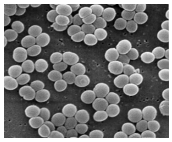
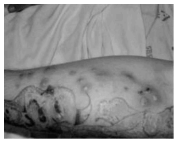
Do Staphylococcal Decolonization Strategies Work?
Dr. Andrew Simor, University of Toronto
A Webber Training Teleclass

Do Staphylococcal Decolonization Strategies Work?

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Sunnybrook Health Sciences Centre
University of Toronto, Toronto, ON

Hosted by Nicole Kenny

I have no disclosures to make with regards to this presentation.

Objectives

- to understand the rationale for staphylococcal decolonization
- to review evidence for decolonization as a strategy for staphylococcal infection prevention
- to consider recommendations for *S. aureus* decolonization

S. aureus Colonization

- major ecologic niche is the anterior nares
- other sites may include pharynx, axillae, perineum, skin lesions or wounds

Prevalence of *S. aureus* Nasal Colonization, 2003-04

	S. aureus	MRSA
Prevalence (%)	28.6	1.5
Estimated no. (in millions)	78.9	4.1

National Health and Nutrition Examination Survey (NHANES) 2001-2004. Gorwitz, J Infect Dis 2008

S. aureus Nasal Carriage

Carriage	% (range)
Persistent	20 (12-30)
Intermittent	30 (16-70)
Non-carriers	50 (16-69)

Kluytmans, Clin Microbiol Rev 1997; Wertheim, Lancet Infect Dis 2005

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S. aureus Colonization Risk Factors

- chronic skin conditions (atopic)
- diabetes mellitus (insulin)
- dialysis
- IVDU
- HIV

Significance of *S. aureus* Nasal Carriage

Nasal carriage of *S. aureus* is a risk for infection in hospital (usually same strain):

- nosocomial bacteremia (RR 30; 95% CI 2.0-4.7) (von Eiff, NEJM 2001; Wertheim, Lancet 2004)
- BSI, exit site infection in dialysis patients (Luzar, NEJM 1990; Kluytmans, ICHE 1996)
- SSI (2-9 X increased risk) (Kluytmans, JID 1995; Perl, NEJM 2002; Kalmeijer, CID 2002)
- ICU-acquired infection (2-5 X increased risk) (Honda, ICHE 2010)

Significance of MRSA Colonization

Colonization with MRSA associated with a greater risk of subsequent infection:

- Nasal carriers of MRSA 3.9 times more likely to develop nosocomial staphylococcal bacteremia than were MSSA carriers (Pujol, Am J Med 1996)
- MRSA colonization at ICU admission associated with higher risk of ICU-acquired *S. aureus* (MRSA) infection; RR 4.1 (Honda, Infect Control Hosp Epidemiol 2010)

Risk of MRSA Colonization Becoming an Infection

- 60 of 209 (29%) adults with newly identified colonization developed a subsequent MRSA infection during 18 months of follow-up (Huang, CID 2003)
- 8 of 38 (21%) with newly identified colonization developed MRSA infection in 1 year of follow-up (Davis, CID 2004)

Decolonization

treatment to eradicate staphylococcal carriage

S. aureus Decolonization

Topical Agents
- mupirocin
- bacitracin
- triclosan
- chlorhexidine
- retapamulin
- lysostaphin
- tea tree oil
- bacterial interference *S. aureus* 502A

Systemic Agents
- rifampin
- TMP/SMX
- ciprofloxacin
- tetracyclines
- novobiocin
- vancomycin

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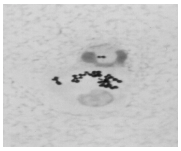
Reasons to Consider Staphylococcal Decolonization

1. to prevent infection in a colonized patient (MSSA/MRSA)
2. to prevent transmission (primarily MRSA) to others

