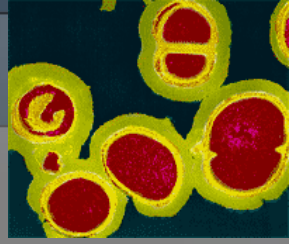


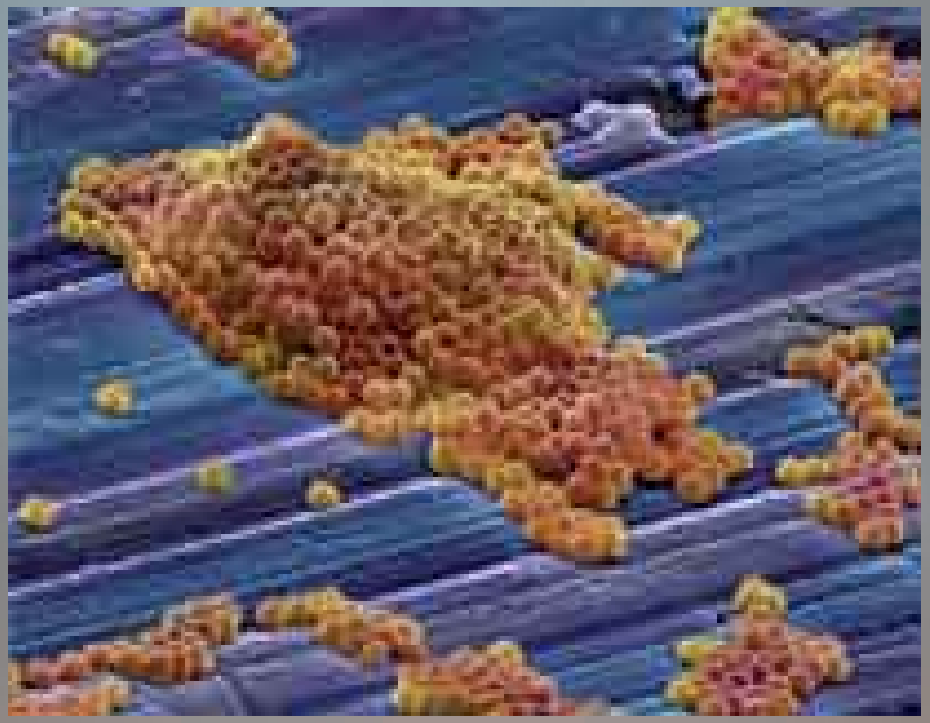
ESCAPE FROM THE INSTITUTION?



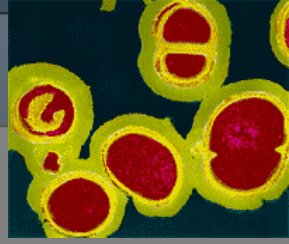


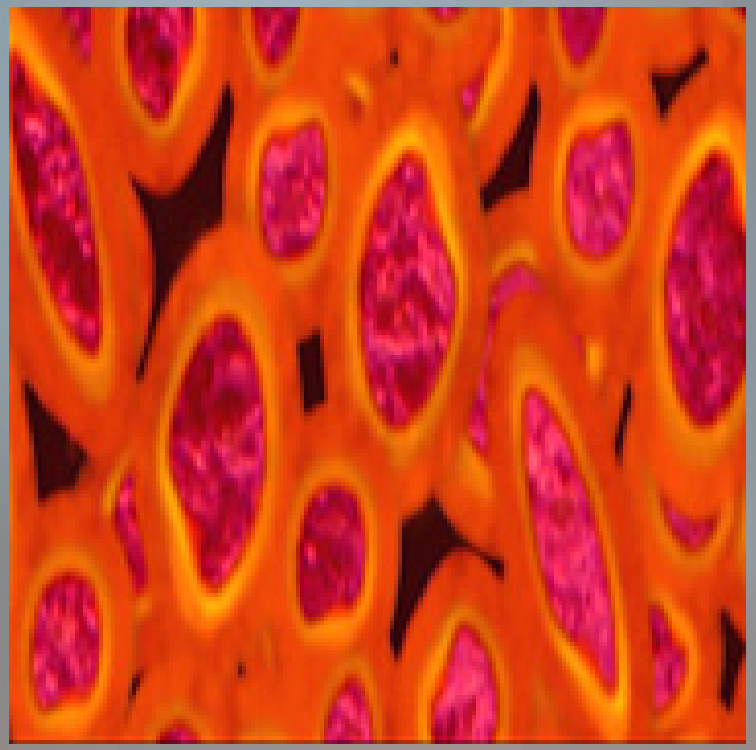
ESCAPE FROM THE INSTITUTION?



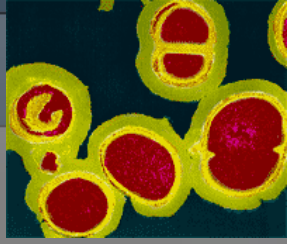


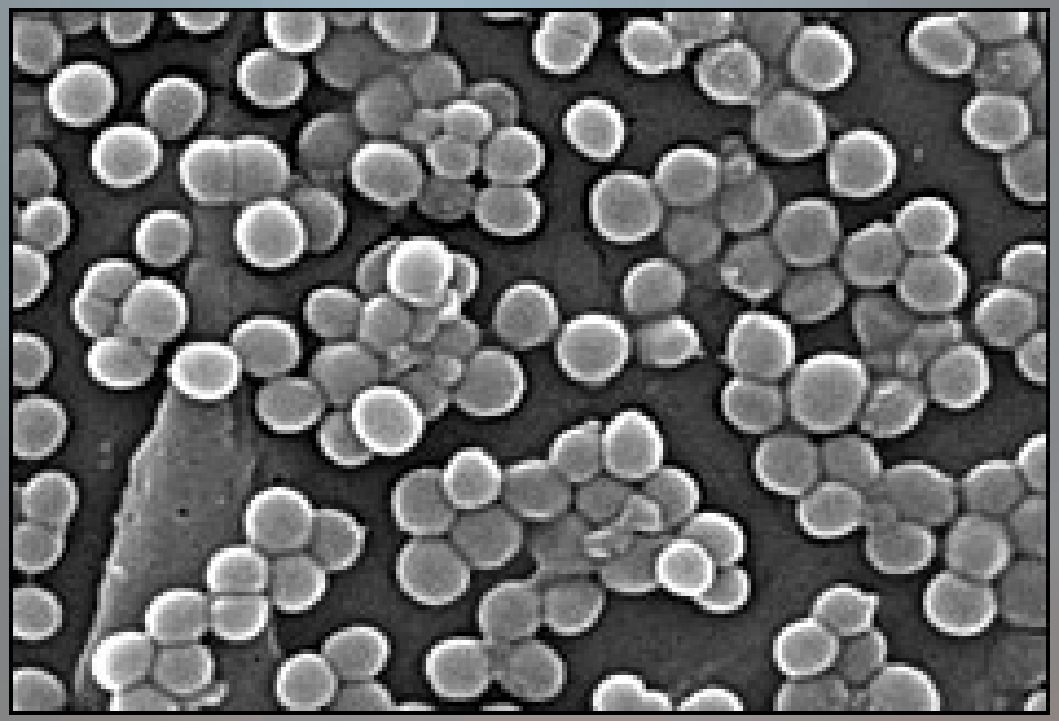
ESCAPE FROM THE INSTITUTION?



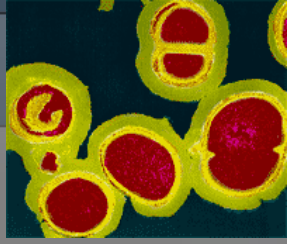


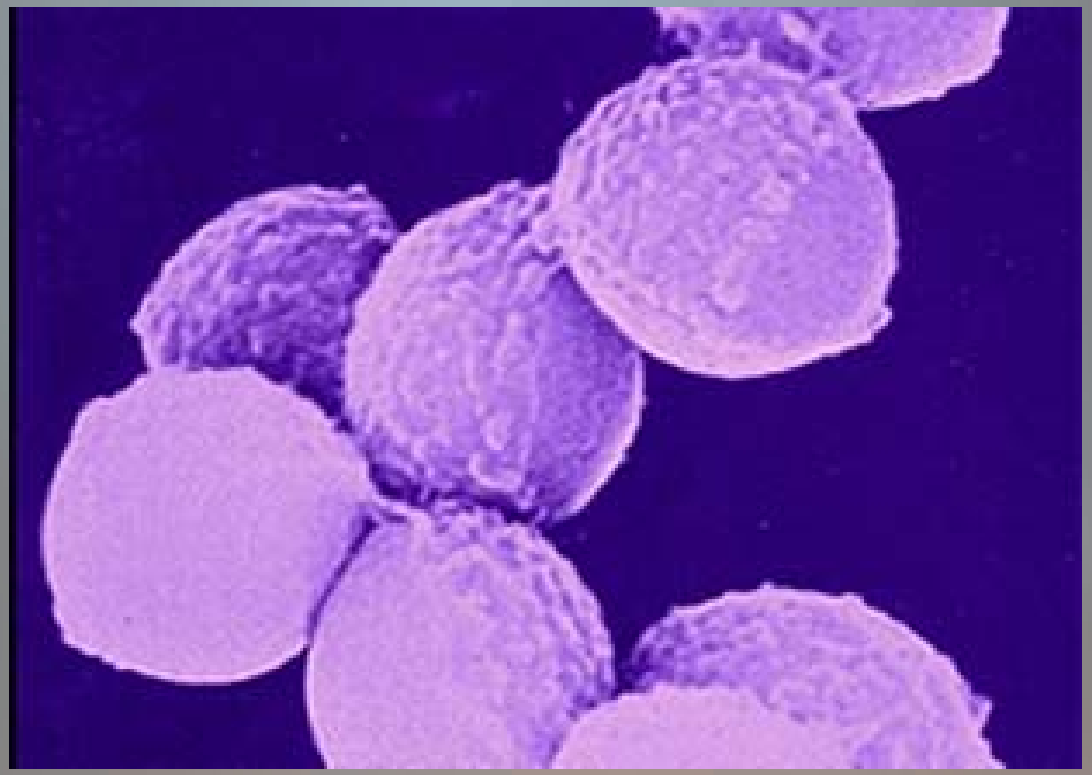
ESCAPE FROM THE INSTITUTION?



