3M℠ Health Care Academy

Nasal Colonization and Surgical Site Infection (SSI) Risk
Disclosure

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- *Registered nurse participants can receive 1.0 contact hour upon course completion*

Presented by:

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Clinical Consultant, Infection Prevention Division
Perioperative Products
Learning Objectives

1. Describe how nasal carriage of *S. aureus* relates to SSI

2. Identify relevant clinical studies related to preoperatively reducing bacteria in the nose

3. Describe guidelines and recommended practices that support nasal intervention
Surgical Site Infections

- Surgical procedures are becoming increasingly more complicated
- Population of surgical patients has more underlying conditions
- These factors increase the risk for developing surgical site infection (SSI)
SSI Epidemiology


SSIs are common complications

- SSI occur in 2-5% of patients undergoing inpatient surgery
- Approximately 160,000-300,000 SSI occur each year in the US
- SSI represent 20% of all HAI in hospitalized patients
- SSI is now the most common and costly HAI
**SSI Epidemiology**


Outcomes associated with SSI

- Up to 60% of SSI may be preventable by use of evidence-based guidelines
- Each SSI increases LOS by approximately 7-11 days
- SSI is associated with 2-11 times higher risk of mortality compared with operative patients without SSI
  - 77% of mortality in patients with SSI is directly attributable to that SSI
- Attributable costs of SSI depend on the type of operative procedure and the infecting pathogen
  - Believed to account for $3.5-10 billion annually in health care expenditures
Process Variability

\[
\frac{\text{Dose of Bacteria} \times \text{Virulence}}{\text{Resistance of the Host}} \times \text{Patient Variability} = \text{Risk}
\]

CDC Guideline For Prevention Of Surgical Site Infection, 1999
http://www.cdc.gov/ncidod/dhqp/gl_surgicalsite.html
Patient Variability: Resistance of the host (patient)

- Age
- Compromised Immune System
- Diabetes
- Remote Site Infection (Not Treated Prior To Surgery)
- Nutritional Status
- Nicotine Use
- Prolonged Preoperative Stay
- Obesity
- Steroid Use
- Duration of Surgery
Process Variability

- Hand hygiene
- Appropriate antimicrobial prophylaxis
- Preoperative bathing
- **Nasal decontamination**
- Oral decontamination
- Hair removal
- Skin preparation
- Surgical hand antisepsis
- Appropriate surgical attire and drapes

- Operating room characteristics
  - Ventilation, traffic, environmental surfaces
  - Sterilization

- Patient management
  - Normothermia
  - Glucose control
  - Oxygenation

- Surgical technique
  - Hemostasis
  - Failure to obliterate dead space
  - Tissue trauma
Reducing Bacteria in the Nares
S. aureus is the leading cause of surgical site infections

## Distribution of Top Ranking Pathogens – 2009-2010

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>SSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>30.4%</td>
</tr>
<tr>
<td>Coagulase Negative Staph (CNS)</td>
<td>11.7%</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>9.4%</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>5.9%</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>5.5%</td>
</tr>
<tr>
<td>Enterobacter spp.</td>
<td>4%</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>4%</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>3.2%</td>
</tr>
<tr>
<td>Proteus spp.</td>
<td>3.2%</td>
</tr>
</tbody>
</table>

Approximately 30% of the population are colonized with *S. aureus* in the nares and 1% carry MRSA

80% of the S. aureus infections are caused by the patient’s own (clonal) nasal flora


**S. aureus** Nasal Carriage and Infection

**Perl TM, et al.**

- NEJM 2002; 346(24): 1871-1877
- Intranasal mupirocin to prevent postoperative *Staphylococcus aureus* infections
- Genotyping revealed that over 80% of the *S. aureus* strains isolated from the nares were identical to those isolated from the surgical site
Nasal carriage of *S. aureus* is a major risk factor for SSI following cardiac open heart surgery.
Cardiac Procedures


- Case control study of 1980 patients undergoing cardiac surgery at University Hospital, Rotterdam
- 10/10 pairs of pre-op nasal isolates and post-op wound isolates were identical
- Nasal carriage of *S. aureus* is a significant risk factor for development of sternal wound infection with *S. aureus*
Nasal carriage of *S. aureus* is a major risk factor for SSI following orthopedic prosthetic joint surgery.
Joint Arthroplasty


