

MRSA

Stephen Ritchie
s.ritchie@auckland.ac.nz

Chris, 52 years old

- extremely fit, Tongan NZer
- “injured” right hip when stepped down off his truck
 - advised to rest, naproxen
- the next day – excruciating pain, fever
 - also history of recurrent boils
 - CRP elevated 117
 - MRI hip : liposclerosing myxofibrous tumour
- later that day.... required ED resuscitation and ICU admission



Treatment

- Drain abscess
- antibiotics
 - MSSA, MRSA or both?
 - culture of MRSA
- femoral head necrosis/osteomyelitis
 - excision of femoral head
 - delayed implantation of THJR

What is MRSA?

S. aureus: a gram positive coccus, with a thick peptidoglycan cell wall

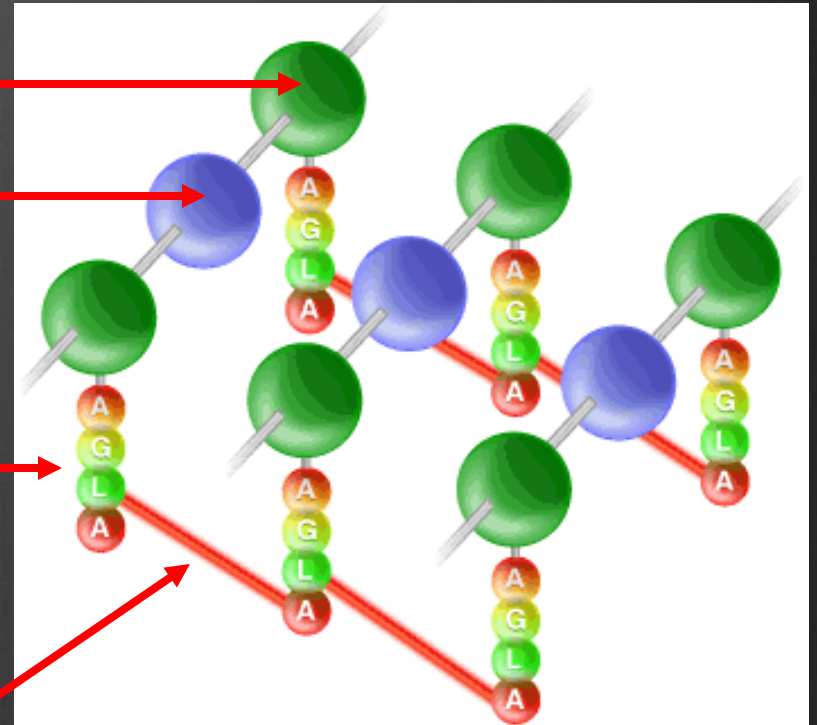
N-acetylmuramic acid (NAM)

N-acetylglucosamine (NAG)