MRSA Decolonization

short-term
surgery
? ICU



long-term
dialysis
recurrent SSTI
infection control

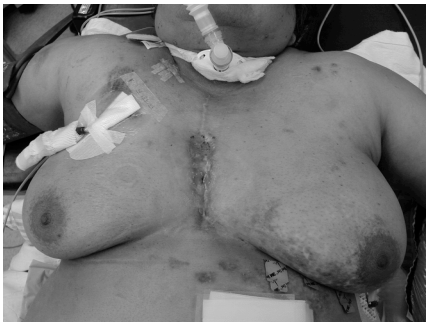
S. aureus Decolonization

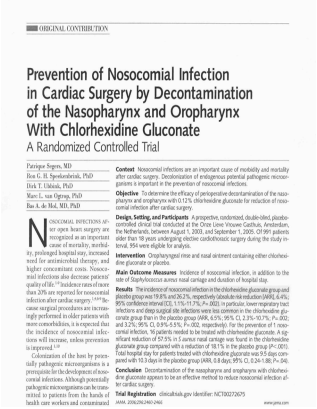
- surgical patients
- non-surgical patients
- ICU patients
- dialysis patients
- recurrent SSTIs
- MRSA decolonization

Mupirocin for *S. aureus* Decolonization in HCWs

MSSA
Reagan, Ann Intern Med 1991
Doebbeling, Clin Infect Dis 1993
Fernandez, J Antimicrob Chemother 1995
MRSA
Casewell, J Antimicrob Chemother 1986
Scully, Arch Intern Med 1992

Staphylococcal Decolonization – Surgical Patients





ORIGINAL CONTRIBUTION

Prevention of Nosocomial Infection in Cardiac Surgery by Decontamination of the Nasopharynx and Oropharynx With Chlorhexidine Gluconate
A Randomized Controlled Trial

- ↓ *S. aureus* carriage in CHG-treated group
- ↓ nosocomial infections, esp. LRTI and deep SSI (20% vs 26%; ARR 6.2%; 95% CI 1.1-11.7; p=0.002)

Segers, JAMA 2006

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Mupirocin Surgical Prophylaxis

- in most RCTs, peri-operative mupirocin had no effect on SSI or *S. aureus* SSI rates
- 2 studies suggested decresed nosocomial *S. aureus* infections (SSI) in staphylococcal carriers treated with mupirocin
  (Perl, N Engl J Med 2002; Bode, N Engl J Med 2010)

Mupirocin Surgical Prophylaxis - RCTs

Reference;	All SSI (%)		*S. aureus* SSI (%)	
Surgery (No.)	mupirocin	placebo	mupirocin	placebo
[1] elective (3,864)	7.9	8.5	2.3	2.4
[2] orthopedic (614)	3.8	4.7	1.6	2.7
[3] G.I. (395)	14.5	10.9	2.1	4.6
[4] cardiac (263)*	13.8	8.6	3.8	3.2
[5] CV, GI, ortho(808)*			2.5	7.9

[1] Perl, NEJM 2002; [2] Kalmeijer, Clin Infect Dis 2002; [3] Suzuki, Br J Surg 2003; [4] Konvalinka, J Hosp Infect 2006; [5]Bode, N Engl J Med 2010

* all *S. aureus* carriers


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Preventing Surgical-Site Infections in Nasal Carriers of *Staphylococcus aureus*

Lonneke G.M. Bode, M.D., Jan A.J.W. Kluytmans, M.D., Ph.D., Heiman F.L. Wertheim, M.D., Ph.D., Diana Bogaers, I.C.P., Christina M.J.E. Vandenbroucke-Grauls, M.D., Ph.D., Robert Roosendaal, Ph.D., Annet Troelstra, M.D., Ph.D., Adrienne T.A. Box, B.A.Sc., Andreas Voss, M.D., Ph.D., Ingeborg van der Tweel, Ph.D., Alex van Belkum, Ph.D., Henri A. Verbrugh, M.D., Ph.D., and Margreet C. Vos, M.D., Ph.D.

