


Prevention of Methicillin-Resistant Staphylococcus Aureus

Size of the Problem and Mechanisms of Control

Health Watch USA Conference
Nov 7, 2014


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MDROs Significance

- Infections from MDROs have twice the mortality rate as other Healthcare Associated Infections (HAIs)
- The percentage of these infections is growing.

From the CDDEP – HW USA Presentation, Samantha Gandra, March 16, 2014





Healthcare Associated Infections

Many Healthcare Associated Infections are Multi-Resistant Drug Organisms

- Affects 1 in 25 Hospitalized Patients
- Top 10 Cause of Death in the United States
<http://www.ahrq.gov/news/newsletters/research-activities/aug11/0811RA3.html>


Nationally, deaths from HAIs equal more than one Boeing 767 crashing every day.

MRSA – How Are We Doing

Data conflicting on meeting goals – No Uniform Reporting System:

- H-Cup Data (USA Today, Dec 2013) – No {460,000 Hospitalizations involving MRSA, 23,000 Deaths}
- UHC (ICHE, 2013) – No "The number of hospital admissions for any MRSA infection per 1,000 hospital admissions overall increased during 2003–2008"
- EIP (JAMA, 2010, 2013) – Yes {Overall 21% decrease, Hospital Onset a 46% decrease}
- NHSN (Dept. HHS, 2014) – No {Data from 1/1/2013 to 3/31/2013: SIR is 1.05, Base Data 2010}
- Pediatric Survey (Pediatrics, 2013) – No "there were no significant reductions in health care-associated MRSA infections in children."



MDROs Significance & HAIs


Account for 20% of HAIs

20% MDRO breakdown

Organism	Percentage
MRSA	8.5%
ESBL	6%
VRE	3%
OTHER	2%
CRE	0.5%

- MDRO - Defined as non-susceptibility to at least one agent in three or more antimicrobial categories


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Methicillin-Resistant Staphylococcus Aureus - MRSA

Proportion of MRSA among S. aureus blood isolates in Europe and North America - 2012

From the CDDEP – HW USA Presentation, Samantha Gandra, March 16, 2014



Methicillin-Resistant Staphylococcus Aureus - MRSA

In Northern Europe – Less than 5% of Staph Cultures are MRSA Positive.

In the United States – 50% of Staph Cultures are MRSA Positive.

In the Region Kentucky Resides – Almost 70% of Staph Cultures are MRSA Positive.

outpatient

2009 EXTENDING CARE

Strong Research In Support of Surveillance

Union of Concerned Scientists:
"Downplaying evidence and playing up false uncertainty"

MRSA – Reporting Requirements

- MRSA is reported for bloodstream infections (lab event).
-- The picture to the right would not be reportable.

Strong Research In Support of Surveillance

Only two major studies with arguably poor designs. STAR*ICU and the JAMA-Swiss Study found Surveillance did not work.(1)

Compared to numerous before & after studies (1) Plus, well controlled studies from Northwestern University (2), Geneva, Switzerland (3) and Sevilla, Spain (4) which found surveillance to be vital in the prevention bundle.

- Kavanagh KT, et al. PMID 24100502
- Robicsek A, et al. PMID 18347349
- Lee AS, et al. PMID 24056477
- Rodriguez-Baño J, et al. PMID 20524852

MRSA Bacteremia in Kentucky

SIR For MRSA Bacteremia – NHSN Data

Acquisition Dates 1/1/2013 to 9/30/2013

KY

Kentucky has the 4th highest incidence in the 50 States.

MRSA Infection Reduction

Reduction In MRSA Infections Well Controlled Studies (Interventions which use surveillance)	No Effect on MRSA Infections (Interventions which used surveillance, but had anomalies with Interventions)
Robicsek A, et al. Ann Intern Med 2008. Mar. 18, 148(6): 409-18	Harbarth S. et al. JAMA. 2008, Mar. 12; 299(10):1149-57
Rodriguez-Baño J, et al. Infect Control Hosp Epidemiol. 2010 Aug;31(8):786-95	Huskings WC, et al. NEJM. Apr. 2011; 364; 1407-1428.
Lee AS, et al. BMJ Open. 2013; 3: e00312	
Reduction In MRSA Infections Before and After Studies (Interventions which use surveillance)	Concluded Surveillance Not Better Than Chlorhexidine
Jain R, et al., NEJM. Apr. 2011; 364: 1419-1430	Huang SS, et al. NEJM. June 2013; 368:2255-2265
Almost 40 other studies.	

MRSA: Robiseck A, et al.