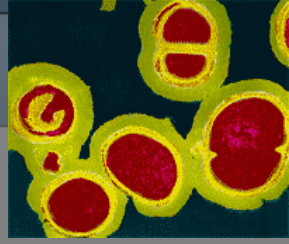


ESCAPE FROM THE INSTITUTION?

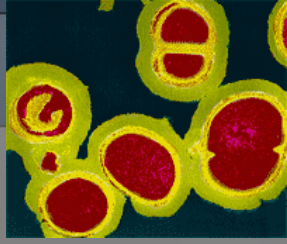


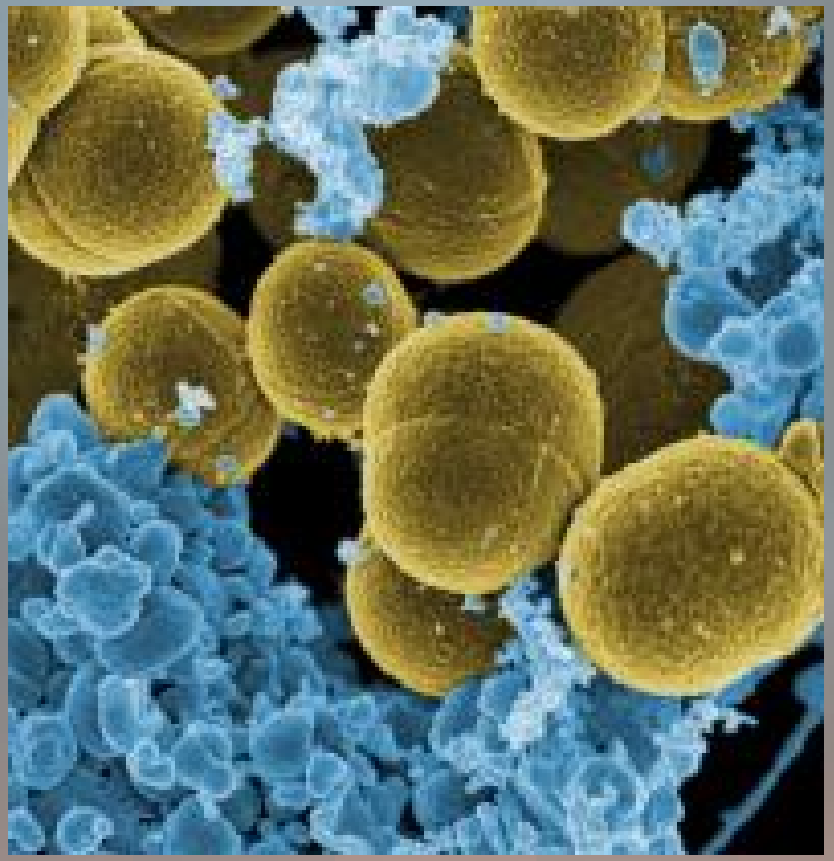


ESCAPE FROM THE INSTITUTION?

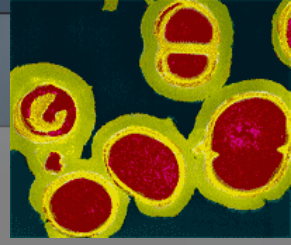


ESCAPE FROM THE INSTITUTION?

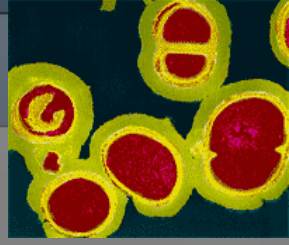




ESCAPE FROM THE INSTITUTION?



ESCAPE FROM THE INSTITUTION?



Clinical Characteristics of Community-associated MRSA Infection

- Develops within 48 hours of hospitalization
- No history of MRSA colonization or infection
- No indwelling medical device
- No history of hospitalization, surgery or hemodialysis within one year

ESCAPE FROM THE INSTITUTION?

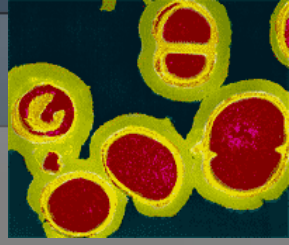
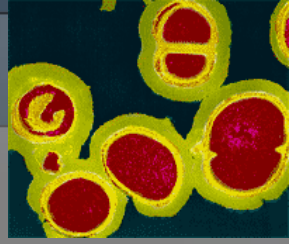


Table 1. Definitions Used for Epidemiologic Classification of Invasive Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infections

Classification	Definition
Health care–associated Community-onset	Cases with at least 1 of the following health care risk factors: (1) presence of an invasive device at time of admission; (2) history of MRSA infection or colonization; (3) history of surgery, hospitalization, dialysis, or residence in a long-term care facility in previous 12 mo preceding culture date
Hospital-onset	Cases with positive culture result from a normally sterile site obtained >48 h after hospital admission. These cases might also have ≥1 of the community-onset risk factors.
Community-associated	Cases with no documented community-onset health care risk factor

Klevens et al, 2007

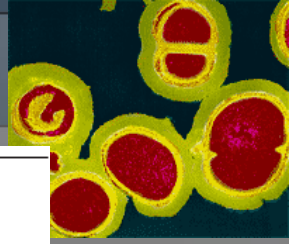
ESCAPE FROM THE INSTITUTION?



CA-MRSA vs. HA-MRSA

* spectrum of disease
* resistance characteristics
* toxins

ESCAPE FROM THE INSTITUTION?



ORIGINAL CONTRIBUTION

Comparison of Community- and Health Care–Associated Methicillin-Resistant *Staphylococcus aureus* Infection

Timothy S. Naimi, MD, MPH
Kathleen H. LeDell, MPH, RN
Kathryn Como-Sabetti, MPH
Stephanie M. Borchardt, MPH
David J. Boxrud, MS
Jerome Etienne, MD, PhD
Susan K. Johnson, BS
Francois Vandenesch, MD, PhD
Scott Fridkin, MD
Carol O'Boyle, PhD, RN
Richard N. Danila, PhD, MPH

Context Methicillin-resistant *Staphylococcus aureus* (MRSA) has traditionally been considered a health care–associated pathogen in patients with established risk factors. However, MRSA has emerged in patients without established risk factors (community-associated MRSA).

Objective To characterize epidemiological and microbiological characteristics of community-associated MRSA cases compared with health care–associated MRSA cases.

Design, Setting, and Patients Prospective cohort study of patients with MRSA infection identified at 12 Minnesota laboratory facilities from January 1 through December 31, 2000, comparing community-associated (median age, 23 years) with health care–associated (median age, 68 years) MRSA cases.

Main Outcome Measures Clinical infections associated with either community-associated or health care–associated MRSA, microbiological characteristics of the MRSA isolates including susceptibility testing, pulsed-field gel electrophoresis, and staphylococcal exotoxin gene testing.

Naimi et al,
JAMA 2003

ESCAPE FROM THE INSTITUTION?

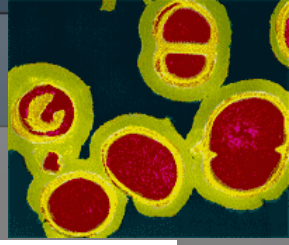


Table 4. Community-Associated and Health Care–Associated Methicillin-Resistant *Staphylococcus aureus* Cases, by Infection Type

Infection Type*	No. (%) of Methicillin-Resistant *S aureus* Cases		*P* Value†
	Community-Associated (n = 131)	Health Care–Associated (n = 937)	
Skin/soft tissue	98 (75)	343 (37)	<.001
Otitis media/externa	9 (7)	11 (1)	<.001
Respiratory tract‡	8 (6)	205 (22)	<.001
Bloodstream	5 (4)	83 (9)	.07
Urinary tract‡	1 (1)	185 (20)	<.001
Other§	10 (8)	110 (12)	.21

*If patients had more than 1 type of infection, only 1 was selected for inclusion in this table. The hierarchy for choosing the type of infection for patients with multiple sources was: bacteremia, bone, pleural fluid, peritoneal fluid, joint, surgical specimen, postoperative wound, eye, ear, sputum, urine, and skin.