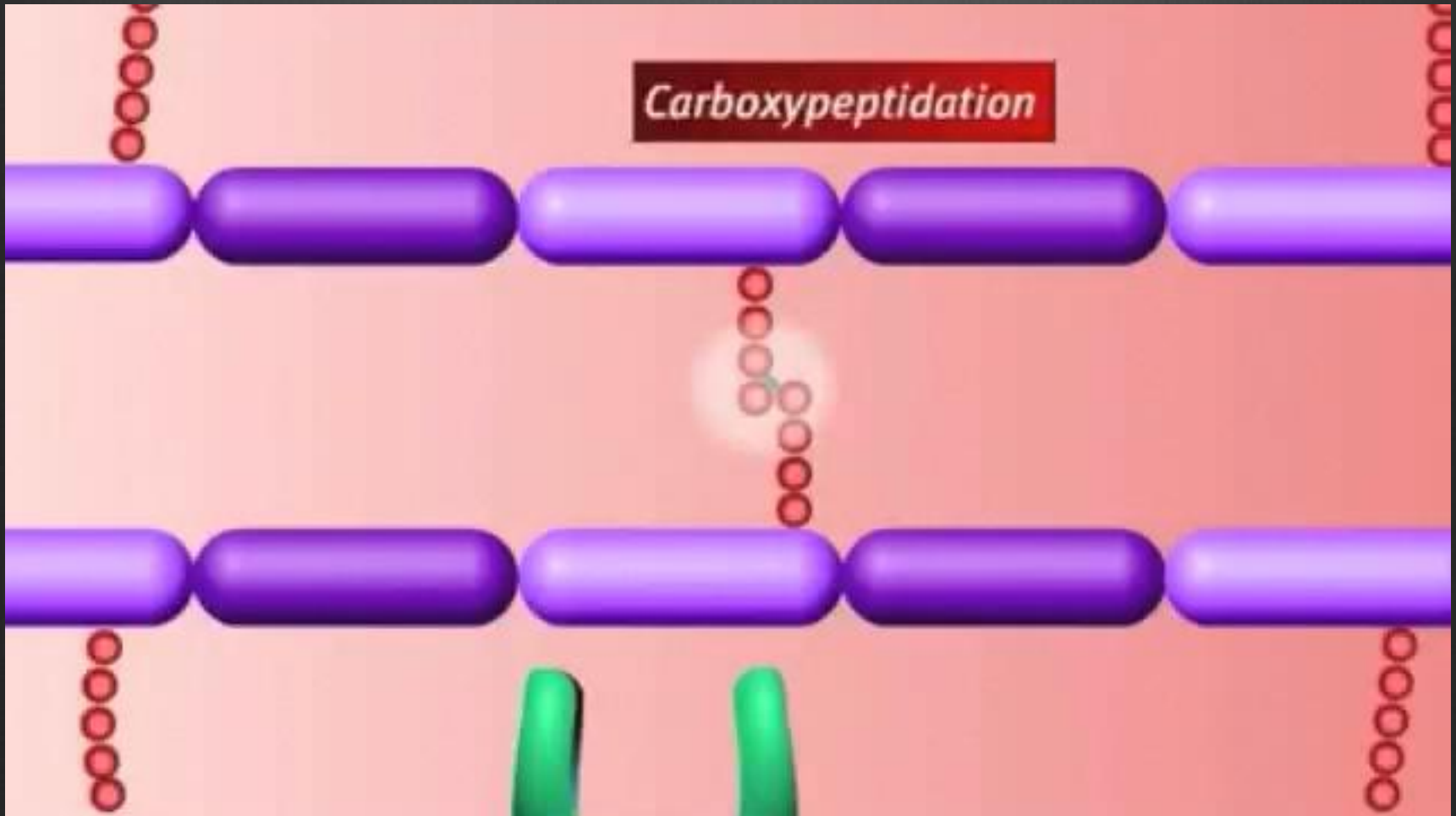
NAMs have peptide chains:
alanine, glutamine, lysine and alanine

cross-link terminal peptides
(lysine to terminal alanine)

TRANSPEPTIDASE

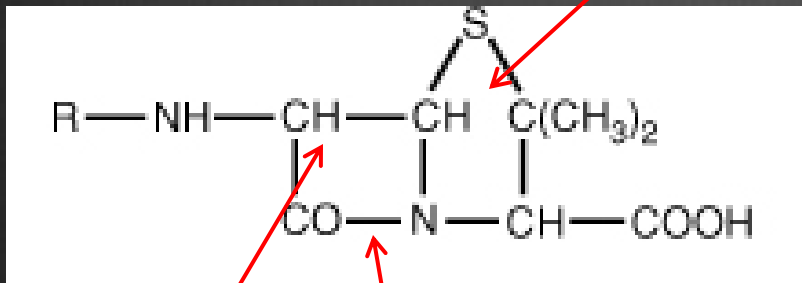


β -lactam resistance: *S. aureus*



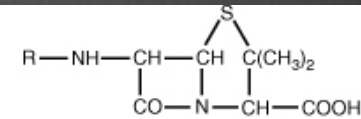
S. aureus - β lactamase

thiazolidine ring



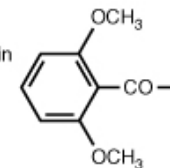
β lactam ring

87% of *S. aureus* produce β lactamase:
hydrolysis of β lactam ring

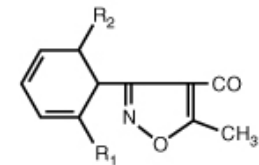
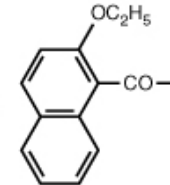


