Screening for *Staphylococcus aureus* before surgery. Why bother?

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Hosted by Paul Webber
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Declaration

The views expressed are of a professional but personal nature and not necessarily those of the RCSI & Beaumont Hospital, Dublin.

I have recently received research funding from Pfizer & Astellas. I have also provided professional advice or education for Cepheid

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Outline

1. Surgical site infections (SSI); prevalence, impact & costs
2. *Staph. aureus* as a pathogen, evolution of resistance & virulence determinants
3. Strategies to reduce post-operative SSI
4. Selective screening & decolonisation or universal decolonisation – the evidence
5. Conclusions

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Key Publications

1. Humphreys H, Becker K, Dolmen PM, *et al*. *Staphylococcus aureus* and surgical site infections: benefits of screening & decolinisation before surgery. *J Hosp Infect* 2016; 295-304.

2. Septimus EJ, Schweizer ML. Decolonisation in prevention of healthcare-associated infection. *Clin Microbiol Review* 2016; 29: 201-222.

3. Poovikunnel T, Gethin G, Humphreys H. Mupirocin resistance; Clinical implications & potential alternatives for the eradication of MRSA. *J. Antimicrobial Chemother* 2015; 70: 2681-2692

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Surgical Site Infection;

Prevalence, Impact & Costs

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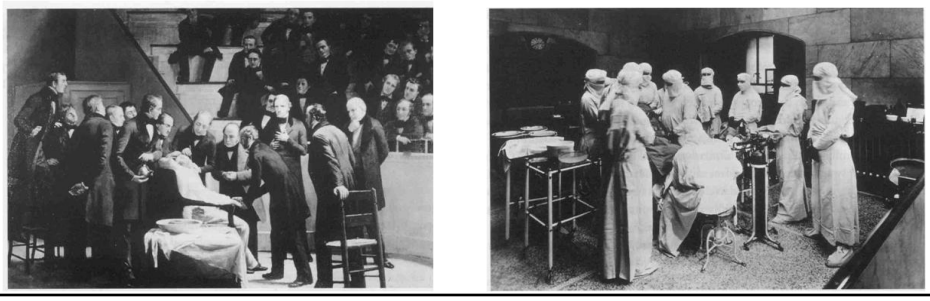
SSI-Worldwide

USA & Europe - 4.5 -7.1/100 hospitalised patients
- 1.7- 41 x 10^6 patients
- 3rd most common HCAI

Resource-poor countries - 15.4/100 hospitalised patients
- Commonest HCAI



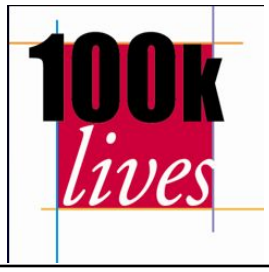
Public Reporting & Performance Indicators

HICPAC

SSI associated with cost, morbidity & mortality Prevention guidelines exist

100,000 Lives Campaign/Surgical Care Improvement Project
SSI amenable to interventions

Am J Infect Control 2005; 217-26
JAMA 2000; 295: 324-327
Clin Microbiol Infect 2008; 14: 892-894



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ECDC Point Prevalence Survey of HCAI & Antimicrobial Use, 2011-2012

- 2800 healthcare workers from 1200 hospitals were trained
- 231,459 patient in 947 hospitals, with a single ward surveyed on a single day
- Prevalence of HCAI was 6% (2.3 – 10.%); 4.8% in primary & 7.2% in tertiary hospitals
- RTI (23.5%), SSI (19.6%), UTI (19%), bloodstream infection (10.7%) & GI infection (7.7%) – 48% due to *Clostridium difficile*

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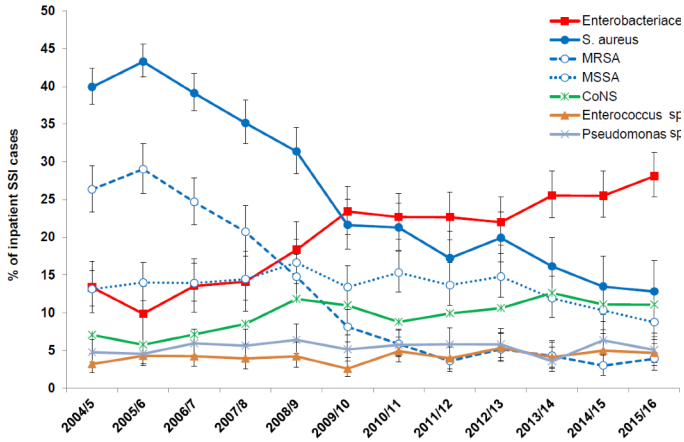
SSI in England, 2015-16