†Refers to the statistical probability that the type of infection among community-associated cases differed from the percentage among health care–associated cases ($\alpha = .05$).

‡Among health care–associated isolates, some respiratory tract isolates were obtained from endotracheal tubes, and some urinary tract isolates were obtained from Foley catheters.

§Included bone, peritoneal fluid, joint, surgical specimen, and postoperative wound.

Naimi et al,
JAMA 2003

ESCAPE FROM THE INSTITUTION?

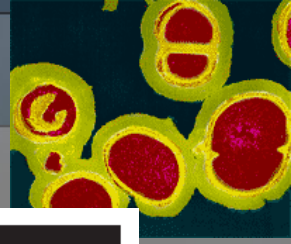


Table 5. Antimicrobial Susceptibility Profiles of Community-Associated and Health Care–Associated Methicillin-Resistant *Staphylococcus aureus* Isolates

Type of Antibiotic	No. (%) Susceptible*		*P* Value†
	Community-Associated (n = 106)	Health Care–Associated (n = 211)	
Oxacillin (methicillin)	0	0	NA
Ciprofloxacin	84 (79)	33 (16)	<.001
Clindamycin	88 (83)	44 (21)	<.001
Erythromycin	47 (44)	18 (9)	<.001
Gentamicin	100 (94)	168 (80)	.001
Rifampin	102 (96)	199 (94)	.64
Tetracycline	98 (92)	194 (92)	.95
Trimethoprim-sulfamethoxazole	101 (95)	189 (90)	.13
Vancomycin	106 (100)	211 (100)	NA

Abbreviation: NA, not applicable.
*Tested at the Minnesota Department of Public Health Laboratory by broth microdilution using National Committee for Clinical Laboratory Standards break points.
†Refers to the statistical probability that the percentage susceptible among community-associated isolates differed from the percentage susceptible among health care–associated isolates ($\alpha = .05$).

Naimi et al,
JAMA 2003

ESCAPE FROM THE INSTITUTION?

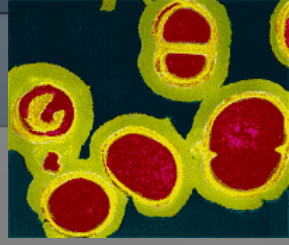


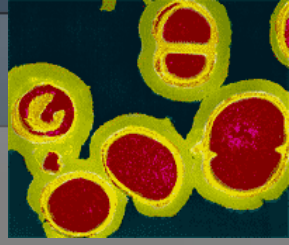
Table 6. Exotoxin Genes and Gene Alleles Among Community-Associated and Health Care–Associated Methicillin-Resistant *Staphylococcus aureus* Isolates

Gene Sequence	No. (%) of Cases With Gene Sequence		Odds Ratio (95% Confidence Interval)*
	Community-Associated (n = 26)	Health Care–Associated (n = 26)	
Exotoxin Gene†			
β Hemolysin	2 (8)	0	Undefined
γ Hemolysin variant	25 (96)	26 (100)	0 (0-1.00)
Leukocidin E-D	24 (92)	26 (100)	0 (0-1.00)
PVL	20 (77)	1 (4)	5.01 (3.49-5.25)
sea	15 (58)	1 (4)	3.03 (2.03-3.22)
seb	6 (23)	1 (4)	3.35 (0.80-5.14)
sec	13 (50)	0	Undefined
sed	5 (19)	14 (54)	0.41 (0.13-0.93)
seg	5 (19)	25 (96)	0.17 (0-0.67)
seh	17 (65)	1 (4)	3.63 (2.47-3.84)
sei	5 (19)	25 (96)	0.17 (0-0.67)
sej	5 (19)	14 (54)	0.41 (0.13-0.93)
sek	16 (62)	0	Undefined
sem	5 (19)	25 (96)	0.17 (0-0.67)
sen	5 (19)	25 (96)	0.17 (0-0.67)
seo	5 (19)	25 (96)	0.17 (0-0.67)
Gene Allele‡			
agr 2	4 (15)	25 (96)	0.20 (0-0.67)
agr 3	17 (65)	1 (4)	3.63 (2.47-3.84)
SCC*mec* II	3 (12)	21 (81)	0.14 (0-0.53)
SCC*mec* IV	22 (85)	3 (12)	5.87 (3.67-6.55)

Abbreviations: AGR, accessory gene regulator; PVL, Panton Valentine leukocidins; SCC, Staphylococcal chromosomal cassette; se, Staphylococcal enterotoxin.
*The corrected odds ratio of being associated with community-associated vs health care–associated case isolates.
†Toxins not present in either community or health care–associated methicillin-resistant *S aureus* included *see*, toxic shock syndrome toxin, leukocidin M, exfoliative toxins A, B, and D, epidermal inhibitor A, and γ hemolysin.
‡Although all isolates had SCC*mec* and *agr* alleles, the total percentage of isolates with the listed allele does not total to 100% because some isolates had alleles that were not shown.

Naimi et al, JAMA 2003

ESCAPE FROM THE INSTITUTION?



RECAP

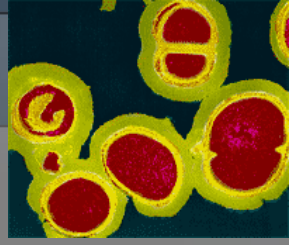
CA-MRSA is distinct from HA-MRSA

CA-MRSA is more likely to cause skin infections

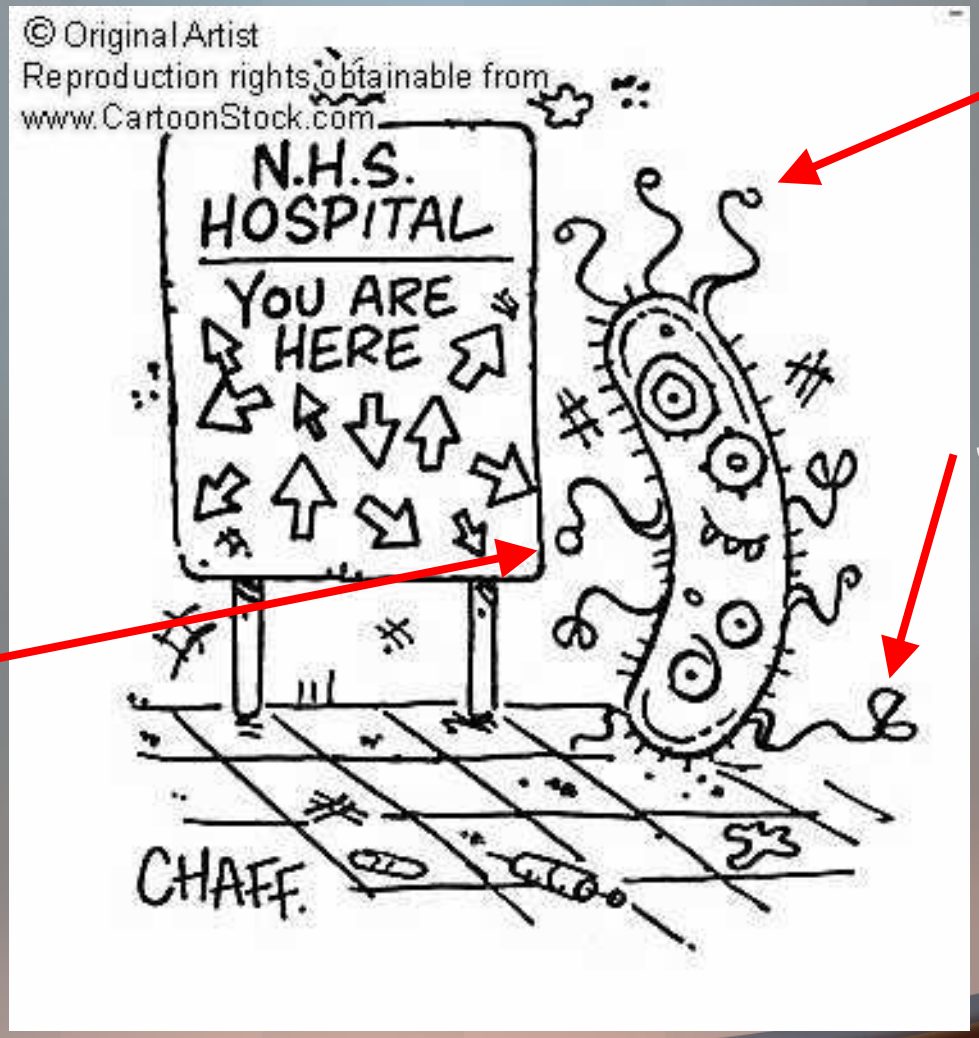
CA-MRSA is more likely to be sensitive to ABX

CA-MRSA has distinct microbiological characteristics, of undetermined significance.

ESCAPE FROM THE INSTITUTION?