Structure of side chain R

Methicillin
2, 6, dimethoxyphenylpenicillin



Nafcillin
2-ethoxy-1-naphthylpenicillin



Oxacillin
3-phenyl-5-methyl-
4-isoxazolympenicillin

R ₂	R ₁
H	H

Cloxacillin
3-(2-chlorophenyl)-5-methyl-
4-isoxazolympenicillin

R ₂	R ₁
Cl	H

Dicloxacillin
3-(2, 6-fluorophenyl)
5-methyl-4-isoxazolympenicillin

R ₂	R ₁
Cl	Cl

Flucloxacillin
3-(2-chloro-6-fluorophenyl)
5-methyl-4-isoxazolympenicillin

R ₂	R ₁
Cl	F

S. aureus - MRSA

- within 1 year of methicillin's introduction in early 1960s
 - = Methicillin Resistant SA
- MRSA are resistant to **all penicillin and cephalosporin antibiotics**

MRSA is a community problem, no longer a hospital problem.



The prevalence of MRSA varies by location, ethnicity and deprivation.

MRSA infections differ between ethnic groups

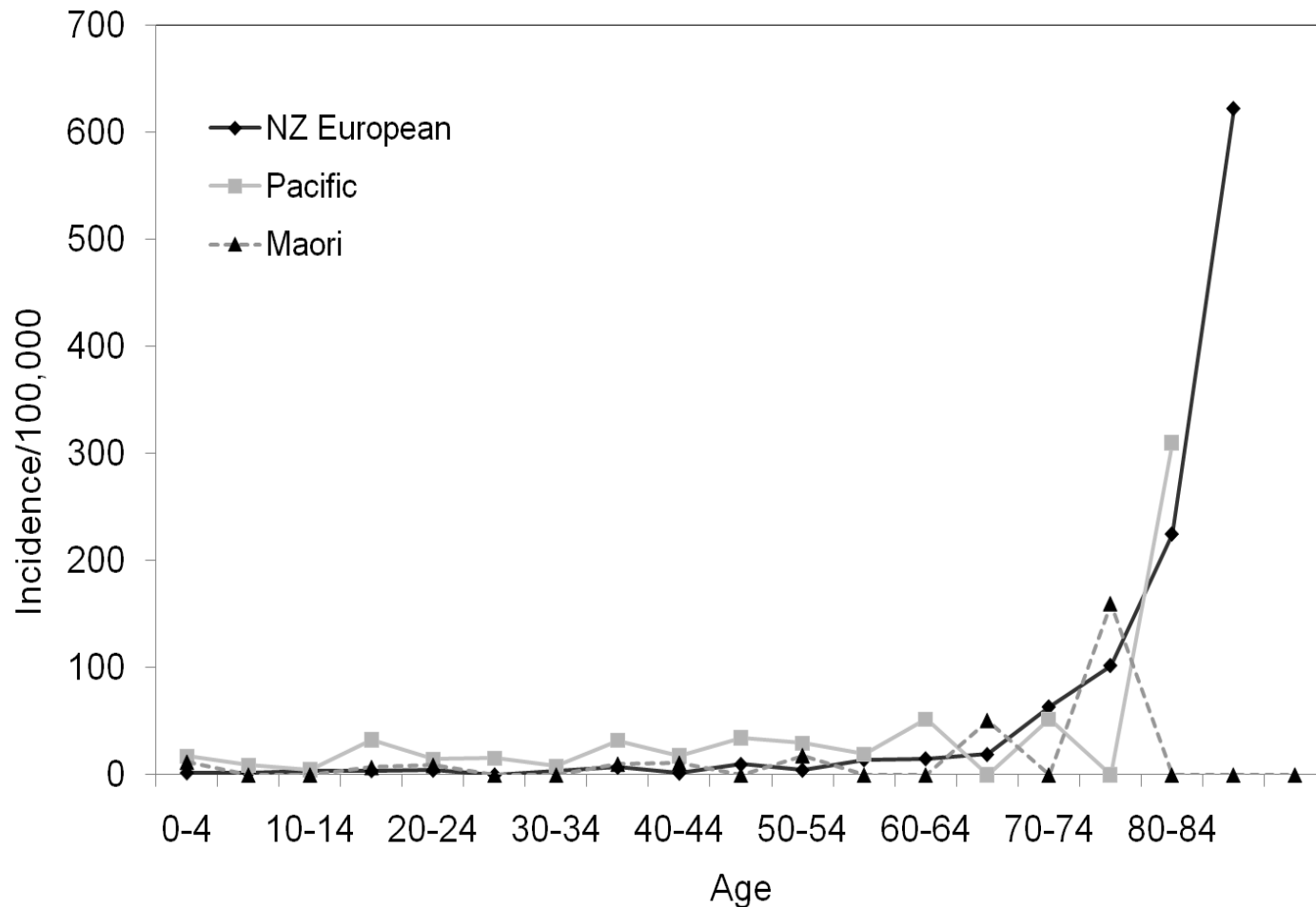
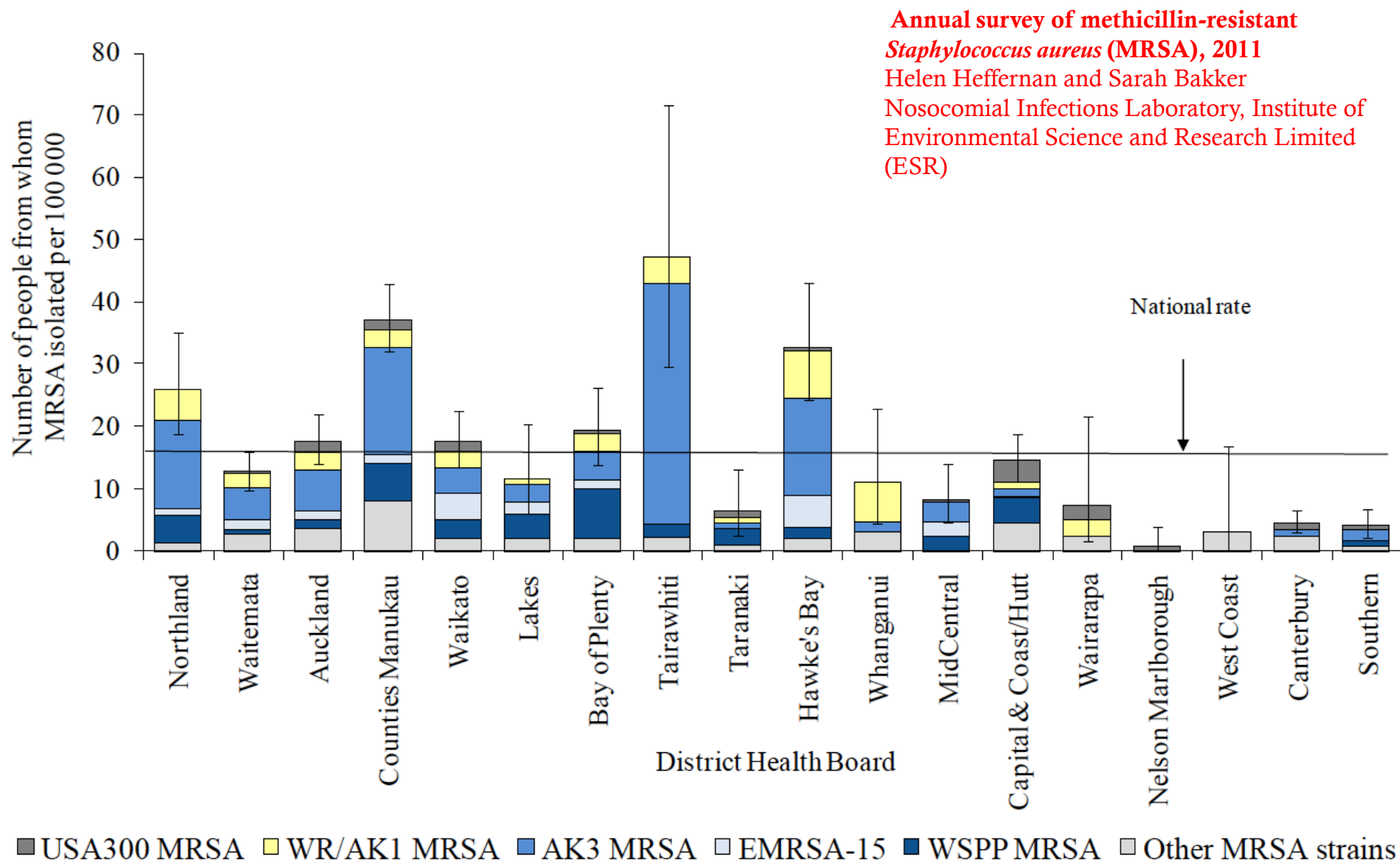


