Antimicrobial Surfaces to Prevent Healthcare-Associated Infection

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Healthcare Associated Infection (HAI)

- 4% to 10% of hospitalized patients affected\(^1,2\)
- Results in death, disability, prolonged stay
- Huge associated costs
- Most HAI are preventable\(^3\)
- Contamination of the environment is not the primary cause of HAI but does contribute

2. Magill SS et al. NEJM 2014;370(13)
3. Umscheid CA et al. ICHE 2011:32
What is the role of the environment in infection transmission?

• The strength of evidence linking environmental contamination with infection is increasing

• Key pathogens such as MRSA, VRE and *C. difficile*
  – Are frequently found in the hospital environment
  – Can persist with weeks to months in the environment
  – Contaminate the hands/gloves of healthcare workers who enter a contaminated environment
  – Can be transmitted from one surface to another on the hands of healthcare workers

Dancer SJ. Clin Micro Rev 2014:27(4)
Prior room occupants

• Patients have a higher risk of acquiring certain infections or pathogens if they are admitted to the room of a patient that had that infection

• Examples
  – MRSA
  – VRE
  – *C. difficile*
  – Acinetobacter

Dancer SJ. Clin Micro Rev 2014:27(4)
Risk of Acquiring Antibiotic-Resistant Bacteria From Prior Room Occupants

• Examined 11,000 admission in 8 ICU
• Looked at whether new MRSA and VRE cases were more common in patients admitted to a room where the last occupant had MRSA or VRE
• >11,000 admissions evaluated and 10,151 could be studied

Huang SS et al. Arch Intern Med 2006:166
11528 ICU Room Stays

1377 (11.9%) Ineligible
- Occupant MRSA Positive Before ICU Admission

10151 (88.1%) Eligible

1454 (14.3%) Exposed
- Prior Occupant MRSA Positive
  - 57 (3.9%) MRSA Positive
    - Acquired MRSA During ICU Stay
  - 1397 (96.1%) MRSA Negative
    - No MRSA Acquired During ICU Stay

8697 (85.7%) Unexposed
- Prior Occupant MRSA Negative
  - 248 (2.9%) MRSA Positive
    - Acquired MRSA During ICU Stay
  - 8449 (97.1%) MRSA Negative
    - No MRSA Acquired During ICU Stay
Risk of Acquiring Antibiotic-Resistant Bacteria From Prior Room Occupants

• MRSA: 3.9% vs. 2.9% (OR 1.4) p=0.04
• VRE: 4.5% vs. 2.8% (OR 1.4) p=0.02
• 40% increased risk if patient admitted to room previously occupied by an MRSA / VRE patient
• Explained 5% of MRSA and 7% of VRE transmission
Author’s Conclusions

• We found a 40% increased odds of transmission of MRSA/VRE attributable to the status of prior room occupants, strongly suggesting a role of environmental contamination, despite room cleaning methods that exceeded national standards.

• This risk accounts for a small fraction of the total cases of acquired MRSA/VRE.
Challenges in Environmental Cleaning

• Complex environment
• Insufficient Resources
• Lack of training / education
• Failure of routine cleaning and disinfection to remove all pathogens

→ We need to optimize environmental cleaning!
Best Practices for Environmental Cleaning for Prevention and Control of Infections
In All Health Care Settings - 2nd edition

Provincial Infectious Diseases
Advisory Committee
(PIDAC)

First Published: December 2009
Revised: May 2012
PIDAC Best Practices Document

• Document developed by PIDAC-IPC with input from stakeholders – now due for revision

• What is new since 2012 that could enhance environmental cleaning?
Focus on new technologies

- Audit and feedback
- No touch disinfection
- Antimicrobial surfaces
What are Antimicrobial Surfaces?