RECAP



PVL

SCC *mecA* IV

seq

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVES:

1) Should we adopt a "search and destroy" strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA a problem worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

* Colonization vs. infection: Should we attempt to eradicate one or both?
* Prevention of acquisition: There are choices better than eradication…
* Risk factors for acquisition: Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA: What are the tools for eradication?
* Eradication regimens: What works?

A SPECTRE IS HAUNTING EUROPE

* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

S. aureus = normal skin flora

Also colonizes:

- perineum, wounds, burns, respiratory secretions, urine, feces

Forms biofilms

A PLANCK UNIT OF PREVENTION IS WORTH A GRAM OF CURE

COLONIZATION

1) Persistent	10-35%
2) Intermittent	20-75%
3) Non-carriers	5-50%

A GRAIN OF PREVENTION IS WORTH A PENNYWEIGHT OF CURE

META-ANALYSIS

* 10 studies, 8350 persons

Table 2. Studies reporting methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in the community.

Study, reference	Year	Location	Sample size (study population)	No. (%) of subjects with *S. aureus*	No. (%) of subjects with MRSA	Proportion of MRSA-colonized subjects with risk factor, %					
						Recent hospitalization	Recent outpatient visit	Chronic illness	Recent antibiotic use	Injection drug use	Contact
Charlebois et al. [48]	2002	San Francisco	833 Adults (homeless and marginally housed)	190 (22.8)	23 (2.8)[a,b]	48	NA	NA	65	91	NA
Abudu et al. [50]	2001	Birmingham, UK	274 Adults (from general practice clinics list)	63 (23.0)	4 (1.5)	50	NA	NA	0	NA	NA
Hussain et al. [16]	2000	Chicago	500 Children (outpatient clinic attendees)	122 (24.4)	3 (0.6)	33[e]	0	0	0	0	0
Shopsin et al. [52]	2000	New York	275 Children and 225 guardians (pediatric clinic attendees)	96 children (34.9) and 63 adults (28)	1 child (0.4) and 0 adults[c]	100	NA	NA	100	NA	NA
Eicher et al. [49]	2000	Minneapolis	94 Children (students)	34 (36.2)	7 (7.4)	NA	NA	NA	86	NA	NA
Muto et al. [54]	1999	Charlottesville, VA	816 Individuals (hospital admissions)	NA	8 (0.98)	67	NA	100	NA	NA	NA
Suggs et al. [51]	1999	Chicago	500 Children (emergency department attendees)	132 (26.4)	11 (2.2)	0	0	36	27	0	0
Kim et al. [53]	1998	Seoul, Korea	420 Children and 501 adults (outpatient clinic attendees)	190 children (45.2) and 98 adults (19.6)	28 children (6.7) and 4 adults (0.8)[d]	25 adults	0	NA	NA	NA	NA
Troillet et al. [55]	1998	Boston	387 Individuals (hospital admissions)	96 (24.8)	10 (2.6)	⩾70	⩾60	100	100	NA	NA
Sá-Leão et al. [56]	2001	Oeiras, Portugal	2111 Children and 1414 adults (day care attendees, Air Force personnel, and students)	1001 (28.4)	7 (0.20)[a]						

NOTE. NA, not assessed.

[a] Excluded subjects with previous hospital contact.

[b] Two subjects with MRSA (0.24% of all subjects) had no identifiable risk factors.

[c] Total, 1 subject (0.20%).

[d] Total, 32 subjects (3.5%).

[e] A 2-week-old infant who was born in the hospital.

Salgado et al, Clin Infect Dis 2003

A CLOVE OF PREVENTION IS WORTH A STONE OF CURE

MET

* 10

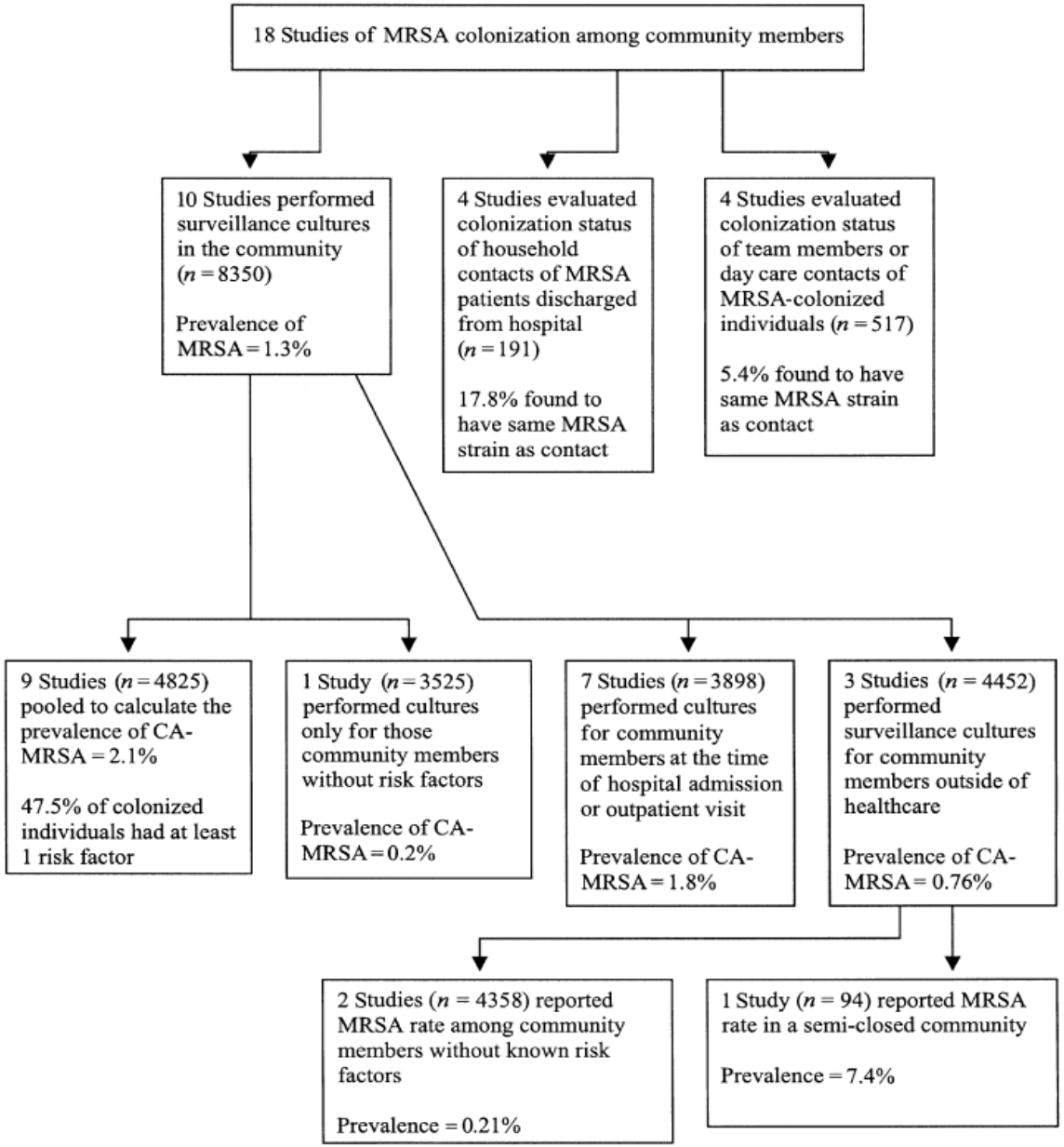


Figure 1. Studies of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in communities. CA, community acquired.

Salgado

A QUINTAL OF PREVENTION IS WORTH A ZENTNER OF CURE

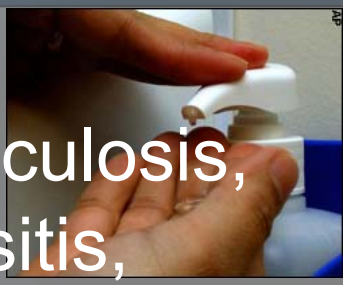
NHANES

* 2001-2002, 9622 persons
  → *S. aureus* in 32.4%
  → MRSA in 0.8%

Non-healthcare

* 4 settings, random sample of 295 persons
  → MRSA 1.0%

Kuehnert et al, J Infect Dis 2006
Rim & Bacon, Infect Control Hosp Epi 2007



Described Sites of Infection for MRSA

- Skin and soft tissue: cellulitis, impetigo, furunculosis, folliculitis, abscess, necrotizing fasciitis, myositis, surgical wounds
- Indwelling catheter: urinary, intravenous, central nervous system shunt
- Bone/joint, including prosthetic
- Pulmonary: necrotizing pneumonia, empyema, VAP
- Endocarditis, pericarditis
- Central nervous system (meningitis, abscess)
- Intraabdominal or renal abscess
- Septic thrombophlebitis with pulmonary embolism
- Severe sepsis with purpura fulminans and Waterhouse-Friderichsen syndrome

A SLIGHTLY GRAVID SWALLOW CARRYING A COCONUT OF PREVENTION IS WORTH AN ASIAN ELEPHANT OF CURE

RECAP

S. aureus (including MRSA) can colonize all sorts of body surfaces

S. aureus carriage may be persistent or intermittent, and is about 25% in the gen pop.

MRSA carriage is < 2% in a risk-factor free population, and is certainly higher in at-risk populations