- Well Controlled Study (surveillance, decolonization and contact isolation).
- MRSA decreased by:
 - 36.2% from baseline to ICU Surveillance.
 - 69.6% from baseline to Universal Surveillance.

Robiseck A, et al., Ann Intern Med 2008. Mar. 18, 148(6): 409-18



MRSA: Lee, et al.

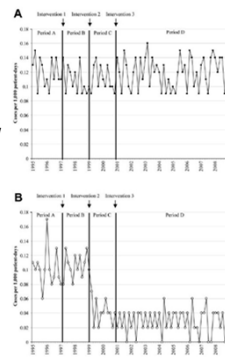
- "In surgical wards with relatively low MRSA prevalence, a combination of enhanced standard and MRSA-specific infection control approaches was required to reduce MRSA rates. *Implementation of single interventions was not effective*, except in clean surgery wards where MRSA screening coupled with contact precautions and decolonisation was associated with significant reductions in MRSA clinical culture and infection rates."

Lee AS, et al., BMJ Open. 2013; 3: e00312



MRSA: Rodriguez-Bano, et al.

- To the right is a drop in MRSA bacteremia observed by Rodriguez-Bano, et al. (Period C represents the time period when active MRSA surveillance, & decolonization in patients and healthcare workers were performed in units where there was MRSA transmission. A: No decrease in MSSA bacteremia, B: Decrease found in MRSA Bacteria.



Rodríguez-Baño J, et al., Infect Control Hosp Epidemiol. 2010 Aug;31(8):786-95



MRSA: The VA Experience

- VA Nursing Homes – 36% decrease in MRSA.
- VA Study – Jain, NEJM, Apr. 14, 2011
 - Decrease of 45% in non-ICU Patients.
 - Decrease of 62% in ICU Patients.

Jain R, et al., NEJM. Apr. 2011; 364: 1419-1430



MRSA: Lee, et al.

- "In clean surgery wards, strategy 2 (*MRSA screening, contact precautions and decolonisation*) was associated with decreasing rates of MRSA clinical cultures (15% monthly decrease, aIRR 0.85, 95% CI 0.74 to 0.97) and MRSA infections (17% monthly decrease, aIRR 0.83, 95% CI 0.69 to 0.99).
- "... no evidence that enhanced HH (hand hygiene) promotion was effective."

Lee AS, et al., BMJ Open. 2013; 3: e00312




MRSA: The VA Experience

- Among VA patients in intensive care units (ICU) between 2007 and 2012, healthcare-associated MRSA infection rates dropped 72 percent—from 1.64 to 0.46 per 1,000 patient days. Infection rates dropped 66 percent—from 0.47 to 0.16 per 1,000 patient days—for patients treated in non-ICU hospital units.


News Release: VA Sharply Reduces Drug-Resistant Staph Infections in Hospitalized Veterans October 8, 2014
<http://www.va.gov/opa/pressrel/pressrelease.cfm?id=2642>



No Reduction Associated With Surveillance



Research for The Effectiveness of Chlorhexidine Is Controversial




MRSA: Harbarth, et al.

- Prior to surgery over half of the known MRSA carriers were not given antibiotics effective against MRSA and because of delays and emergency intervention, 31% of the carriers were identified as MRSA carriers only after surgery.
- Of the patients who developed a MRSA infection and were known carriers prior to surgery, only 43% received prophylaxis against MRSA and almost 60% did not receive optimal decolonization of MRSA prior to surgery.
- 10 MRSA Carriers, known prior to surgery, did not receive MRSA prophylaxis and developed an MRSA Infection.

Harbarth S. et al., JAMA. 2008, Mar. 12; 299(10):1149-57


This study effectively was negated by Lee, et al. Harbarth, S. was the corresponding author of this study.



MRSA: Huang, et al.

- Found a significant decrease in MRSA clinical cultures associated with daily bathing with chlorhexidine.
- "Changes in important metrics: According to www.clinicaltrials.gov, 6 months after the study completion date, the registry's records for the study were updated by adding a measure for all-pathogen bloodstream infections and eliminating the measures for central line- associated bloodstream infections and MRSA urinary cultures."
- "The all-pathogen bloodstream infection (primarily skin commensal organisms) and nosocomial MRSA clinical culture measures showed a statistically significant improvement over the control. MRSA bacteremia reduction was not significant."


Huang SS, Septimus E, Kleinman K, Moody J, Hickok J, Avery TR, Lankiewicz J, Gombosev A, Terpstra L, Hartford F, Hayden MK, Jernigan JA, Weinstein RA, Fraser VJ, Haffnerffer K, Cui E, Kaganov RE, Lolans K, Perlin JB, Platt R; the CDC Prevention Epicenters Program, the AHRQ DECIDE Network and Healthcare-Associated Infections Program. Targeted versus Universal Decolonization to Prevent ICU Infection. N Engl J Med. 2013 May 29; [Epub ahead of print] PMID: 23718152.