- 2 Dutch hospitals, 808 pts with nasal *S. aureus* detected by real-time PCR
- Mupirocin + CHG body wash vs placebo X 5 days

Mupirocin Surgical Prophylaxis

808 surgical patients

441 Mup-CHG		367 placebo	RR (95% CI)
4 (0.9)	deep SSI	16 (4.4)	0.21 (0.07-0.62)
7 (1.6)	superficial SSI	13 (3.5)	0.45 (0.18-1.11)
6 (1.2)	other infection	3 (0.7)	

Bode, N Engl J Med 2010

Study Limitations

- real-time PCR for prompt initiation of intervention
- no MRSA (all MSSA)
- decreased *S. aureus* SSI rates, but no data on overall SSI rates

Bode, N Engl J Med 2010

Mupirocin to Prevent Infections in non-Surgical Patients (RCTs)

Reference (No.)	Patients	Infection rate (%) mupirocin	placebo
[1] (1,627)	colonized inpatients, the Netherlands	2.6	2.8
[2] (98)	MRSA inpatients, Geneva	1.5	2.8
[3] (127)	colonized LTCF, USA 50% MRSA	5	15

[1] Wertheim, Ann Intern Med 2004; [2] Harbarth, Antimicrob Agents Chemother 1999; [3] Mody, Clin Infect Dis 2003

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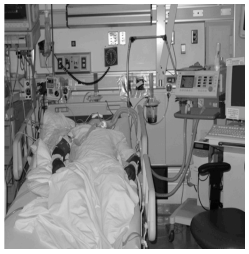
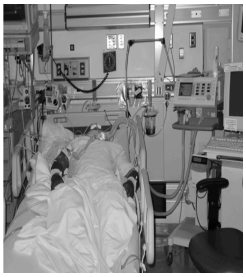
S. aureus Decolonization - ICU

- quasi-experimental before-after study, medical ICU; real-time PCR screening; mupirocin + CHG baths
- ICU-acquired *S. aureus* infections decreased: 3.5 to 1.3 per 1,000 pt-days (RR 0.37, 95% CI 0.14-0.90)



Fraser, Infect Control Hosp Epidemiol 2010

MRSA in the ICU



Prevalence of MRSA on admission to ICU[1]: 8% (range: 5-20%)

Rate of MRSA acquisition in ICU[2]: 5% (range: 2-12%)

[1] Lucet, Arch Intern Med 2003; Huang, J Infect Dis 2007; Ridenour, Infect Control Hosp Epidemiol 2007
[2] Warren Infect Control Hosp Epidemiol 2006; Climo, Crit Care Med 2009; Marshall, Infect Control Hosp Epidemiol 2009

MRSA Decolonization in the ICU

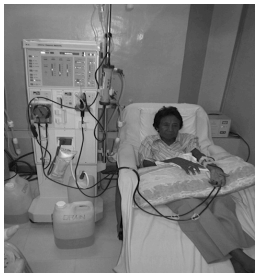
- Before-after observational studies in ICUs and NICUs using mupirocin and/or CHG body wash have shown reduced MRSA infection rates
  (Muller, Crit Care 2005; Sandri, Infect Control Hosp Epidemiol 2006; Ridenour, Infect Control Hosp Epidemiol 2007; Milstone, Infect Control Hosp Epidemiol 2010; Batra, Clin Infect Dis 2010)

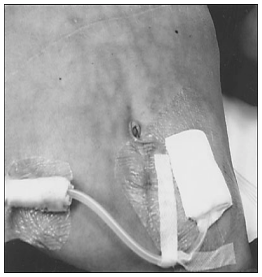
MRSA Decolonization

- A cluster randomized trial to prevent MRSA infections in ICUs (45 hospitals):
  - ASC + Contact Precautions
  - ASC + Precautions + Decolonization
  - Universal decolonization

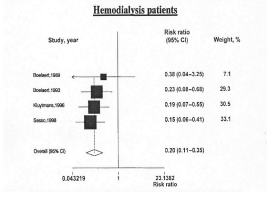
Platt, Medical Care 2010

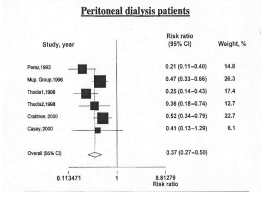
Staphylococcal Decolonization - Dialysis Patients