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVES:

1) Should we adopt a "search and destroy" strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA a problem worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

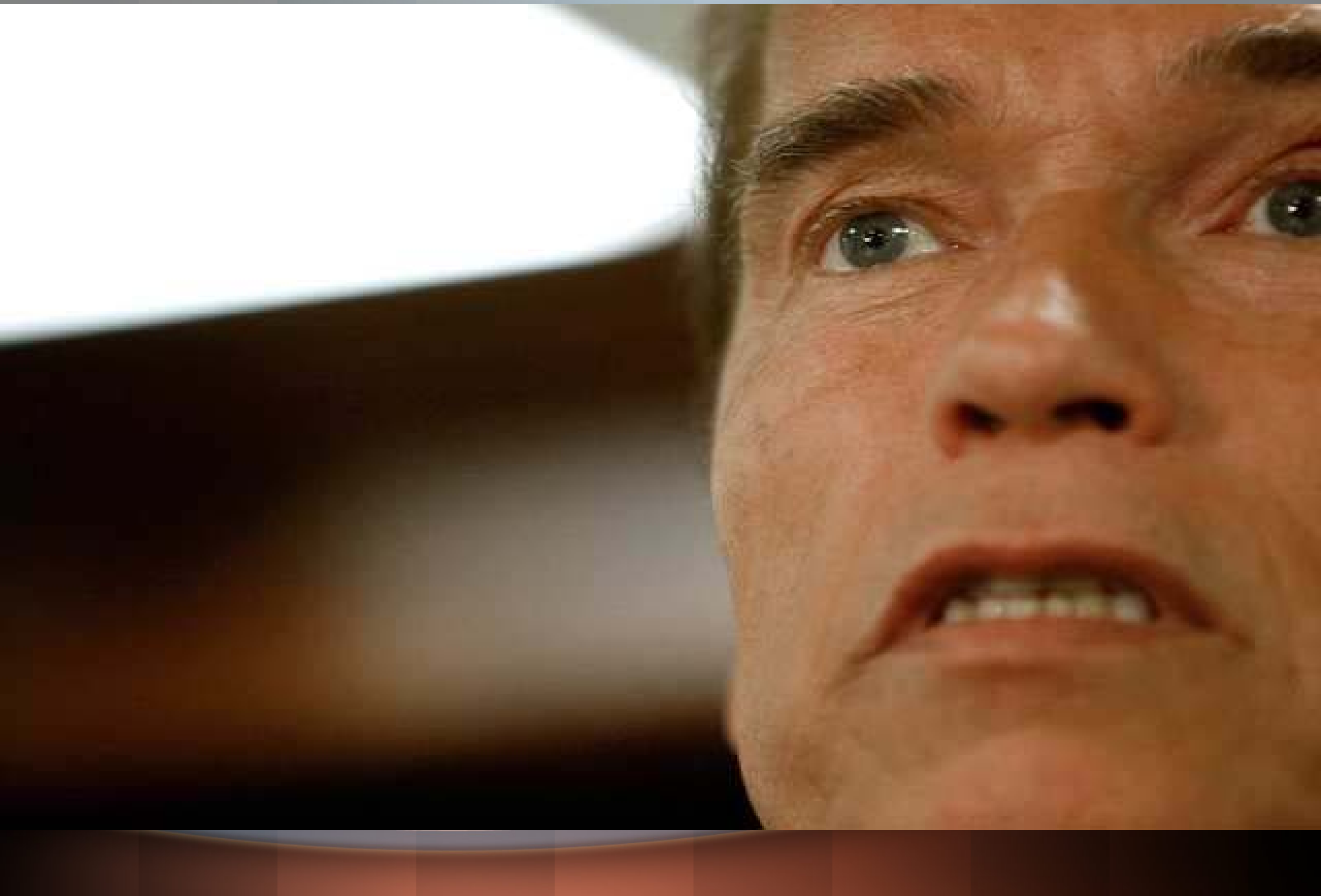
AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

* Colonization vs. infection: Should we attempt to eradicate one or both?
* Prevention of acquisition: There are choices better than eradication…
* Risk factors for acquisition: Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA: What are the tools for eradication?
* Eradication regimens: What works?

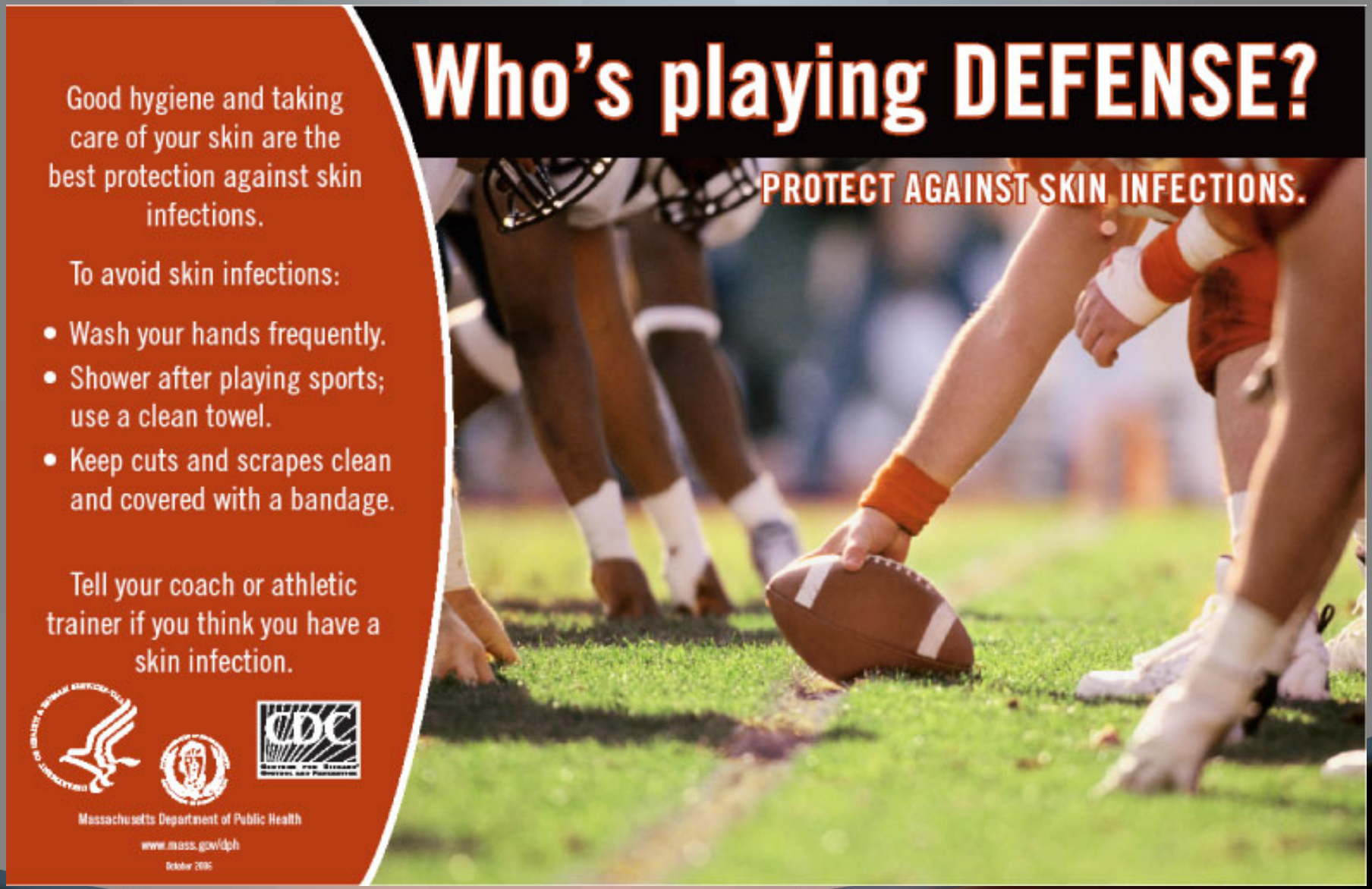
A SPECTRE IS HAUNTING EUROPE

* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

PREVENTION OF ACQUISITION



PREVENTION OF ACQUISITION



PREVENTION OF ACQUISITION

PREVENTION OF ACQUISITION

PREVENTION OF ACQUISITION

CDC Recommendations

* wounds clean and covered
* clean hands with soap & water, or alcohol-based gel
* do not share items that may transmit bacteria
* avoid activities with uncovered wounds
* clean equipment and clothes that come into contact with wounds

Gorwitz et al, CDC 2006

PREVENTION OF ACQUISITION

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Clone of Methicillin-Resistant *Staphylococcus aureus* among Professional Football Players

Sophia V. Kazakova, M.D., M.P.H., Ph.D., Jeffrey C. Hager
Matthew Matava, M.D., Arjun Srinivasan, M.D., Larry Phel
Bernard Garfinkel, M.D., Thomas Boo, M.D., Sigrid McAllister, B.
Jim Anderson, B.S., A.T.C., Bette Jensen, M.M.Sc., Doug D
David Lonsway, M.M.Sc., Linda K. McDougal, M.S., Matthew A
Victoria J. Fraser, M.D., George Killgore, Dr.P.H., Fred C. Te
Sara Cody, M.D., and Daniel B. Jernigan, M.D., M.