MRSA: Huskins, et al.

- "... when contact precautions were specified, gloves were used for a median of 82% of contacts, gowns for 77% of contacts, and hand hygiene after 69% of contacts,"
- Results of admission MRSA cultures took 5 days to get back.

Huskins WC, et al., NEJM. Apr. 2011; 364; 1407-1428.




Change in Metrics Raise Concerns

Changes to NCT00980980 on 2012_06_19
Type of info changed: Protocol, Misc.

	Before (Updated 2011_10_24)	After (Updated 2012_06_19)
1	<clinical_study>	<clinical_study>
2	<measure> Nosocomial MRSA Bloodstream and Urinary Cultures	<measure> MRSA Bloodstream Infection
3	<measure>	<measure>
4	<measure> Routinely reported central line-associated blood stream infections (CLABSIs)	<measure> ICU-attributable All-pathogen Bloodstream Infection
5	<measure>	<measure>
6	<time_frame> 18 months	<time_frame> 18 months
7	<time_frame>	<time_frame>
	<last_release_date> 2011-10-24	<last_release_date> 2012-06-19
	<last_release_date>	<last_release_date>
	<clinical_study>	<clinical_study>

From www.clinicaltrials.gov



MRSA: Derde, et al.

- Derde et al. (Lancet, 2014), also observed a significant decrease in MRSA acquisitions with improved hand hygiene and unit-wide daily chlorhexidine body washes protocols.
There was not a significant decrease in vancomycin-resistant Enterococcus or Enterobacteriaceae acquisitions .
- There is also concern regarding the promotion of bacterial resistance. *Disturbingly, Derde et al. reported a 13 to 14% incidence of MRSA resistance to chlorhexidine.*



Effectiveness of CHX

- Maiwald and Chan could find *"no evidence that chlorhexidine without alcohol was effective"* and that many trials compared chlorhexidine plus alcohol (two antiseptics) to povidone-iodine alone (one antiseptic) with some trials then attributing the clinical efficiency to chlorhexidine alone.

Maiwald M, Chan ES. Pitfalls in evidence assessment: the case of chlorhexidine and alcohol in skin antiseptics. *J Antimicrob Chemother.* 2014; **69**(8):2017-21. doi: 10.1093/jac/dku121. Epub 2014 Apr 28.



Effectiveness of CHX

- Climo, et al. compared reduction in primary bloodstream infections with daily bathing using 2% chlorhexidine gluconate washcloths to daily bathing with nonantimicrobial washcloths.
- They did not observe a decrease in MRSA or VRE bloodstream infections in the chlorhexidine group compared to the nonantimicrobial washcloth group.
- They did observe a decrease in CLABSIs and multi-resistant drug organism acquisitions, *although the decrease for MRSA acquisitions did not reach statistical significance (p=0.29). The largest decrease in bloodstream infections was for coagulase-negative staphylococci.*

Climo MW, Yokoe DS, Warren DK, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. *N Engl J Med.* 2013; **368**(6):533-42. doi: 10.1056/NEJMoa1113849.

Chlorhexidine Resistance

- The recent observation that MRSA strains carrying the antiseptic resistance genes *qacA/B* can be clinically resistant to chlorhexidine raises a note of caution against its unfettered use. The dissemination of chlorhexidine-resistant MRSA would have implications for the decolonization of individual patients and for preventing transmission.

Edgeworth JD. Has decolonization played a central role in the decline in UK methicillin-resistant *Staphylococcus aureus* transmission? A focus on evidence from intensive care. *J Antimicrob Chemother.* 2011 Apr;66 Suppl 2:i141-7. doi: 10.1093/jac/dkq325. Epub 2010 Sep 18.



Effectiveness of CHX

- Rotter, et al. (1988) who found that preoperative bathing with chlorhexidine did not reduce surgical infections compared to bathing with a detergent.

Rotter ML, Larsen SO, Cooke EM, et al. A comparison of the effects of preoperative whole-body bathing with detergent alone and with detergent containing chlorhexidine gluconate on the frequency of wound infections after clean surgery. The European Working Party on Control of Hospital Infections. *J Hosp Infect* 1988; **11**:310-320.

Multiple Studies Are Finding Reduced Susceptibility to Chlorhexidine

Organisms causing CLABSIs were more likely to have reduced chlorhexidine susceptibility in patients bathed daily with chlorhexidine,

Suwanarat N, et al. High prevalence of reduced chlorhexidine susceptibility in organisms causing central line-associated bloodstream infections. *Infect Control Hosp Epidemiol.* 2014 Sep;35(9):1183-6.