Public Health, England

Figure 11: Trends in micro-organisms reported as causing inpatient SSIs, proportions with lower and upper 9
surgical categories*, NHS hospitals, England



*excludes breast, cardiac (non-CABG), cranial and spinal surgery

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SSI Variation

- Varies according to procedure 'clean', 'contaminated', patient risk factors (e.g. age, diabetes mellitus), duration, technical competence, etc.
- 11% for cardiac surgery, 7% for vascular surgery & 2.4% for orthopaedic surgery
- Highest, usually > 20%, for emergency, colo-rectal surgery with perforation
- SSI rate increases x 2.9 if nasal colonisation for *Staph. aureus*

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SSI Impact & Costs

Length of stay – 10 additional days

Costs - €19 billion in Europe

Numbers – 70,000 SSIs out of 80 million procedures in US

Also, more hospital visits
- **need for home help**
- **more equipment**
- **? societal costs, e.g. loss of income**
- **tax, disability payments, etc.**

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What About After Hospital Discharge?

1. **Data from existing IT systems, e.g. pharmacy**
2. **Direct observation by healthcare professional**
3. **Telephone interviews**
4. **Patient questionnaire**

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In-Patient *versus* Post-Discharge Diagnosis

	Superficial	Deep	Organ/ space	Total
During hospitalisation	149	14	5	168
Post discharge	122	57	32	216
Re-admission	28	39	26	93
Follow-up	19	2	2	23
OPD + questionnaire	64	7	2	73

Infect Control Hosp Epidemiol 2006; 27: 1324-1329

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Surgical Site (Wound) Infection

	Uninfected	MSSA	MRSA
Death	2%	7%	21%
Mean hospital stay after surgery	5d	14d	23d
Hospital charges	$29,000	$53,000	$92,000

Clin Infect Dis 2003;36:592-98

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Staph. aureus as a pathogen;

Evolution of Resistance &

Virulence Determinants

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MICROCOCCUS POISONING. By Alex. Ogston, M.D.,
Surgeon to the Aberdeen Royal Infirmary.

(*Continued from* vol. xvi. *p.* 567).

Sapræmia.

(σαπρός, putrid; αἷμα, blood.)

A Scottish surgeon in Aberdeen first showed that many pyogenic lesions were associated with cluster-forming micro-organisms

Also described bloodstream infection or septicaemia

J Anat Physiol 1882; 17 part 1: 24-58

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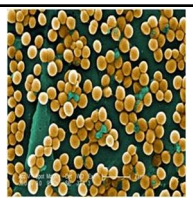

Colonisation & Infection

Colonisation

The bacteria are **carried** by the individual/patient, but he/she is well

Infection

The bacteria causes illness, with symptoms & possible adverse consequences

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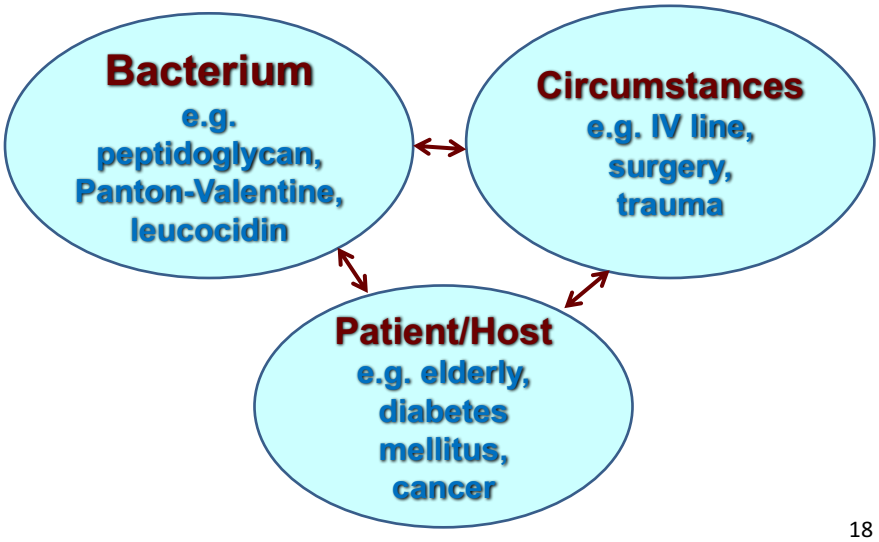
Pathogenesis