ABSTRACT

BACKGROUND

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an emerging cause of infections outside of health care settings. We investigated an outbreak of abscesses due to MRSA among members of a professional football team and examined the transmission and microbiologic characteristics of the outbreak strain.

Kazakova et al, NEJM 2005

PREVENTION OF ACQUISITION

IN THE HOSPITAL

- Handwashing!
- Isolation of MRSA-positive patients
- Cohorting of MRSA-positive patients
- Contact precautions – gowns, gloves, et al

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVES:

1) Should we adopt a "search and destroy" strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA a problem worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

* Colonization vs. infection: Should we attempt to eradicate one or both?
* Prevention of acquisition: There are choices better than eradication…
* Risk factors for acquisition: Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA: What are the tools for eradication?
* Eradication regimens: What works?

A SPECTRE IS HAUNTING EUROPE

* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

RISK FACTORS FOR ACQUISITION

- Long-term care facility
- Hemodialysis
- Indwelling catheter

- Intravenous drug abuse
- Military
- Incarceration
- Athletes
- Homelessness
- Men who have sex with men

RISK FACTORS FOR ACQUISITION

- Tattoos
- Native Americans, Pacific Islanders
- Contact with persons at day care centers

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVES:

1) Should we adopt a "search and destroy" strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA a problem worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

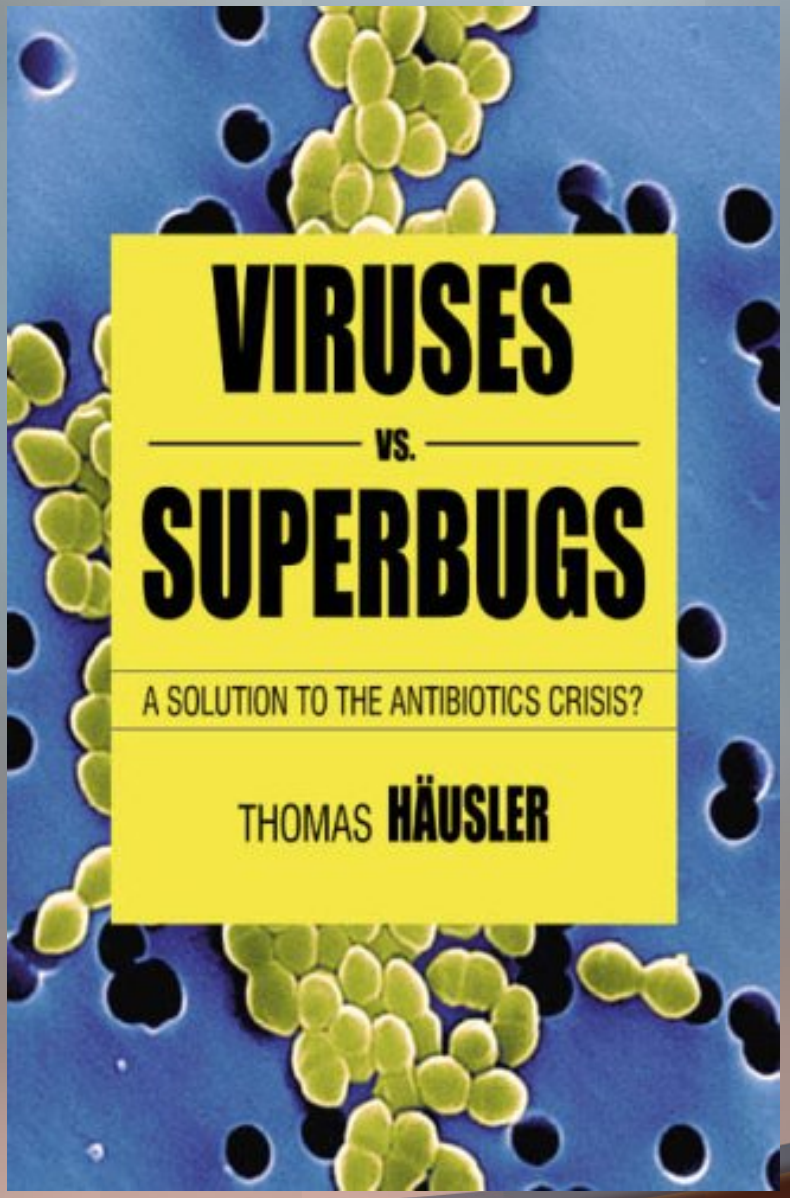
AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

* Colonization vs. infection: Should we attempt to eradicate one or both?
* Prevention of acquisition: There are choices better than eradication…
* Risk factors for acquisition: Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA: What are the tools for eradication?
* Eradication regimens: What works?

A SPECTRE IS HAUNTING EUROPE

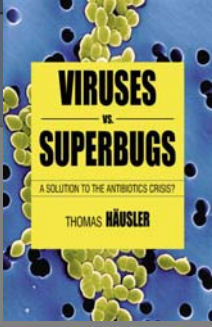
* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

TREATMENT MODALITIES



TREATMENT MODALITIES

- Topical agents
- Oral agents
- Parenteral agents



MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVES:

1) Should we adopt a "search and destroy" strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA a problem worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

* Colonization vs. infection: Should we attempt to eradicate one or both?
* Prevention of acquisition: There are choices better than eradication…
* Risk factors for acquisition: Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA: What are the tools for eradication?
* Eradication regimens: What works?

A SPECTRE IS HAUNTING EUROPE

* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

ERADICATION REGIMENS

ERADICATION REGIMENS

ERADICATION REGIMENS

ERADICATION REGIMENS

CDC Recommendations

- "To date, there is no data to support the use of agents to eliminate *S. aureus* colonization… for patients with MRSA infection or their close contacts."
- However, recommend considering decolonization if:

  1) multiple documented recurrences of MRSA

  2) ongoing MRSA transmission in a well-defined, closely-associated cohort

  AND, ONLY IF standard prevention measures do not work.
- No appropriate regimens have been established for community
- Culture and target vs. universal treatment?
- Do so simultaneously, for short courses, with topicals if possible.

Gorwtiz et al., CDC 2006.

ERADICATION REGIMENS

SHEA Recommendations

- "Consider MRSA decolonization therapy for both patients and HCWs [healthcare workers] as an adjunctive measure for controlling spread of MRSA in selected populations when appropriate."
- Perform with susceptibility testing to select agents
- Avoid widespread or prolonged use.

- Active surveillance cultures
- Hand hygeine
- Barrier precautions: gloves, gown, masks
- Antibiotic stewardship

Muto et al., Infect Control Hosp Epi 2003

ERADICATION REGIMENS

Cochrane Review: Antimicrobial drugs for treating methicillin-resistant *Staphylococcus aureus* colonization.

- Only 6 studies were randomized controlled trials, comparing treatment to no treatment, placebo, or alternative regimen.
- Total = 384 participants.

oral fusidic acid vs no treatment

mupirocin vs placebo

ripampin vs minocycline vs rif + mino vs no treatment
mupirocin vs topical fusidic acid vs TMP-SMX

ciprofloxacin + rifampin vs TMP-SMX

novobiocin + rifampin vs TMP-SMX

- "There is insufficient evidence to support use of…therapy for eradicating nasal or extranasal MRSA."

Loeb et al, Cochrane 2007

ERADICATION REGIMENS

RCT: Eradication protocol

Chlorhexidine 2% wash	Daily x7 days
mupirocin 2% intranasally	TID x7 days
Rifampin 300mg	BID x7 days
doxycycline 100mg	BID x7 days

vs.

no treatment

Simor et al, Clin Infect Dis 2007

ERADICATION REGIMENS

RCT: Eradication protocol [chx/mup/doxy/rif]

Randomized, but open-label.

Primary endpoint: detection of MRSA at 3 months

Inclusion: MRSA screening on admission or as part of outbreak investigation

Exclusion: on ABX, prior MRSA decol attempt w/in 6 months, allergy to medications, known ABX resistance to study drugs, inability to take meds PO or via PEG, pregnancy/breastfeeding, known hepatic cirrhosis or LFT abnormalities, planned surgery w/in 3 months.