Meta-analysis: Mupirocin Prophylaxis in Dialysis Patients





↓ 78% *S. aureus* BSI ↓ 66% *S. aureus* peritonitis

Tacconelli, Clin Infect Dis 2003

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S. aureus Decolonization in Hemodialysis (RCTs)

Reference (No.)	Treatment	*S. aureus* infections	RR (95% CI)
[1] (44)	RFP + Bac None	11.1% 46.2%	0.61 (0.41-0.90)
[2] (34)	Mupirocin Placebo	1.0/100 mos 4.1/100 mos	0.24 (0.03-1.9)
[3] (36)	Mupirocin None	0.35/1000days 5.95/1000days	0.06 (0.01-0.46)

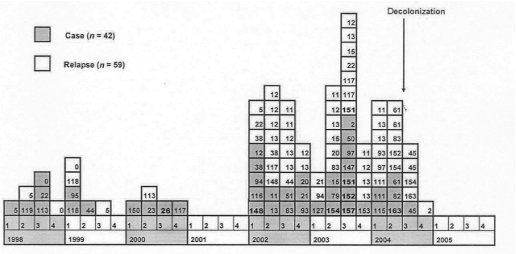
[1] Yu, N Engl J Med 1986; [2] Boelaert, Nephrol Dial Transplant 1989;
[3] Sesso, J Am Soc Nephrol 1998

S. aureus Decolonization in Peritoneal Dialysis (RCTs)

Reference (No.)	Treatment	*S. aureus* infections	RR (95% CI)
[1] (267)	Mupirocin Placebo	0.1/100 mos 0.2/100 mos	0.66 (0.47-0.92)
[2] (133)	Mupirocin Gentamicin	0.52/pt-yr 0.34/ pt-yr overall peritonitis rates	*P*=0.03

[1] The Mupirocin Study Group, J Am Soc Nephrol 1996;
[2] Bernardini, J Am Soc Nephrol 2005

Use of Mupirocin + Antiseptics in a Furunculosis Outbreak due to Methicillin-Susceptible *S. aureus* (PVL+)



Wiese-Posselt, Clin Infect Dis 2007

Failure of Mupirocin Decolonization in a CA-MRSA Outbreak

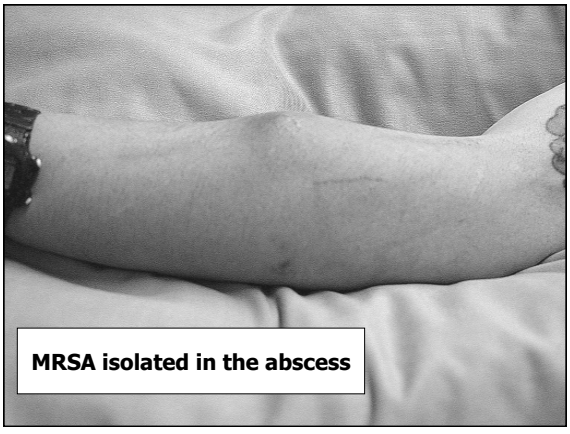
- CA-MRSA outbreak among members of a high school football team
- only 36% compliance with recommended treatment
- mupirocin failed to prevent subsequent infections

Rihn, Pediatr Infect Dis J 2005

Mupirocin to Prevent Recurrent SSTIs (RCTs)

Reference (No.)	Patients	Infection rate (%)	
		mupirocin	placebo
[1] (34)	MSSA; monthly treatment X 1 yr	26 infections	52 infections
[2] (134)	CA-MRSA, military recruits	10.6	7.7

[1] Raz, Arch Intern Med 1996; [2] Ellis, Antimicrob Agents Chemother 2007



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MRSA Decolonization

- many observational studies with mupirocin or other agents, as part of infection control measures in hospitals and nursing homes (Hill, J Antimicrob Chemother 1998; Cederna, ICHE 1990; Strausbaugh, ICHE 1992; Sandri, ICHE 2006; Ridenour, ICHE 2007; Bowler, ICHE 2010)
- retrospective observational study, 3 Chicago hospitals, MRSA screening on admission, decolonization at MD's discretion: transient eradication of MRSA, but no reduced risk of subsequent infection (Robicsek, ICHE 2009)