- Surfaces that are easily cleanable
- Surfaces that resist contamination
- Surfaces that actively eliminate bacteria
PIDAC Recommendations (2012)

- Surfaces should be durable, cleanable, and unable to support microbial growth
- Surfaces features that should be avoided (as they increase the risk of microbial growth)
  - Surfaces that hold moisture
  - Wood surfaces
  - Porous surfaces (e.g. textiles)
  - Surfaces with seems
- Surfaces that are preferred
  - Metals and hard plastics
- But what about surfaces that actively kill or reduce microbial growth?
Antimicrobial Surfaces

• Antimicrobials surfaces are surfaces designed to
  – Kill bacteria
  – Resist bacterial adhesion
  – Prevent biofilm formation

• Mechanisms
  – Biocide leaching (release of a cytotoxic compound)
  – Contact killing (disruption of cell membranes in contact with the surface)
  – Adhesion prevention (via a super-hydrophobic covering)

• Research has identified surfaces or surface coatings with persistent antimicrobial properties

  1. Abreu AC et al. JAC 2013:68;2718-2732
Antimicrobial Surfaces

• Potential value
  – Reduce contamination of surfaces
  – Delay recontamination of surfaces

• Surfaces and surface coatings under study
  – Metals (e.g. Copper, Silver)
  – Antimicrobials, Antiseptics
  – Micro-scale patterned surfaces (e.g. Sharklet™)
Microorganism contaminated surface → Direct transfer → Healthcare worker → Patient

Microorganism contaminated surface → Direct transfer → Antimicrobial Surface Coating

Microorganism contaminated surface → Direct transfer → Healthcare worker → Patient

Page K et al. J Material Chem 2009
PIDAC recommendations (2012)

• Treated surfaces have not been well studied in clinical settings
• Little data exists to show how these antimicrobial chemicals will endure after exposure to frequent cleaning, or whether they will prevent disease.
• The only surface that has been shown to be effective in reducing bacterial load in field testing in hospitals is copper
• The use of copper-containing materials for surfaces in the hospital environment may prove to be an adjunct for the prevention of HAIs but requires further evaluation. It does not replace the need for routine cleaning and disinfections.

54. Surfaces treated with antimicrobial substances are not recommended.
Potential Advantages

• Routine and discharge cleaning/disinfection is periodic – recontamination occur rapidly
• Other novel technologies (e.g. no-touch disinfection) are also periodic
• Routine cleaning/disinfection is not always effective at removing pathogens
• Antimicrobial surfaces work ‘24/7’ to reduce microbial contamination and may add to routine cleaning / disinfection
• But what is the evidence?
Questions

• What antimicrobial surface options are there?
• Have they been tested in a real clinical environment?
• Do they reduce contamination?
• Do they reduce infection?
• Other questions?
  – Which type of surface?
  – Which and how many objects must be coated / treated?
  – Are they durable?
PIDAC Approach

• Systematic review of the literature
• Use of the Grading recommendations Assessment, Development, and Evaluation (GRADE) approach
• GRADE is a systematic and transparent methodology to aid in guideline recommendation development
  – Strength of evidence
  – Strength of recommendation
• Being piloted by PIDAC-IPC
GRADE strength of evidence

• For a specific intervention and outcome, how strong is the evidence of benefit (or harm)?
• Categories = high, moderate, low or very low quality evidence
• Determined by study design (e.g. from ‘high’ for randomized controlled trials to ‘very low’ for uncontrolled before-after studies)
• Strength of evidence can be downgraded based on
  – Risk of bias, inconsistency, indirectness, imprecision, publication bias
GRADE strength of recommendation

• Determined by
  – Strength of evidence
  – Balance of benefit versus harm
  – Resource requirement
  – Patients’ values and preferences
Methods

• Systematic review of the literature
• Review of MEDLINE and other relevant databases
• Inclusion Criteria
  – Study design – controlled clinical trials, quasi-experimental studies, cohort or case control studies
  – Setting – patient rooms in hospitals or long term care facilities
  – Intervention – antimicrobial materials that do not require reapplication incorporated into or onto surfaces
  – Outcomes – infection rates, transmission of drug resistant bacteria, microbial contamination of surfaces
• Synthesis of data, evaluation of risk of bias, GRADE strength of evidence
Results

6011 citations identified from literature search and reference review

225 duplicate articles excluded

5786 non-duplicate publications

5551 articles excluded based on title/abstract review

235 full text articles reviewed

224 articles excluded due to:
Not hospital or LTCF setting (n=100)
Did not evaluate antimicrobial surface (n=60)
Not an experimental, quasi-experimental, cohort or case-control study (n=43)
Did not use HAI, ARO or microbial contamination/bioburden as an outcome (n=19)
Not published in English (n=2)