Groups similar for all conditions except PEG (24% vs 8%, p=0.08)

Data collection:

Ant nares, perianal area, skin lesions, medical device exit sites
Study onset, weekly x4 wks, monthly x7 mos for up to 8 mos

Follow-up: high percentage lost

Simor et al, Clin Infect Dis 2007

ERADICATION REGIMENS

RCT: Eradication protocol [chx/mup/doxy/rif]

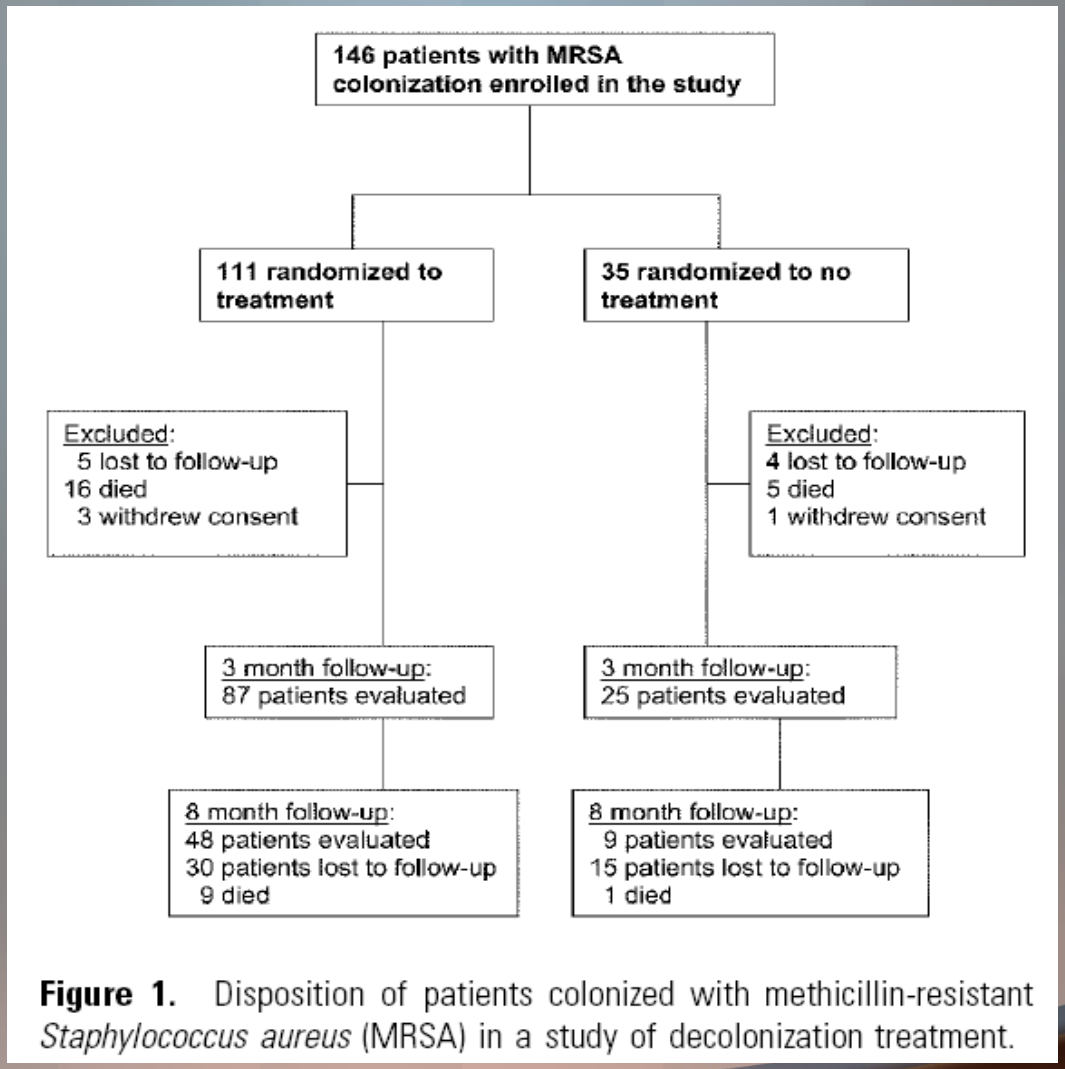


Figure 1. Disposition of patients colonized with methicillin-resistant *Staphylococcus aureus* (MRSA) in a study of decolonization treatment.

Simor et al, Clin Infect Dis 2007

ERADICATION REGIMENS

RCT: Eradication protocol [chx/mup/doxy/rif]

At 3 months:

87 evaluated for tx group: 64 (**74%**) remained MRSA-negative

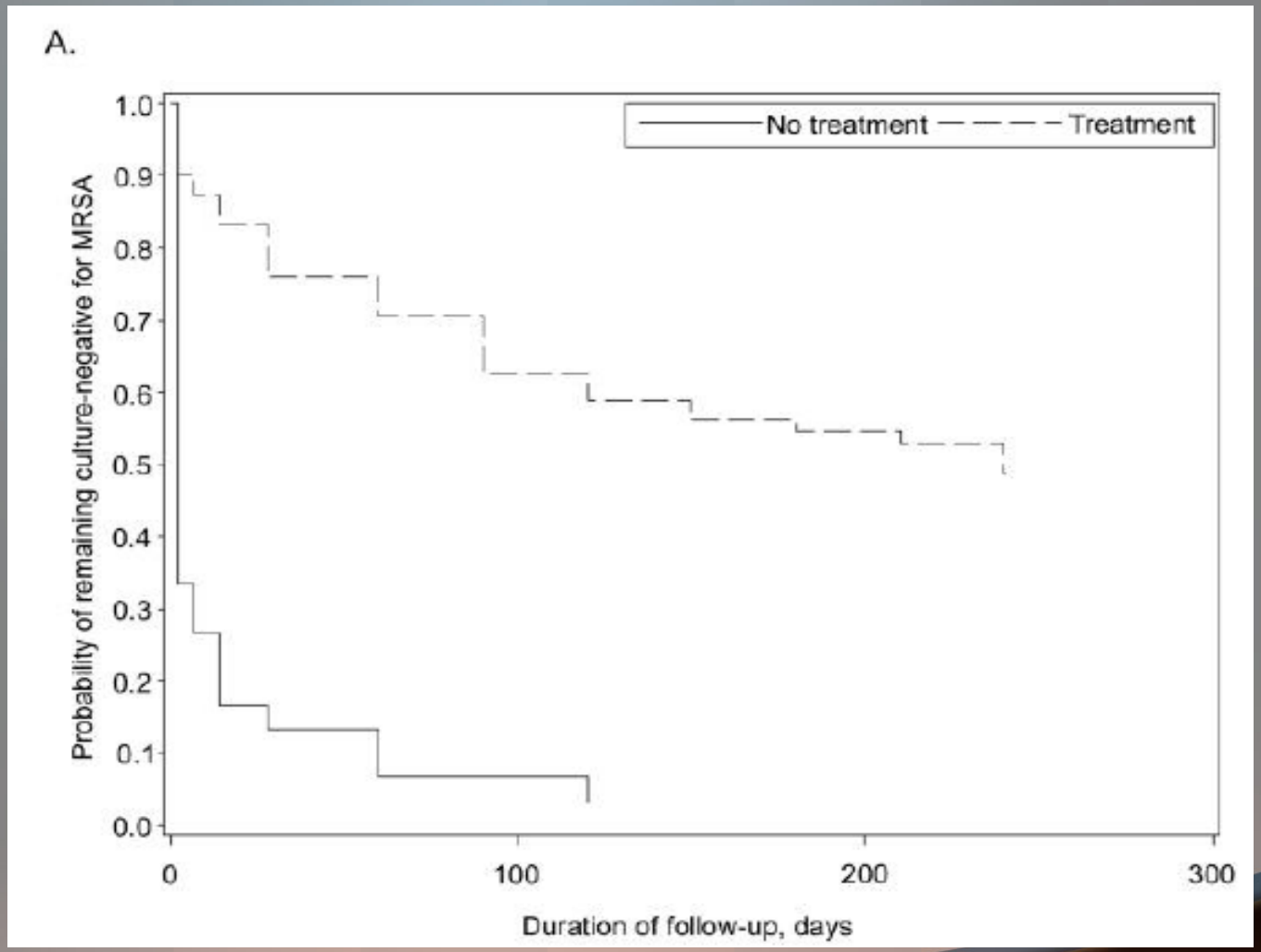
25 evaluated for no tx group: 8 (**32%**) were MRSA-negative

- Compliance with decol therapy: 92% completed ≥ 6 days
- 4 patients discontinued tx for adverse effects (reported in 22)
- 13 (18%) had new strains of MRSA
- 21 of 110 isolates (19%) had high-level mupirocin resistance (5, 5% had low-level resistance)
- No MRSA infections developed during study
- Univariate analysis: variables assoc w/ recol = mupirocin-resistance at baseline

Simor et al, Clin Infect Dis 2007

ERADICATION REGIMENS

RCT: Eradication protocol [chx/mup/doxy/rif]



Simor et al, Clin Infect Dis 2007

ERADICATION REGIMENS

RECAP

Very little has been proven about the efficacy of eradication regimens.

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVES:

1) Should we adopt a "search and destroy" strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA a problem worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

* Colonization vs. infection: Should we attempt to eradicate one or both?
* Prevention of acquisition: There are choices better than eradication…
* Risk factors for acquisition: Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA: What are the tools for eradication?
* Eradication regimens: What works?