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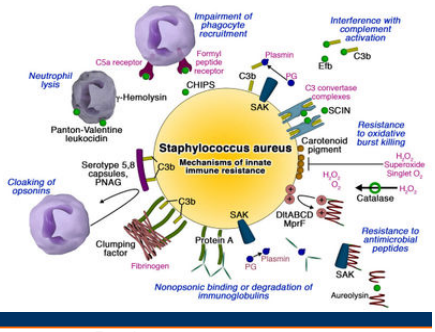
S. aureus Virulence Factors

- Pathogen of humans & animals
- Expresses many potential virulence factors
- Pathogenesis is multifactorial



David Coleman

Medscape® www.medscape.com

Virulence factor	Mechanism of action	Examples
Membrane-damaging toxins	Lyse host cell membranes	Leukotoxins, leukocidin (PVL), hemolysins
Extracellular proteins	Inhibit neutrophil recruitment	CHIPS, Eap
Surface factors	Inhibit phagocytic engulfment	Capsule, protein A
	Confer lysozyme resistance	*O*-acetyltransferase
Biochemical properties	Scavenge oxygen-free radicals	Carotenoids
	Enhance survival in phagocytes	Superoxide dismutase enzymes
Exotoxins	Damage host tissues	Superantigens, toxic shock syndrome toxin, enterotoxin
	Prevent T-cell proliferation and antibody production	
Antimicrobial resistance	Inherent and acquired mechanisms	β-Lactamase production renders resistance to β-lactam agents
		Acquisition of *mecA* gene renders resistance to methicillin
		Efflux pumps
Invasins	Promote bacterial spread in tissues	Leukocidins, kinases, hyaluronidases

CHIPS, chemotaxis inhibitory protein of staphylococci; Eap, extracellular adherence protein; PVL, Panton–Valentine leukocidin.

Source: Curr Opin Pul Med © 2007 Lippincott Williams & Wilkins

Recent Changes in *S. aureus* Epidemiology

A. Increase followed by decrease in MRSA in many hospitals such as BSI (EARS-Net)
B. Emergence & spread of CA-MRSA with presentations in acute hospitals
C. Livestock-associated MRSA, often in low prevalence countries
D. New clonal lineages, e.g. SCC*mec* XI with the divergent *mecC*

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Community-Acquired MRSA in the Netherlands

- > 29% of pig farmers & 39% of pigs MRSA+ve
- Sequence Type (ST) 398, unusual in humans
- Overuse of antibiotics in pigs, e.g. tetracyclines, or international trade in pigs

Clin Microbiol Infect 2008; 14: 519-521

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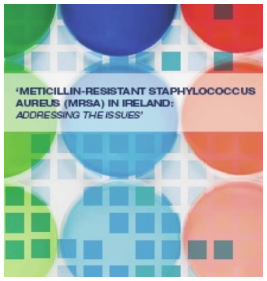
Costs of MRSA in Ireland

- 25,000 patients get HCAI annually
- €850/day leads to €233.75m
- MRSA accounts for 10% of HCAI
- MRSA costs the healthcare system €23m; does not allow for additional costs of MRSA



MRSA in Ireland: Addressing the Issues (2010)

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Strategies to Reduce Post-Operative SSI

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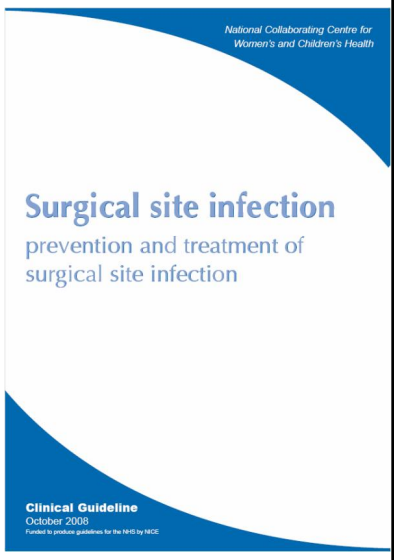
Healthcare Bundle for SSIs
Derived from NICE

Pre-Operative
e.g. hair removal,
staff theatre wear
antibiotic prophylaxis

Intra-Operative
e.g. hand decontamination
antiseptic skin preparation
wound irrigation

Post-Operative
e.g. changing dressings
topical antimicrobial agents
debridement



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New WHO Recommendations to Prevent SSI

1. Meta-analyses, Cochrane methods & Guideline Development Group
2. Pre-operative measures, e.g. preoperative bathing, antibiotic prophylaxis, etc.
3. Intra-operative measures, e.g. body temperature, category of drapes, etc.
4. Post-operative measures, e.g. ward dressings, etc.