11 articles included

2 articles included in review of reduced HAI/ARO

11 articles included in review of reduced microbial contamination
Study Design

• All 11 studies looked at microbial contamination
• Interventions assessed included
  – Copper (7)
  – Organosilane (2)
  – Silver (1)
  – Metal alloy – not specified (1 study)
• Surfaces evaluated ranged from hard surfaces (e.g. bedrails, light switches) to textiles (e.g. curtains, clothes)
• Number of surfaces included per room ranged from 1 to ‘all’
• 10 of 11 studies reported on ‘overall bacterial contamination’
• Some studies looked at specific pathogens like MRSA (4), VRE (4) or C. difficile (3)
Study Design

• Studies were controlled trials (9) or before-after studies (2)
• 8 studies done on a single ward
• Did not report potential confounding factors
  – Adherence to environmental cleaning practices
  – Hand hygiene
• All industry sponsored/supported or included authors from industry
Microbial Contamination

• 5/7 copper studies showed a reduction in overall microbial contamination
• Median reduction in contamination was $<1 \log_{10}$ ($<1$ to 2 logs)
• Limited data for other surfaces
  – 2 Organosilane studies with opposite results
  – 1 silver study showing $1 \log_{10}$ reduction
Infection Outcomes

• 2 studies evaluated clinically important outcomes\textsuperscript{1,2}

1. Salgado et al. ICHE 2013;34;479-486
Salgado et al.

• ‘RCT’ of copper alloy surfaces in 3 ICU
• 8 intervention rooms and 8 control rooms
• Six standard items were replaced with copper items in the intervention rooms
  – Bed rails, bed table, IV poles, arms of visitor’s chair plus 2 of: call button, computer mouse, monitor bezel, laptop palm rest
• Patients assigned by usual hospital practices to intervention or control room (or other room)
• Outcome = HAI and MRSA/VRE colonization
Salgado et al. Results

650 patients (unique identifiers) initially randomized

614 randomized unique patients included in analysis

Exclusions:
- 12 missing primary outcome only
- 3 missing study room only
- 21 missing both

294 assigned to receive care in ICU rooms with copper-surfaced objects

137 received care in rooms where all six copper-surfaced objects remained in room for entire LOS

320 assigned to receive care in ICU rooms without copper surfaced objects

277 received care in rooms where no copper surfaced object was placed in room for entire LOS
Salgado et al. Results