- Meta-analysis of five clinical studies
- On average, nasal carriage of *S. aureus* increases the risk of SSI by nearly 6-fold
  - OR = 5.92, 95% CI [1.15-30.39]; p = 0.033

- Retrospective cohort study
- 9863 procedures with nasal MRSA PCR screening
- Surgery type
  - Abdominal 29.8%, ortho 21.8%, neuro 19.7%, Cardiothoracic and vascular 16.7%
  - 4.3% with at least 1 positive MRSA PCR day of or within 30 days of procedure
- 1.86% PCR positive developed SSI compared to 0.2% PCR negative (p < 0.0001)
- **Multivariate analysis:** positive MRSA PCR was an independent risk factor for SSI
  - OR, 9.20; 95% CI, 3.81-20.47, p < 0.0001
Guidelines and Recommendations

2008 APIC Guide for the Prevention of Mediastinitis SSI

• Nasal decolonization with mupirocin is recommended for the prevention of mediastinitis due to the risk of *S. aureus* as the causative organism and the ease of program implementation
Guidelines and Recommendations

2010 APIC Guide to the Elimination of Orthopedic Surgical Site Infections

• Nasal carriage of *Staphylococcus aureus* is a modifiable risk factor for SSI
• Screening and decolonization protocols should be standardized
• One of the concerns with the use of intranasal mupirocin ointment is development of resistance

APIC Guide to the Elimination of Orthopedic Surgical Site Infections, 2010
http://apic.org/Resource_/EliminationGuideForm/34e03612-d1e6-4214-a76b-e532c6fc3898/File/APIC-Ortho-Guide.pdf

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Guidelines and Recommendations

2014 SHEA/IDSA Practice Recommendation

- If unacceptably high SSI rates exist for surgical populations despite implementation of the basic SSI prevention strategies then applying standard infection control methods for outbreak investigation and management are recommended, including:
  - Screen surgical patients for *S. aureus* and decolonize preoperatively for high risk procedures including some orthopedic and cardiac procedures
  - Routine preoperative decolonization with mupirocin without screening and targeted use is not currently recommended due to concerns about evolving resistance

Reducing *S. aureus* in the Nares Prior to Surgery

**Bactroban Nasal® (mupirocin calcium ointment, 2%)**
- Indicated for institutional outbreaks of MRSA*
- Greater than 90% of subjects/patients in clinical trials had eradication of nasal colonization 2 to 4 days after therapy was completed*

**mupirocin challenges**
- Full 5-day treatment does not fit into pre-surgical logistics
- Poor patient compliance
- Antibiotic resistance

Antiseptic Prep – 5% Povidone Iodine

- One-time application 1 hour before incision
- Provides a 99.5% reduction of *S. aureus* in the nares at 1 hour
- Maintains this log reduction for at least 12 hours
- Patented formula designed specifically for the nose—presents unique challenges compared to prepping skin

### Example for 12-hour Time Point
Baseline: 4.72 logs or 52,000 *S. aureus* – 2.37 logs killed = 220 bacteria remaining at 12 hours
Antiseptic Prep – 5% Povidone Iodine

**Advantages**
- Resistance has not been shown,\(^1\) supports antibiotic stewardship
- Broad spectrum
- Easy to implement in pre-op
- No need to change current protocols
  - i.e., screening
- Directly observed application ensures compliance\(^2\)
- Demonstrated efficacy in helping reduce SSI risk

**Limitations**
- A small number of patients may be sensitive to povidone iodine-containing products
- Reduces bacteria, does not eradicate

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1. 3M Study 05-011322
Summary

- Nasal carriage of *S. aureus* increases risk of SSI, and is of increased focus for high risk surgical procedures.
- If *S. aureus* SSI is higher than benchmark despite effective basic SSI risk reduction strategies then implementation of *S. aureus* decolonization program is recommended.
- Intranasal mupirocin has been used historically to decolonize the nares and is associated with compliance burdens.
- 5% PI formulated specifically for intranasal application is an option that provides directly observed, just in time application with demonstrated efficacy in helping to reduce the risk of SSI.
Clinical Evidence-Implementation
Clinical Trial Designs – Hierarchy of Evidence