Lancet Infect Dis 2016; 16: e276-87 & e288-303

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WHO & Decolonisation of *S. aureus*

Surgery	Recommendation	Strength	Quality of Evidence
Cardiothoracic & orthopaedic	Decolonise known carriers with mupirocin & CHG	Strong	Moderate
Other surgery	Decolonisation is suggested	Conditional	Moderate

CHG = chlorhexidine

Lancet Infect Dis 2016; 16: e27-87

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Selective Screening & Decolonisation or Universal Decolonisation- the Evidence

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Decolonisation to Prevent *S. aureus* SSI-1

- Studies vary in quality & category of surgery
- Some limited to MRSA
- Often combined with other interventions
- Methods of testing vary; culture & molecular

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Decolonisation to Prevent *S. aureus* SSI-2

- Best evidence for cardio-thoracic & orthopaedics
- Elective more than emergency unless PCR
- Plausible that there might be benefits for neurosurgery & plastic surgery
- SSI after GI, liver & gall bladder surgery caused by enteric bacteria

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Nasal Decolonisation of *S. aureus*

Conventional	Unconventional
Mupirocin	Tea tree oil
Bacitracin	Photodynamic therapy
Retapamulin	Omiganan pentahydrochloride
Povidone - iodine	Lysostaphin
Alcohol	Honey

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Skin Decolonisation of *S. aureus*

Selective	Digestive Tract Decontamination
Chlorhexidine (CHG)	Tobramycin, polymixin & amphothericin B
Hexachlorophane	
Povidone-iodine	Directed mainly against GNBs & in ICU
Triclosan	
Bleach	Has been combined with CHG

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Dutch Study of SSI & *S. aureus*

1. PCR screening at admission, multi-centre
2. No MRSA detected
3. +ve received a 5 day course of mupirocin/CHG
4. SSI rate lower in treatment group (3.4% vs 7.7%)
5. Mean hospital stay less by 2 days

N Engl J Med 2010; 362: 9-17

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Point-of-Care Universal Screening

- Cluster randomised cross-over trial on four admission wards in London with wash-out periods
- Admission & discharge screening by culture or/& PCR (Xpert™ MRSA, Cepheid)
- PCR was 69% sensitive, 97% specific, PPV 29%, NPV 99%
- Total days not isolated higher if culture

J Hosp Infect 2017;95: 245-52

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Point-of-Care Universal Screening

Variables	Culture	PCR
No. screened	4978 (75%)	5039 (72%)
MRSA +ve	113 (1.8%)	109 (1.6%)
MRSA acquisition by discharge	23 (0.46%)	24 (0.48%)
Acquisition/1,000 patient days	5.39	4.6

J Hosp Infect 2017; 95: 245-52

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Rapid Screening for MRSA

- Beaumont Hospital study of 462 (ward, ED) & 27 ICU patients during 3 periods
- 22-33% MRSA +ve
- 27% not screened if culture used & 11% if PCR used ($p<0.01$)
- 24% of patients pre-emptively isolated without PCR compared to 7% with PCR ($p>0.001$)

Infect Control Hospital Epidem 2010; 31: 374-381

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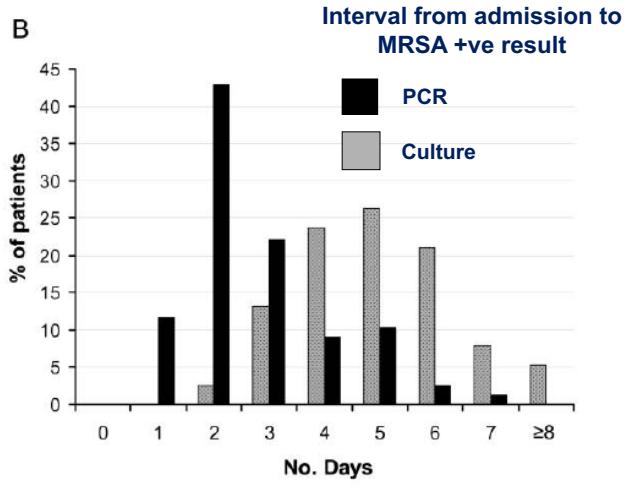
Rapid Screening for MRSA Using PCR- Does It Make a Difference?