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Copper</th>
<th>Noncopper</th>
<th>Total</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td>.17</td>
</tr>
<tr>
<td>&lt;40 years</td>
<td>23 (7.82)</td>
<td>38 (11.91)</td>
<td>61 (9.95)</td>
<td></td>
</tr>
<tr>
<td>40–64 years</td>
<td>147 (50.00)</td>
<td>162 (50.78)</td>
<td>309 (50.41)</td>
<td></td>
</tr>
<tr>
<td>≥65 years</td>
<td>124 (42.18)</td>
<td>119 (37.30)</td>
<td>243 (39.64)</td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>185 (62.93)</td>
<td>199 (62.19)</td>
<td>384 (62.54)</td>
<td>.85</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
<td>.25</td>
</tr>
<tr>
<td>Asian</td>
<td>5 (1.74)</td>
<td>8 (2.61)</td>
<td>13 (2.19)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>78 (27.18)</td>
<td>100 (32.57)</td>
<td>178 (29.97)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>198 (68.99)</td>
<td>197 (64.17)</td>
<td>395 (66.50)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>4 (1.39)</td>
<td>2 (0.65)</td>
<td>6 (1.01)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (0.70)</td>
<td>0 (0)</td>
<td>2 (0.34)</td>
<td></td>
</tr>
<tr>
<td>Infection at admission</td>
<td>140 (47.62)</td>
<td>169 (52.81)</td>
<td>309 (50.33)</td>
<td>.20</td>
</tr>
<tr>
<td>APACHE II score</td>
<td></td>
<td></td>
<td></td>
<td>.51</td>
</tr>
<tr>
<td>&lt;20</td>
<td>119 (40.48)</td>
<td>111 (34.69)</td>
<td>230 (37.46)</td>
<td></td>
</tr>
<tr>
<td>20–30</td>
<td>120 (40.82)</td>
<td>145 (45.31)</td>
<td>265 (43.16)</td>
<td></td>
</tr>
<tr>
<td>31–40</td>
<td>49 (16.67)</td>
<td>58 (18.13)</td>
<td>107 (17.43)</td>
<td></td>
</tr>
<tr>
<td>&gt;40</td>
<td>6 (2.04)</td>
<td>6 (1.88)</td>
<td>12 (1.95)</td>
<td></td>
</tr>
<tr>
<td>Site*</td>
<td></td>
<td></td>
<td></td>
<td>.43</td>
</tr>
<tr>
<td>MSKCC (6 rooms)</td>
<td>108 (36.73)</td>
<td>113 (35.31)</td>
<td>221 (35.99)</td>
<td></td>
</tr>
<tr>
<td>MUSC (6 rooms)</td>
<td>97 (32.99)</td>
<td>121 (37.81)</td>
<td>218 (35.50)</td>
<td></td>
</tr>
<tr>
<td>RHJVA (4 rooms)</td>
<td>89 (30.27)</td>
<td>86 (26.88)</td>
<td>175 (28.50)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Copper $(n = 294)$</td>
<td>Noncopper $(n = 320)$</td>
<td>Total</td>
<td>$P$</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-------------------</td>
<td>-----------------------</td>
<td>-------</td>
<td>-----</td>
</tr>
<tr>
<td><strong>Primary outcome: new HAI or colonization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No HAI or colonization</td>
<td>273 (92.86)</td>
<td>279 (87.19)</td>
<td>552 (89.90)</td>
<td></td>
</tr>
<tr>
<td>HAI and/or colonization</td>
<td>21 (7.14)</td>
<td>41 (12.81)</td>
<td>62 (10.10)</td>
<td>.020</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAI only</td>
<td>10 (3.40)</td>
<td>26 (8.12)</td>
<td>36 (5.86)</td>
<td>.013</td>
</tr>
<tr>
<td>Colonization only</td>
<td>4 (1.36)</td>
<td>12 (3.75)</td>
<td>16 (2.61)</td>
<td>.063</td>
</tr>
<tr>
<td><strong>ICU length of stay</strong></td>
<td></td>
<td></td>
<td></td>
<td>.96</td>
</tr>
<tr>
<td>0–2 days</td>
<td>72 (24.49)</td>
<td>73 (22.81)</td>
<td>145 (23.62)</td>
<td></td>
</tr>
<tr>
<td>3–4 days</td>
<td>95 (32.31)</td>
<td>108 (33.75)</td>
<td>203 (33.06)</td>
<td></td>
</tr>
<tr>
<td>5–7 days</td>
<td>63 (21.43)</td>
<td>69 (21.56)</td>
<td>132 (21.50)</td>
<td></td>
</tr>
<tr>
<td>&gt;7 days</td>
<td>64 (21.77)</td>
<td>70 (21.88)</td>
<td>134 (21.82)</td>
<td></td>
</tr>
<tr>
<td>Died in ICU</td>
<td>42 (14.29)</td>
<td>50 (15.63)</td>
<td>92 (14.98)</td>
<td>.64</td>
</tr>
</tbody>
</table>
Salgado et al. Results

- Intervention and control patients similar
  - But trend to sicker patients in non-copper room
  - No data on presence of catheters or central lines, antibiotic use, or mechanical ventilation
- Large reduction in HAI
  - 3.4% (10/294) in copper room vs. 8.1% (26/320) in non-copper room
  - 58% relative risk reduction!
  - Most of reduction due to fewer bloodstream infections (3 vs. 11) and fewer ‘other’ infections (0 vs. 5) [p=0.013]
- Trend to large reduction in antibiotic resistant organism transmission
  - 1.4% (4/294) in copper room vs. 3.8% (12/320) in non-copper room [p=0.063]
  - 64% relative risk reduction
# Risk of Bias

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Salgado <em>et al.</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Was the allocation sequence adequately generated?</td>
<td>Red</td>
</tr>
<tr>
<td>Was the allocation adequately concealed?</td>
<td>Red</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Yellow</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>Green</td>
</tr>
<tr>
<td>Were incomplete outcome data adequately addressed?</td>
<td>Yellow</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>Red</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>Yellow</td>
</tr>
<tr>
<td>Was the study free from selective outcome reporting?</td>
<td>Green</td>
</tr>
<tr>
<td>Was the study free of other sources of bias?</td>
<td>Green</td>
</tr>
</tbody>
</table>

Red = high risk of bias, Green = low risk of bias, Yellow = unclear risk of bias
Lazary et al.