- **Systematic Reviews**
  - Meta-analyses

- **Experimental Studies**
  - Randomization
  - Control over use of intervention

- **Quasi-experimental**
  - No randomization

- **Observational Studies**
  - No control over allocation of intervention
  - No randomization

- **Descriptive Studies**:
  - No comparative group
  - Description of exposed subjects

**Quality of evidence**
Clinical Trial Designs – Hierarchy of Evidence for Nasal Antisepsis

- Systematic Reviews
- Meta-analyses
- Randomized Controlled
- Quasi-experimental
- Cohort Studies
- Case Control Studies
- Case Series
- Case Reports

Phillips, et al.
Rezapoorn, et al.
Bebko, et al.
Rivera, et al.
Hogenmiller, et al.
Waibel, et al.
Osborn & Reynolds
Torres, et al.
Flynn & Carr
Brown, et al.

“Before and After” Bundle

3M™ Skin and Nasal Antiseptic
Clinical Study Rationale

Protocol to reduce the risk of SSI consisted of:
- CHG bathing the night before and the morning of surgery nasal
- Nasal mupirocin ointment twice daily for 5 days preoperatively

Barriers to protocol:
- 86% compliance to mupirocin regimen
- 8% of patients reported difficulty obtaining mupirocin due to cost
- Concerns regarding reports of mupirocin resistance

These barriers led to search for an alternative

Clinical Studies- Phillips M et al., ICHE 2014

Preventing Surgical Site Infections: A Randomized, Open-Label Trial of Nasal Mupirocin Ointment and Nasal Povidone-Iodine Solution
Clinical Studies Phillips

Randomized trial comparing SSI after arthroplasty or spine fusion surgery. Patients receiving two applications of Sage® 2% CHG cloths were randomized to:

- one time treatment of 3M™ Skin and Nasal Antiseptic or
- five days of Bactroban Nasal® mupirocin ointment prior to surgery

The primary end point was deep SSI within 3 months of surgery

Results: Intent to treat (n=1,697); Per protocol (n= 1,539)

- Significantly more adverse events were reported by patients in the mupirocin group (8.9%) than patients in the antiseptic group (1.8%) (p<0.05 for all treatment related symptoms)

Conclusion Phillips:

- 5% nasal PI may be considered as an alternative to mupirocin in a multifaceted approach to reduce SSI

Other observations:
- Compared to mupirocin in terms of cost and efficacy, 5% nasal PI provides more value, defined as quality of outcomes divided by cost
- Application of 5% nasal PI by the patient care team just prior to surgery may ensure greater compliance
Clinical Studies Bebko

Prospective study comparing SSI in elective orthopedic surgery with hardware before and after implementation of a preoperative decontamination protocol:

- Sage® 2% CHG cloths and Peridex™ 0.12% CHG oral rinse night before and morning of surgery AND
- 3M™ Skin and Nasal Antiseptic morning of surgery

The primary end point was 30 day SSI rates

Results:

- 100% compliance to protocol
- Multivariate logistic regression: Decontamination protocol = Significant independent protective factor against SSI (OR 0.24 [95% CI, 0.08-0.770]; p = 0.02)

Conclusion Bebko

“Universal decontamination using this low-cost protocol may be considered as an additional prevention strategy for SSIs”...

Other observations:

• Wider implementation without the need of SA carrier screen and treat may allow for cost savings.

• Advantages to the protocol include shorter duration, cost effectiveness (compared to PCR based protocols), and potentially fewer concerns about antibiotic resistance.
Clinical Studies Torres

Retrospective study comparing infection rate and cost difference between two preoperative protocols in THA and TKA surgery

- MRSA screening, carriers treated with mupirocin preoperatively twice daily for 5 days (control)
- Received one application of 3M™ Skin and Nasal Antiseptic in preop (intervention)

Both groups: CHG bathing for 5 days before surgery; operative leg cleansed with CHG wipe in preop

Results

- 1,853 patients were included
- No difference in SSI rate between groups: 0.8% in both groups (p = 1.0)
- Significant difference in the mean cost per case: control group: $121.16 versus intervention group: $27.21 (p≤ 0.01)
- Savings of $93.95/patient