Infect Control Hosp Epidemiol 2010; 31: 374-381

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Logistical Issues

- **Decolonisation with prior screening requires planning, education, etc**

Table II
Education requirements for patients undergoing screening and decolonization before surgery

Theme	Specifics
Hand hygiene	Importance of personal hygiene
	Asking healthcare workers if they have decontaminated their hands
Staphylococcus aureus	What is MRSA/MSSA?
	Measures to prevent transmission
	Importance of environmental cleaning
Decolonization	What are mupirocin and CHG?
	Where to access and how to apply decolonization agents
	Importance of compliance

MRSA, meticillin-resistant *S. aureus*; MSSA, meticillin-susceptible *S. aureus*; CHG, chlorhexidine.

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Universal Decolonisation - 1

Q. Why screen as ~ 30% are carriers and adds to delay & expense

A. Unnecessary use of mupirocin & CHG with emergence of resistance

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Universal Decolonisation - 2

- Represents a horizontal intervention, i.e. measures for all patients
- Largely used in critical care but –
  - very ill patients
  - not directed at preventing SSI
  - possible benefits in preventing BSI
- Economic models target short-term benefits
- Well planned non-emergency surgery should allow for screening

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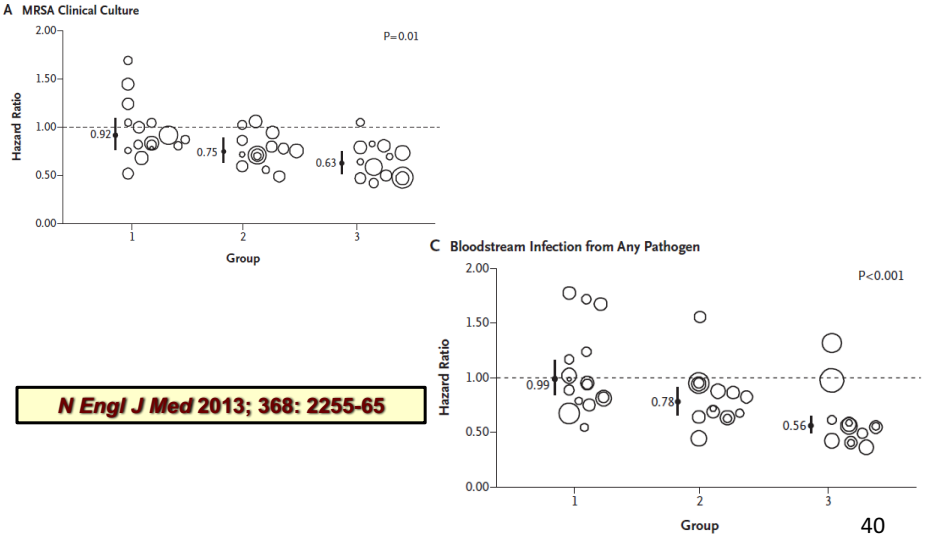
Targeted *versus* Universal Decolonisation to Prevent ICU Infection



N Engl J Med 2013; 368: 2255-65

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Prevention of Surgical Site Infections: Decontamination With Mupirocin Based on Preoperative Screening for *Staphylococcus aureus* Carriers or Universal Decontamination?

David J. Hetem,[1] Martin C. J. Bootsma,[2,3] and Marc J. M. Bonten[1,2]

Clin Infect Dis 2016; 62: 631-6

"The current evidence on the occurrence of high-level mupirocin resistance in CoNS does not constitute an important risk for high-level mupirocin resistance in *Staph. aureus.*"

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S. aureus & Mupirocin Resistance - 1

Low level - MICs 8 – 128/256 mg/l
Amino acid substitutions
Clinical significance uncertain

High level - MICs ≥ 512 mg/l
Plasmid – localised *mup A* gene
Can transfer to *Staph. epidermidis*

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S. aureus & Mupirocin Resistance -2

- Mupirocin resistance associated with resistance to other antimicrobial agents such as clindamycin & levofloxacin
- Resistance to antiseptics/biocides such as CHG (*qacA* & *qacB*) amongst coagulase negative staphylococci
- Increased use of mupirocin associated with increased resistance

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J Antimicrob Chemother 2015; **70**: 2681–2692
doi:10.1093/jac/dkv169 Advance Access publication 3 July 2015

Journal of Antimicrobial Chemotherapy

Mupirocin resistance: clinical implications and potential alternatives for the eradication of MRSA