- Uncontrolled before-after study of copper impregnated textiles in 1 long term care ward
- Regular textiles (linens, patient gowns) replaced by copper oxide impregnated textiles
- HAI rates were compared 6 months before and 6 months after replacement of textiles
Lazary et al. Results

- Patients during the intervention period were less likely to have urinary catheters (22% vs. 31%) or pressure sores (17% vs. 26%) or to be on corticosteroids (19% vs. 30%).
- 27.2 vs. 20.8 HAI per 1000 patient day baseline vs. intervention period (p=0.05)
- 24% reduction in HAI with intervention
- Most of the reduction due to fewer GI (1 vs. 13) and eye (9 vs. 20) infections
Interpretation

• Both studies showed reductions in HAI
• Lazary et al. at high risk of bias
  – High risk study design, not blinded
  – Differences in population at baseline
• Salgado et al. at moderate risk of bias
  – Not really a randomized study
  – Incomplete blinding
  – Possible differences in populations at baseline and unmeasured confounders
  – Implausible benefit?
• Neither reported adherence to routine cleaning
<table>
<thead>
<tr>
<th>Study</th>
<th>Outcome</th>
<th>Control</th>
<th>Copper surfaces</th>
<th>Relative risk</th>
<th>Relative risk reduction</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salgado et al.</td>
<td>HAI per patient</td>
<td>26/320</td>
<td>10/294</td>
<td>0.42 ($P=0.013$)</td>
<td>58%</td>
<td>🟢🟢🟢</td>
</tr>
<tr>
<td>Lazary et al.</td>
<td>HAI per patient day</td>
<td>118/4337</td>
<td>82/3940</td>
<td>0.76 ($P=0.046$)</td>
<td>24%</td>
<td>🟢🟢🟢</td>
</tr>
<tr>
<td>Salgado et al.</td>
<td>ARO per patient</td>
<td>12/320</td>
<td>4/294</td>
<td>0.36 ($P=0.063$)</td>
<td>64%</td>
<td>🟢🟢🟢</td>
</tr>
</tbody>
</table>

Abbreviations: 🟢🟢🟢🟢 = low quality of evidence, 🟢🟢🟢🟢 = very low quality of evidence
Conclusions

• Among potentially useful antimicrobials surfaces, only copper surfaces have been widely tested in the clinical environment
• Only 2 studies looked at clinical outcomes
• Copper surfaces reduce overall bacterial contamination ~50% to 90% (0 to 1 log)
• Both show a reduction in HAI but both were at moderate to high risk of bias
Conclusions

• GRADE quality of evidence – there is very low quality evidence supporting the use of copper to reduce HAI
  – Salgado downgraded from high to low quality due to lack of proper randomization, incomplete blinding
  – Overall body of evidence downgraded due to risk of publication bias and imprecision

• PIDAC will need to derive a recommendation based on this evidence
Unanswered Questions

• What are the key surfaces associated with infection transmission?
• What degree of antimicrobial contamination is ‘significant’?
• Is the antimicrobial effect of copper durable?
• What is the cost of copper relative to other surfaces and interventions?
Future Research

• Copper studies should be prioritized
• We need better study designs, careful measurement of confounding factors, and focus on clinical outcomes
• Some non-industry funded studies
• Head to head comparisons
  – Copper versus silver
  – Copper versus UV light
  – Copper versus fluorescent marking
PIDAC revised recommendation

Surfaces treated with antimicrobial substances are not recommended (2012)
Final Thought

• No technology will replace the need for trained and dedicated environmental services staff performing manual cleaning

• Emerging technologies should complement and facilitate the role of environmental services staff
Questions?