Conclusion Torres

There were significant cost savings with no difference in infection rates; therefore, the 5% povidone-iodine nasal antiseptic is financially and clinically successful.
Clinical Studies Flynn
Study comparing SSI between cohorts after spine surgery before and after implementation of 3M™ Skin and Nasal Antiseptic

- All patients undergoing surgery from 01/09-08/10; before nasal antiseptic (control)
- All patients undergoing surgery from 09/10-11/11; after nasal antiseptic implemented (intervention)

Results:

- 9,135 patients were included
- Significant reduction in SSI rate:
  - control group: (1.22%; 63/5,154 patients) versus
  - intervention group: (0.45%; 18/3,981 patients) (p=0.0029)
- There was no trend in the infection rate prior to the intervention (p= 0.18)
- The infection rate for any month pre-intervention was 1.04 times the infection rate of the previous month (95% CI, 0.98 to 1.10)

Preoperative use of the 5% nasal antiseptic prior to surgical intervention resulted in a statistically significant decrease in postoperative infections.
Clinical Studies Rivera

Before-and-after intervention study comparing SSI rates in hip or knee arthroplasty surgery

- 01/12-09/13- patients encouraged to bathe with CHG or antibacterial soap 2 days preop; no nasal intervention performed (control)
- 10/13-03/16- patients instructed to bathe with CHG soap 3 days preop; 3M™ Skin and Nasal Antiseptic applied in preop (intervention)

Results:

- 8,961 patients were included
- Significant reduction in total SSI rate:
  - control group: (1.52%; 38/2,507 patients)
  - intervention group: (0.70%; 45/6,454 patients)
  - (p=0.0006)
- Significant reduction in SA/MRSA SSI rate:
  - control group: (0.76%; 19/2,507 patients)
  - intervention group: (0.33%; 21/6,454 patients)
  - (p=0.0095)

Conclusion Rivera

The rates of total and SA/MRSA SSI after joint replacement were significantly lower in the post-intervention timeframe when compared to baseline.
Clinical Studies Waibel
Before-and-after intervention study comparing SSI rates in total joint arthroplasty surgery

Rationale: Lean process improvement reduced infections in 2009; infections increased again in 2011

Intervention:
• Realignment of lean process improvements that were successful in 2009 in reducing THA/TKA infections
• 3M™ Skin and Nasal Antiseptic morning of surgery

Results:

**MRSA SSIs vs. Total SSIs in THA/TKA**

- 3M Skin and Nasal trial began on 2/12 for all total joint patients
- Zero MRSA infections were identified after intervention implementation; actual readmission cost savings of $62,302

*Note: 3M Skin and Nasal trial began 2/12 for all total joint patients


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Clinical Studies Hogenmiller
Before-and-after intervention study comparing SSI rates in total joint arthroplasty surgery

Best practice bundle:
- Sage® 2% CHG cloths
- 3M™ Skin and Nasal Antiseptic applied in preop
- Warming 30 min preop and in surgery with 3M™ Bair Paws™ System
- Antibiotic infusion completed 10 min prior to incision
- Team huddle to review checklist and coordinate start time for opening of instruments

Results:

The number of THA/TKA SSIs was reduced to zero in the 7-month period following implementation of the best practice bundle.

Clinical Studies Osborn
Before-and-after intervention study comparing SSI rates in spine fusion surgery

Intervention:
• Jan 2013 embedded infection preventionist in the OR
• June 2013 implemented bundle:
  • 3M™ Skin and Nasal Antiseptic morning of surgery
  • CHG bathing
  • Prewarming with 3M™ Bair Paws System

Results:
- 61% reduction in spine fusion infections in 12 months resulting in a cost savings of $228,635
- Surgeries without the intervention had 5 times the number of infections

Osborn N, Reynolds L. Embedding an Infection Preventionist (IP) in the OR. Presented at the AORN Surgical Conference and Expo, Denver, CO, March 2015.
Evidence-Does Formulation Matter?
Efficacy study (ex vivo)

Compare the efficacy of PI formulations against MRSA on porcine vaginal mucosa

- Explants infected with MRSA (USA 300) or high level mupirocin resistant isolate (476 or 920)