T. Poovelikunnel[1,2*†], G. Gethin[3†] and H. Humphreys[2,4†]

Key findings

- Resistance ranges from 1-81%
- Chlorhexidine resistance genes among MRSA isolates, 65-91%
- High level mupirocin resistance (HLMR) linked with multi-drug resistance
  - clindamycin, tetracycline, erythromycin & levofloxacin

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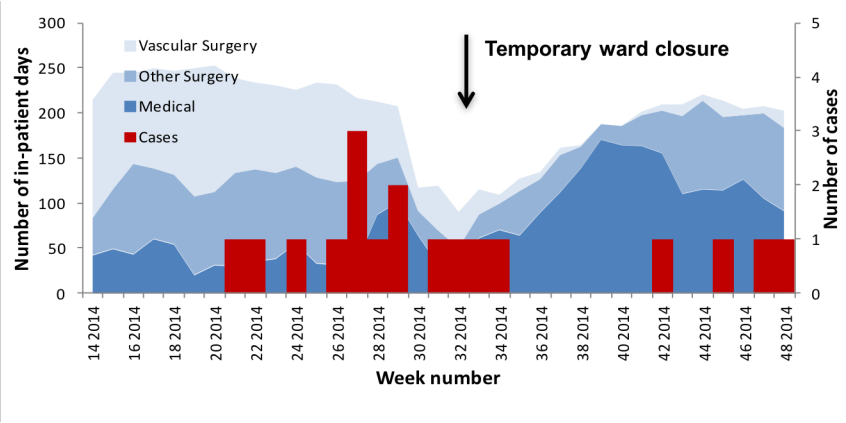
Mup. Res MRSA (spa type t127 or t922) Outbreak



- Median age 73 years, 78% male
- 31 colonised, 8 infections
- 42%, vascular, 37% medical & 20% other surgical patients

Patricia Garvey *et al*

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REDUCE MRSA Trial & Mup/Chlor Resistance

- 7/12 baseline & 18/12 intervention periods
- Most isolates collected from nose on 1st day of hospitalisation; 3,173 (43%) tested
- No difference in MIC_{50} /MIC_{90} for chlorhexidine resistance
- 7.1% LLMR & 7.5% HLMR but no difference between phases & introduction
- 0.6% had *gac* gene

J Clin Microbiol 2016; 54: 2735-42

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Preliminary Results from RCT of Mupirocin *versus* Natural Honey

- Patient recruitment
  - March 2014 to March 2016
- Outcome of ~100 patients enrolled & completed the study
- Natural honey non-inferior & multi-site MRSA a risk factor for decolonisation failure

Toney Poovelikunnel, *et al.*

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Conclusions

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- SSI are amongst the most important HCAIs & *S. aureus* the commonest cause
- Horizontal measures are important pre-intra- & post operatively
- Evidence & plausibility are strong to screen & selectively decolonise before cardio-thoracic & orthopaedic surgery

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- Molecular testing can preclude the need for universal decolonisation before surgery
- Studies are required outside of orthopaedic & cardio-thoracic surgery
- Unnecessary & widespread use of topical antibiotics & biocides should not occur

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www.webbertraining.com/schedulepl.php	
April 6, 2017	TECHNOLOGIC INNOVATIONS TO PREVENT CATHETER-RELATED BLOODSTREAM INFECTIONS Speaker: **Prof. Mark Rupp**, University of Nebraska Medical Center
April 25, 2017	*(FREE European Teleclass … Denver Russell Memorial Teleclass Lecture)* DO'S AND DONT'S FOR HOSPITAL CLEANING Speaker: **Dr. Stephanie Dancer**, Health Protection Scotland
April 27, 2017	COST ANALYSIS OF UNIVERSAL SCREENING VS. RISK FACTOR-BASED SCREENING FOR MRSA Speaker: **Dr. Virginia Roth**, University of Ottawa
May 5, 2017	*(FREE … WHO Teleclass - Europe)* SPECIAL LECTURE FOR 5 MAY Speaker: **Prof. Didier Pittet**, World Health Organization, Geneva *Sponsored by the World Health Organization Infection Control Global Unit (www.who.int/gpsc/en)*
May 18, 2017	THE AIRBORNE SPREAD OF INFECTIOUS AGENTS: SURVIVAL AND DECONTAMINATION OF HUMAN PATHOGENS IN INDOOR AIR Speaker: **Prof. Syed A. Sattar**, University of Ottawa Faculty of Medicine
	(European Teleclass)

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