MRSA chlorhexidine resistance is an independent factor predictive of decolonization failure.

Lee AS, et al. Impact of combined low-level mupirocin and genotypic chlorhexidine resistance on persistent methicillin-resistant *Staphylococcus aureus* carriage after decolonization therapy: a case-control study. *Clin Infect Dis.* 2011 Jun 15;52(12):1422-30.



Research Indicates Daily Chlorhexidine Has a Risk of Worsening Bacterial Resistance

- Because Chlorhexidine is used externally it affects the entire microbiome of the facility.
- The extremely drug resistant strain of Klebsiella can develop reduced susceptibility to Chlorhexidine.

Naparstek L, et al. Reduced susceptibility to chlorhexidine among extremely-drug resistant strains of Klebsiella pneumoniae. J. Hosp. Infect. 2012. 81:15–19.



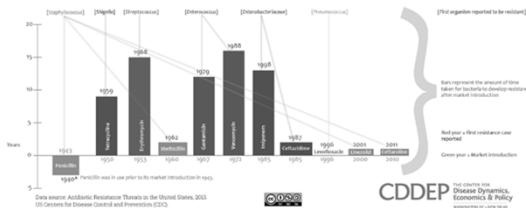
Preop MRSA Surveillance

- Harbarth S. et al. JAMA. 2008, Mar. 12; 299(10):1149-57 Found no effect but serious flaws.
- Lee AS, et al. BMJ Open. 2013; 3: e00312 Was a well controlled multi-national study which found a beneficial effect. Harbarth, S was the corresponding author of this study.
- Multiple other studies most of which did not control for secular trends (were before and after studies) also found a beneficial effect.



Chlorhexidine Resistance

First reported cases of bacterial resistance against key antibiotics



Preop MRSA Surveillance

- MRSA Carriers Have a Higher Risk for Developing MRSA Infections.
- Screening determines the length of preoperative decolonization. (One vs. five days of chlorhexidine.)
- Type of Antibiotic Used Pre-Op May Depend Upon Carrier State.



Allegations of Industrial Influence

- Questions of Conflict-of-Interest and Industrial Influence first arose around a major study published in the NEJM (2010) regarding the effectiveness of a chlorhexidine-Alcohol antiseptic. (1,2)
- This study was part of a \$40 million Dept. of Justice Settlement with CareFusion and an alleged 11 million dollar kickback. (3)

1. Brian J. Influential patient safety board cut ties with doc before CareFusion kickbacks case. Mass Device. Jan. 22, 2014.
2. Allen M. Hidden Financial Ties Rattle Top Health Quality Group. Propublica. Jan. 28, 2014
3. Department of Justice. CareFusion to Pay the Government \$40.1 Million to Resolve Allegations That Include More Than \$11 Million in Kickbacks to One Doctor. Jan. 9, 2014.



UK - National Health Service

The United Kingdom's National Health Service's best practices include MRSA screening of:

- Orthopaedics, cardiothoracic and neurosurgical patients;
- Emergency orthopaedic and trauma admissions;
- Critical care admissions;
- All elective surgical patients;
- Previous MRSA carriers; oncology/chemotherapy patients;
- Renal patients;
- Patients admitted from high risks settings such as nursing homes and care homes and;
- All emergency admissions.




http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_063187.pdf

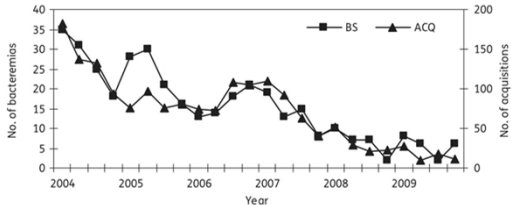
UK - National Health Service

“... the logical conclusion of risk factor assessments and the results of modelling studies is that the most appropriate approach to the reduction in MRSA carriage in the population, and resultant MRSA infections, is the universal screening of all admissions to hospital.”

Screening for Methicillin-resistant Staphylococcus aureus (MRSA) colonization. A strategy for NHS trusts: summary of best practices.
http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/p/rod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_063187.pdf



Comparison between trend reductions in MRSA bacteraemias and MRSA acquisitions at a single UK hospital.



Year	No. of bacteraemias (BS)	No. of acquisitions (ACQ)
2004	35	180
2005	25	120
2006	15	100
2007	20	110
2008	10	60
2009	5	40

Edgeworth J D J. Antimicrob. Chemother. 2011;66:ii41-ii47

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