MRSA Decolonization

"…there is insufficient evidence to support use of topical or systemic antimicrobial therapy for eradicating MRSA"

Loeb, Cochrane Database Syst Rev 2003

Reasons for Failure to Eradicate MRSA Colonization

- use of drugs with marginal activity, or that induce resistance (ciprofloxacin, fusidic acid)
- (Peterson, Arch Intern Med 1990; Chang, Diagn Microbiol Infect Dis 2000)
- intranasal therapy ineffective for GI reservoir of the organism (Boyce, J Clin Microbiol 2005)
- Host factors (skin lesions, catheters, medical devices, comorbidities

Variables Associated with MRSA Persistence/Re-colonization

Variable	Risk	95% CI	P value
MRSA at >1 site[1]	HR=1.73	1.04-2.87	0.035
Fluoroquinolone exposure	HR=1.81	1.01-3.26	0.048
Mupirocin-resistance[2]	RR=9.37	2.76-31.87	0.0003
Decolonization therapy	RR=0.12	0.04-0.36	0.0002
Residence in a LTCF[3]	OR=1.8	1.1-3.2	0.03
Decubitus ulcer	OR=2.3	1.2-4.4	0.01
Mupirocin-resistance	OR=4.1	1.6-10.7	0.003

[1] Harbarth, Clin Infect Dis 2000; [2] Simor, Clin Infect Dis 2007;
[3] Robicsek, Infect Control Hosp Epidemiol 2009

Mupirocin Resistance in *S. aureus*

- mupirocin resistance rates increasing globally, especially in MRSA (Cookson, J Antimicrob Chemother 1998; Yoo, Antimicrob Agents Chemother 2006)
- resistance is associated with extensive mupirocin use (Miller, ICHE 1996; Vasquez, ICHE 2000; Vivoni, ICHE 2005)
- resistance (high-level) associated with treatment failure (Cookson, J Antimicrob Chemother 1998; Walker, ICHE 2003; Simor, Clin Infect Dis 2007)

MRSA Decolonization

Can decolonization with mupirocin be improved by adding?

- antiseptic body wash (CHG)
- systemic antibiotics (Simor, Clin Infect Dis 2007)
- decolonization of household contacts or hot water laundering of clothes and bedding

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Decolonization Practices among IDSA Members (1)

- IDSA Emerging Infections Network survey, April 2005, to determine decolonization use (483 [57%] responses)
- 17% routine pre-op decolonization of *S. aureus* carriers (83% cardiac surgery); 94% with mupirocin
- 20% MRSA decolonization for infection control (47% in outbreaks; 38% all colonized); 92% with mupirocin

West, Infect Control Hosp Epidemiol 2007

Decolonization Practices among IDSA Members (2)

- 85% used decolonization for patients with recurrent furunculosis due to CA-MRSA
- most used mupirocin + antiseptic body wash; 55% also used oral antimicrobial agent
- no data on outcome/efficacy

West, Infect Control Hosp Epidemiol 2007

MRSA Decolonization in European ICUs and Surgical Units

- routine antiseptic washing (eg. chlorhexidine) in 66%
- routine decolonization with mupirocin in 63%

Hansen, Infection 2010

S. aureus Decolonization Recommendations

- no routine decolonization pre-op or in nonsurgical patients; perhaps consider in surgical patients known to be *S. aureus* carriers
- consider in dialysis patients, but risk of mupirocin resistance in the long-term

S. aureus Decolonization Recommendations

- possibly useful in patients with recurrent skin/soft tissue infection (need more data for CA-MRSA)
- mupirocin susceptibility testing should be done prior to use for decolonization
- MRSA as an infection control measure needs to be studied; consider in outbreaks or select patients

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