A SPECTRE IS HAUNTING EUROPE

* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

DUTCH HEALTH CARE

THE NETHERLANDS

- Densely populated
- Universal access to healthcare
- 100-150 hospitals, 300-1200 beds each

Dutch Health Council

- Reports 1966, 1976, 1990 → ICP, infection control guidelines

Dutch Working Party on Infection Control (WIP)

- Guidelines, literature repository, facilitate discussion
- Support from national Chief Medical Officer

Working Group of Hospital Epidemiologists

- Research, discussion, training

DUTCH HEALTH CARE

National Institute of Public Health and Environmental Protection (RIVM)

- Surveillance; 150 to 200 MRSA isolates from 30-50 different hospitals

PREZIES (prevention of hospital infection by surveillance)

- Surgical infections → ICU infections, vascular device-related infection
- 80% Dutch hospital participation

DUTCH HEALTH CARE

Low prevalence of MRSA

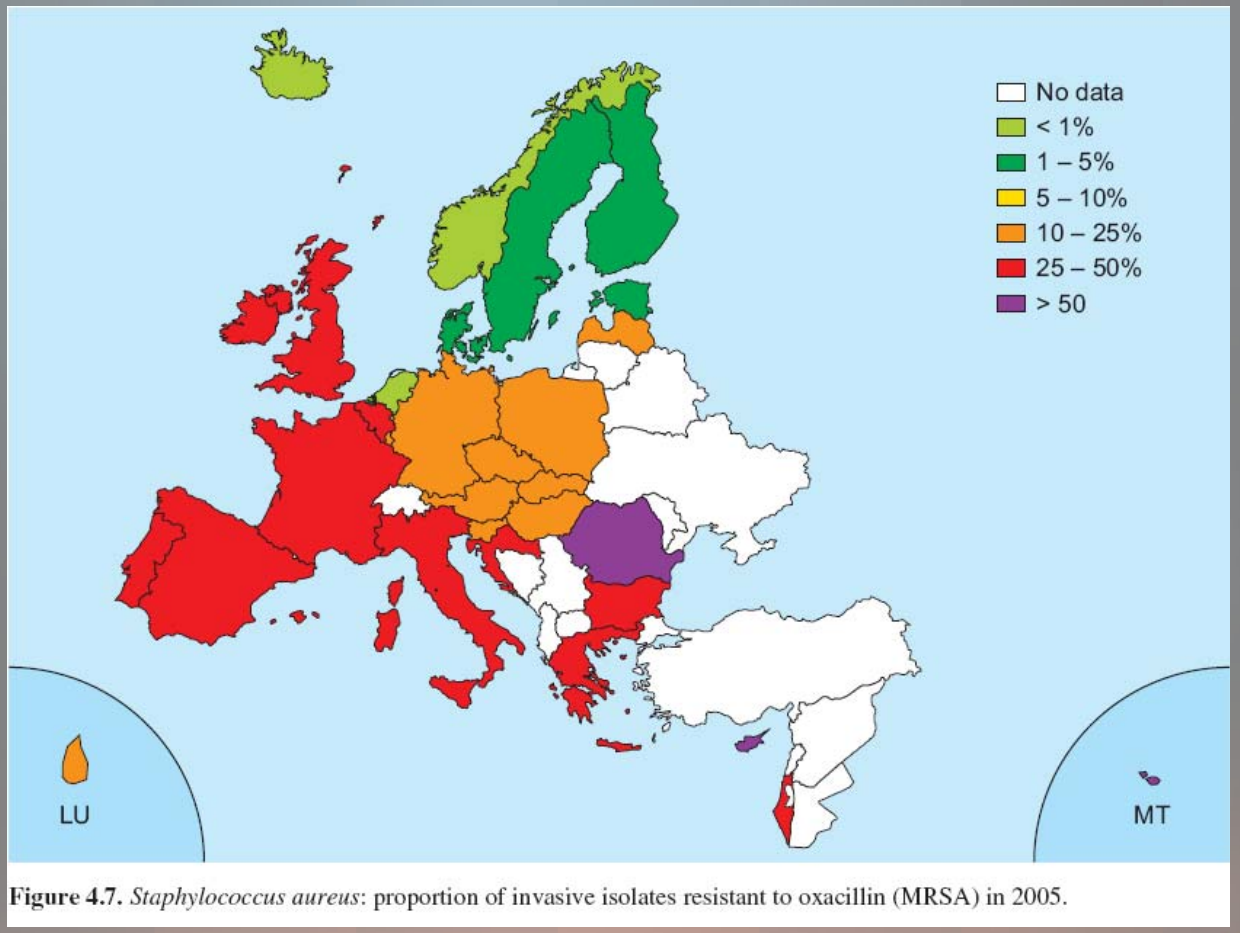


Figure 4.7. *Staphylococcus aureus*: proportion of invasive isolates resistant to oxacillin (MRSA) in 2005.

EARSS, 2006

DUTCH HEALTH CARE

Dutch Risk Factors

- Prior carriage
- Importation from foreign hospitals
- Chronic/persistent skin conditions

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVES:

1) Should we adopt a "search and destroy" strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA a problem worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

* Colonization vs. infection: Should we attempt to eradicate one or both?
* Prevention of acquisition: There are choices better than eradication…
* Risk factors for acquisition: Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA: What are the tools for eradication?
* Eradication regimens: What works?

A SPECTRE IS HAUNTING EUROPE

* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

THE DUTCH METHOD

Routine surveillance

Risk stratification for patients and providers

Strict isolation protocols

Decolonization

THE DUTCH METHOD

Categories of Patient and Caretaker Carriage	
1: proven MRSA carrier	Current cultures with MRSA
2: high risk of being a carrier	Patients receiving care in a foreign hospital (for more than 24hrs, less than 2 months before admission) Foreign patients receiving dialysis Patients from a facility with ongoing MRSA epidemic Patients with contact of unexpected MRSA carrier Patients who are category 1, with treatment for carriage without proven negative cultures Children who are adopted People who have contact with pigs Staff who have unprotected contact with MRSA carriers

Infection Prevention Working Party 2007

THE DUTCH METHOD

Categories of Patient and Caretaker Carriage

3: moderately elevated risk of being a carrier	Patients in their first year following MRSA eradication (with negative cultures) Dutch patients receiving hemodialysis abroad Patients cared for in a foreign hospital with persistent risk factors (skin lesions, chronic respiratory or urinary tract infection) People who come in close contact with live veal calves (at veal calf farms) Staff who have had protected contact with MRSA carriers Staff who have worked in a foreign hospital (for more than 24hrs, less than 2 months prior) Staff who regularly work at a foreign hospital, or who escort patients across Dutch borders Staff who have been carriers (with current negative cultures) within one year of present
4. no elevated risk of being a carrier	Patients who have been cared for in a foreign hospital more than 2 months ago (without persistent lesions) Staff who have been successfully eradicated more than a year prior Staff who have had negative cultures after unprotected contact with MRSA carriers

Infection Prevention Working Party 2007

THE DUTCH METHOD

Measures Taken to Limit Spread of MRSA, Based on Patient Category	
Category 1 Category 2	Care provided in strict isolation Providers must wear surgical mask, cap, coat with long sleeves and cuffs Care provided by fewest number of providers Staff with skin disorders (eczema or psoriasis) excluded from contact with patients A list of staff who have contact with the patient is kept
Category 3	Screening cultures on admission “Restraint should be exercised with regard to transfer, examination and treatment of the patient until results of the cultures are known.” Patient with cultures positive for MRSA are assigned to category 1 Patient with cultures negative for MRSA are assigned to category 4
Category 4	No additional measures

Infection Prevention Working Party 2007

MRSA: We Don't Want It, But Can We Eradicate It?

OBJECTIVES:

1) Should we adopt a "search and destroy" strategy to eradicate MRSA?

MRSA: (NOW NO LONGER JUST A) NOSOCOMIAL INFECTION

* Prevalence and severity: Are sequelae of MRSA a problem worth solving?
* Escape from the institution: What are the attributes of the organism warranting consideration?

AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

* Colonization vs. infection: Should we attempt to eradicate one or both?
* Prevention of acquisition: There are choices better than eradication…
* Risk factors for acquisition: Should we focus eradication efforts on a specific population?
* Treatment modalities for MRSA: What are the tools for eradication?
* Eradication regimens: What works?

A SPECTRE IS HAUNTING EUROPE

* Dutch health care setting: Is the Dutch setting more or less conducive to eradication?
* The Dutch method: What methodology do the Dutch use?
* Search and destroy: What is the evidence?

SEARCH AND DESTROY

SHOULD WE ADOPT A "SEARCH AND DESTROY" STRATEGY?

1) Increasing prevalence; likely significant impact on health and cost
2) Characteristics of HA-MRSA and CA-MRSA
3) Colonization and infection
4) Prevention: in combination with eradication
4) At risk populations as well as the general population
5) Eradication regimes require further research
6) Limitations of the American healthcare setting
7) Established protocols and recommendations

SEARCH AND DESTROY

What we didn't cover, but may play a role:

- Evidence (and non-compliance) for handwashing
- Complicated (and somewhat controversial) topic as antibiotic use driving resistance, as a risk factor for MRSA, and what potential benefit the Dutch derive from a restrictive prescribing policy.
- Role of environmental reservoirs
- Role of zoonotic reservoirs
- MRSA in long-term care facilities
- A serious cost-benefit analysis
- Potential sequelae for patient care (see Stelfox, JAMA 2003 290:1899-1905)
- Britney: a psychoanalysis case report

MRSA: We Don't Want It, But Can We Eradicate It?