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

Hilary Humphreys
Royal College of Surgeons in Ireland (RCSI) & Beaumont Hospital, Dublin, Ireland

Hosted by Paul Webber
paul@webbertraining.com

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March 30, 2017

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

Key Publications


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Surgical Site Infection;  
Prevalence, Impact & Costs  

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  

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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

JAMA 2000; 295: 324-327
Clin Microbiol Infect 2008, 14: 892-894

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%); 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
SSI in England, 2015-16
Public Health, England

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

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, colorectal 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.

### 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

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

*Infect Control Hosp Epidemiol 2006; 27: 1324-1329*

### Surgical Site (Wound) Infection

<table>
<thead>
<tr>
<th></th>
<th>Uninfected</th>
<th>MSSA</th>
<th>MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Death</strong></td>
<td>2%</td>
<td>7%</td>
<td>21%</td>
</tr>
<tr>
<td><strong>Mean hospital stay after surgery</strong></td>
<td>5d</td>
<td>14d</td>
<td>23d</td>
</tr>
<tr>
<td><strong>Hospital charges</strong></td>
<td>$29,000</td>
<td>$53,000</td>
<td>$92,000</td>
</tr>
</tbody>
</table>

*Clin Infect Dis 2003;36:592-98*
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**Staph. aureus as a pathogen;**

**Evolution of Resistance &**

**Virulence Determinants**

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

Pathogenesis

Bacterium
e.g. peptidoglycan, Panton-Valentine, leucocidin

Circumstances
e.g. IV line, surgery, trauma

Patient/Host
e.g. elderly, diabetes mellitus, cancer

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**S. aureus Virulence Factors**

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

David Coleman

<table>
<thead>
<tr>
<th>Virulence factor</th>
<th>Mechanism of action</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membrane-damaging toxins</td>
<td>Lyse host cell membranes</td>
<td>Leukocidins, leukocidin (PVL), hemolysins</td>
</tr>
<tr>
<td>Extracellular proteins</td>
<td>Inhibit neutrophil recruitment</td>
<td>CHIPS, Exp</td>
</tr>
<tr>
<td>Surface factors</td>
<td>Inhibit phagocytic engulfment</td>
<td>Capsule, protein A</td>
</tr>
<tr>
<td>Biochemical properties</td>
<td>Cortile lysozyme resistance</td>
<td>O-acetyltransferase</td>
</tr>
<tr>
<td>Exotoxins</td>
<td>Enhance survival in phagocytes</td>
<td>Superoxide dismutase enzymes</td>
</tr>
<tr>
<td>Antimicrobial resistance</td>
<td>Prevent T-cell proliferation and antibody production</td>
<td>β-Lactamase production renders resistance to β-lactam agents</td>
</tr>
<tr>
<td>Invasion</td>
<td>Promote bacterial spread in tissues</td>
<td>Acquisition of mecA gene renders resistance to methicillin</td>
</tr>
</tbody>
</table>

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

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. SCCmec 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

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

### Healthcare Bundle for SSIs

**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*

### WHO & Decolonisation of S. aureus

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Recommendation</th>
<th>Strength</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiothoracic &amp; orthopaedic</td>
<td>Decolonise known carriers with mupirocin &amp; CHG</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>Other surgery</td>
<td>Decolonisation is suggested</td>
<td>Conditional</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

CHG = chlorhexidine

*Lancet Infect Dis 2016; 16: e27-87*
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**Selective Screening & Decolonisation or Universal Decolonisation - the Evidence**

**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

Nasal Decolonisation of S. aureus

<table>
<thead>
<tr>
<th>Conventional</th>
<th>Unconventional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mupirocin</td>
<td>Tea tree oil</td>
</tr>
<tr>
<td>Bacitracin</td>
<td>Photodynamic therapy</td>
</tr>
<tr>
<td>Retapamulin</td>
<td>Omiganan pentahydrochloride</td>
</tr>
<tr>
<td>Povidone - iodine</td>
<td>Lysostaphin</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Honey</td>
</tr>
</tbody>
</table>
Skin Decolonisation of S. aureus

<table>
<thead>
<tr>
<th>Selective</th>
<th>Digestive Tract Decontamination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorhexidine (CHG)</td>
<td>Tobramycin, polymixin &amp; amphotericin B</td>
</tr>
<tr>
<td>Hexachlorophane</td>
<td></td>
</tr>
<tr>
<td>Povidone-iodine</td>
<td>Directed mainly against GNBs &amp; in ICU</td>
</tr>
<tr>
<td>Triclosan</td>
<td></td>
</tr>
<tr>
<td>Bleach</td>
<td>Has been combined with CHG</td>
</tr>
</tbody>
</table>

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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### Variables

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

*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 Epidemiol 2010; 31: 374-381*

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

![Interval from admission to MRSA +ve result](image)

*Infect Control Hosp Epidemiol 2010; 31: 374-381*
Logistical Issues

- Decolonisation with prior screening requires planning, education, etc

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

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

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

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
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

Targeted versus Universal Decolonisation to Prevent ICU Infection

“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 \textit{Staph. aureus}.”

\textbf{S. aureus & Mupirocin Resistance - 1}

\textbf{Low level -} \begin{itemize}
  \item MICs 8 – 128/256 mg/l
  \item Amino acid substitutions
  \item Clinical significance uncertain
\end{itemize}

\textbf{High level -} \begin{itemize}
  \item MICs \geq 512 mg/l
  \item Plasmid – localised \textit{mup A} gene
  \item Can transfer to \textit{Staph. epidermidis}
\end{itemize}
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

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

T. Poovelikutten, G. Gethin and H. Humphreys

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*

**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.*

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

- 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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Thank you

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www.webbertraining.com/schedule1.php

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Speaker</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 6, 2017</td>
<td>TECHNOLOGIC INNOVATIONS TO PREVENT CATHETER-RELATED BLOODSTREAM INFECTIONS</td>
<td>Prof. Mark Rupp, University of Nebraska Medical Center</td>
<td></td>
</tr>
<tr>
<td>April 25, 2017</td>
<td>(FREE European Teleclass... Denver Russell Memorial Teleclass Lecture) DO'S AND DONT'S FOR HOSPITAL CLEANING</td>
<td>Dr. Stephanie Dancer, Health Protection Scotland</td>
<td></td>
</tr>
<tr>
<td>April 27, 2017</td>
<td>COST ANALYSIS OF UNIVERSAL SCREENING VS. RISK FACTOR-BASED SCREENING FOR MRSA</td>
<td>Dr. Virginia Roth, University of Ottawa</td>
<td></td>
</tr>
<tr>
<td>May 5, 2017</td>
<td>(FREE...WHO Teleclass...Europe) SPECIAL LECTURE FOR 5 MAY</td>
<td>Prof. Didier Pittet, World Health Organization, Geneva</td>
<td></td>
</tr>
<tr>
<td>May 18, 2017</td>
<td>THE AIRBORNE SPREAD OF INFECTIOUS AGENTS: SURVIVAL AND DECONTAMINATION OF HUMAN PATHOGENS IN INDOOR AIR</td>
<td>Prof. Syed A. Satar, University of Ottawa Faculty of Medicine</td>
<td></td>
</tr>
</tbody>
</table>

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