Figure 3. MRSA infection point-prevalence rates by district health board, 2011



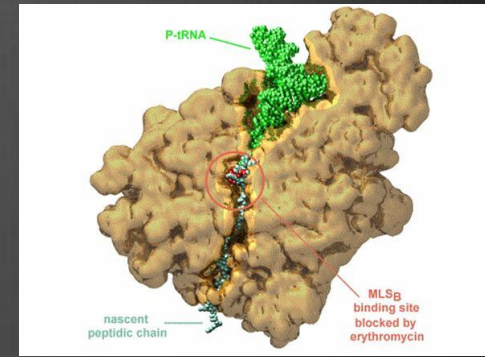
MRSA treatment

treatment options for MRSA

1. clindamycin
2. co-trimoxazole
3. doxycycline

Organism (No tested#)	Labtests	
	<i>Staphylococcus aureus</i> (MSSA) (33,130)	<i>Staphylococcus aureus</i> (MRSA) (3,679) (10% of <i>S. aureus</i>)
Penicillin	13	R
Flucloxacillin	S	R
Amoxicillin		R
Amox/clav	S	R
Cefaclor	S	R
Erythromycin	91	80
Clindamycin	92	87
Tetracycline	98	97
Cotrimoxazole	99	99
Trimethoprim*	91	97
Nitrofurantoin*	100	100
Norfloxacin*	96	74
Fosfomycin*		
Ciprofloxacin	99r	73r
Gentamicin		
Ceftriaxone		
Fusidic acid	75	59
Mupirocin	80	89
Chloramphenicol (topical)	S	S
Neomycin (topical)	S	S
Polymyxin/colistin (topical)	R	R
% ESBL Positive		

clindamycin



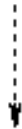
- susceptibility inferred from erythromycin
- effective treatment of skin infection
- has been trialed in SA and OM
 - *The Pediatric Infectious Disease Journal* • Volume 29, Number 12, December 2010
- as good as cephalexin for treating boils caused by MRSA
 - PEDIATRICS Volume 127, Number 3, March 2011:e573

co-trimoxazole

dihydropteroate diphosphate + p-aminobenzoic acid (PABA)

*dihydropteroate
synthetase* **X** ← sulfonamides

dihydropteroic acid



dihydrofolic acid

*dihydrofolate
reductase* **X** ← trimethoprim

tetrahydrofolic acid



purines for DNA

co-trimoxazole

- sulfamethoxazole/ trimethoprim (400/80)
- with rifampicin, similar to β lactam IV for treatment of OM