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 3M™ Skin and Nasal Antiseptic (5% PI)</td>
</tr>
<tr>
<td>• Clorox Healthcare™ Nasal Antiseptic (10% PI)</td>
</tr>
<tr>
<td>• Betadine® Solution (10% PI)</td>
</tr>
<tr>
<td>• untreated (control)</td>
</tr>
</tbody>
</table>

- Mucin wash to simulate mucociliary clearance
- Evaluated at 1, 6 and 24 hours post wash

Log Reduction

- To keep the individual numbers of microbes manageable, microbiologists usually express them using scientific notation.
- Taking the log value of a large number, such as the number of cells killed in a test, transforms it into a smaller one that is easier to work with.
- “Log reduction” is a mathematical term used to show the relative number of live microbes eliminated from an anatomical site by an antimicrobial product.
- Number of bacteria remaining depends on number initially present (baseline)
- One log reduction = 10 fold (90%) reduction in the number of bacteria
- Example:
  - Baseline – start with 100 live bacteria = 2 logs
  - Reduction = 1 log
  - Remaining – left with 10 live bacteria = 1 log
Results

MRSA Log$_{10}$ Reduction (mean reduction across all isolates)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Timepoint</th>
<th>1 hour</th>
<th>6 hours</th>
<th>24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>3M Skin and Nasal Antiseptic</td>
<td></td>
<td>5.8 ± 0.26*</td>
<td>6.6 ± 0.47*</td>
<td>6.9 ± 0.41*</td>
</tr>
<tr>
<td>Clorox Healthcare Nasal Antiseptic</td>
<td></td>
<td>4.1 ± 0.42</td>
<td>3.5 ± 0.4</td>
<td>2.4 ± 0.51</td>
</tr>
<tr>
<td>Betadine Solution</td>
<td></td>
<td>4.8 ± 0.41</td>
<td>4.1 ± 0.60</td>
<td>1.9 ± 0.37</td>
</tr>
</tbody>
</table>

* denotes significant difference from other treatments (p≤0.05)

3M Skin and Nasal Antiseptic was significantly more effective than Clorox and Betadine at reducing MRSA at 1, 6 and 24 hours.
Conclusion

3M Skin and Nasal Antiseptic was persistent and superior to Clorox Healthcare Nasal Antiseptic and Betadine Solution for reducing MRSA (including MRSA high-level mupirocin-resistant isolates) burden over 24 hours.
Clinical Studies

Randomized controlled trial comparing *S. aureus* cultures at baseline and after application of nasal treatment in patients undergoing total joint arthroplasty

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized to either:</td>
</tr>
<tr>
<td>• Off the shelf 10% povidone iodine (10%PI)</td>
</tr>
<tr>
<td>• 3M™ Skin and Nasal Antiseptic (5% PI)</td>
</tr>
<tr>
<td>• Saline (control)</td>
</tr>
</tbody>
</table>

Nasal swabs were taken preoperatively prior to nasal treatment (baseline), and again at 4 hours and 24 hours after treatment.

• 429 patients were randomized, of which 95/429 (22.1%) were positive at baseline for S. aureus and 13.6% of these were MRSA.
• 5% PI formulation demonstrated significantly more effective intranasal decolonization of S. aureus over the 4 hour time interval (p=0.003).
• 10% PI no different than saline (control)
Conclusion

The specially formulated 5% PI solution, which contains a specific adherent polymer, remains in the nares for a longer period, which may explain its better efficacy.
### Not all formulations are created equal

<table>
<thead>
<tr>
<th></th>
<th>Polymeric solution with swabs for nasal use</th>
<th>Povidone iodine saturated swabs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active Ingredient</strong></td>
<td>5% PI</td>
<td>10% PI</td>
</tr>
<tr>
<td><strong>Formulation</strong></td>
<td>Patented formula designed specifically for the nose</td>
<td>?</td>
</tr>
<tr>
<td><strong>Proven efficacy in the nose</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Clinical studies with SSI outcome</strong></td>
<td>9</td>
<td>0</td>
</tr>
</tbody>
</table>

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Summary of Clinical Evidence

One time application of 5% PI Nasal Antiseptic helps reduce the risk of SSI when part of a comprehensive preoperative protocol1-9

It is cost effective1-3

It has better antimicrobial efficacy in the nose than 10% PVP-I10


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Questions?
Thank you