Long-Term Follow-Up Trial of Oral Rifampin-Cotrimoxazole Combination versus Intravenous Cloxacillin in Treatment of Chronic Staphylococcal Osteomyelitis[▽]

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, June 2009, p. 2672–2676

- as good as placebo to treat boils

Randomized Controlled Trial of Trimethoprim-Sulfamethoxazole for Uncomplicated Skin Abscesses in Patients at Risk for Community-Associated Methicillin-Resistant *Staphylococcus aureus* Infection

[Ann Emerg Med. 2010;56:283-287.]

doxycycline

- similar to co-trimoxazole in treatment of boils

Prospective Randomized Trial of Empiric Therapy with Trimethoprim-Sulfamethoxazole or Doxycycline for Outpatient Skin and Soft Tissue Infections in an Area of High Prevalence of Methicillin-Resistant *Staphylococcus aureus*[▽]

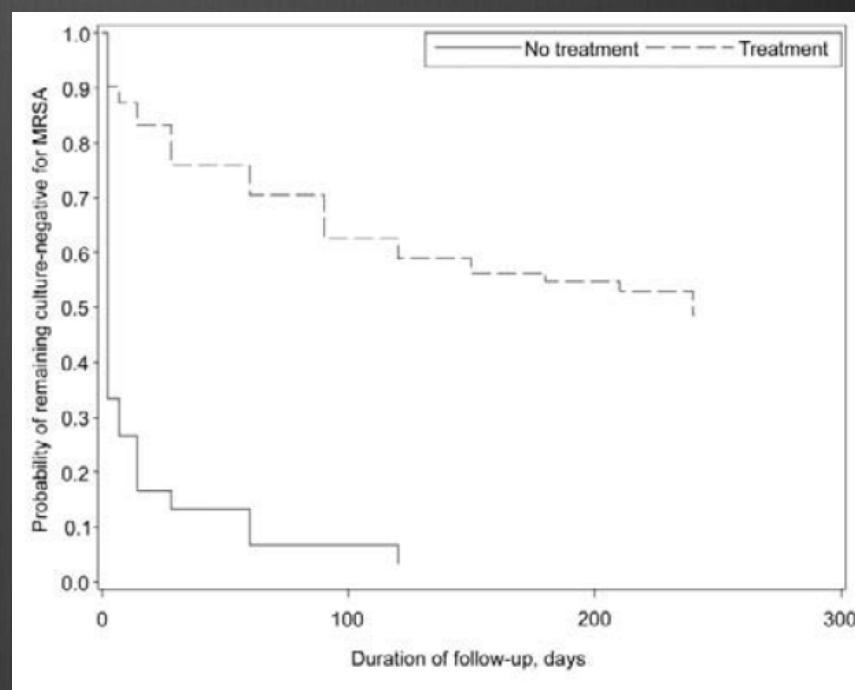
ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 2007, p. 2628–2630

MRSA eradication

Randomized Controlled Trial of Chlorhexidine Gluconate for Washing, Intranasal Mupirocin, and Rifampin and Doxycycline Versus No Treatment for the Eradication of Methicillin-Resistant *Staphylococcus aureus* Colonization

178 • CID 2007:44 (15 January) • Simor et al.

- open label trial of 112 hospital inpatients



summary MRSA

1. infection and transmission occurs in the community
2. the MRSA population is dynamic
3. all penicillins and cephalosporins are ineffective
4. non-complicated boils do not require treatment
5. treatment options are poorly studied but are usually effective
6. eradication for the sake of eradication is not warranted

Should healthcare workers be screened for MRSA carriage?

Journal of Hospital Infection 77 (2011) 285–289



ELSEVIER

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin



Review

Should healthcare workers be screened routinely for meticillin-resistant *Staphylococcus aureus*? A review of the evidence

G. Hawkins*, S. Stewart, O. Blatchford, J. Reilly

Health Protection Scotland, Glasgow, UK