Science Behind Infection Prevention

Matt Scholz
Corporate Scientist

3M™ Company
Webinar Objectives

1. Discuss the concept of using bundles,
2. Understand the cost and challenges of doing various clinical study designs,
3. Understand the importance of formulated drug products
4. Describe some of the latest developments in Infection Prevention including
   a. Nasal Decolonization,
   b. Preoperative patient preps,
   c. Technology to reduce BSIs,
   d. Technology to reduce VAP, Technology to reduce CAUTI.
Housekeeping

- 50 minute presentation followed by question and answer period.
- Today’s topic does not qualify for CE credit due to brand usage/commercial content.
- To ask a question, click on the live questions tab under the video window and type your question in the box and hit send. Questions will be addressed after the video presentation. Questions can be entered at any time.
Science Behind Infection Prevention

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Bundles, Bundles, Bundles…

- **Bundles** = a collection of proven or scientifically sound interventions that should positively influence a desired outcome. Pioneered by IHI

- **Why use the bundle?**
  - Set of best practices supported by clinical studies and/or scientific basis
  - Structured way to improve outcomes.
  - Small set of processes simply checked for compliance
Level of Proof

• Why can’t someone just show me which product is best?
  – Inherent variability of biological samples
  – Cannot always do a Randomized Controlled Clinical Trial with controls (FDA/Clinician)
  – Cannot always afford a RCT
  – Types of Clinical trials
    • RCTs: parallel, cross over, cluster, etc.
    • Observational (prospective analytical observational study)
    • Case controlled (retrospective, analytical, obs study)
    • Prevalence Study (disease state at one point in time)
    • Case Series (descriptive, observational, series of cases)
    • Case Report (anecdotal evidence)
Sample size calculations: clinical trial of treatment A vs. no treatment

- Hypothesis: no effect of treatment A vs. no treatment
- Assume: Infection rate = 1%
- Goal: demonstrate 25% reduction in infection rate.

- For alpha = 0.05 and power = 80%:
  \[ N \sim 44 \, 000 \]

- For alpha = 0.05 and power = 90%:
  \[ N \sim 60 \, 000 \]

http://www.health.ucalgary.ca/~rollin/stats/ssize/b2.html
Meta-analysis

• Meta-analysis = Statistical analysis of results from a collection of studies to integrate the findings
  - Collect “like” studies with predetermined criteria
  - Statistically analyze aggregate data

– Pros:
  • Ability to reach statistical significance by combining a collection of smaller studies
  • Able to formulate new hypotheses

– Issues with Meta-analyses
  • Often studies are combined that should not be
  • Not as strong as a large RCT
Evidence

FDA View¹:
For NDA Approval need:
- “substantial evidence” – 2 well controlled independent studies (only 1 in special circumstances)
- Drug vs. placebo
- Phase I, II, and III studies
- Meta-analysis or pooled studies will not suffice
- Result must be CLINICALLY RELEVANT

• Meta-analysis has been used to establish OTC status

Anello, J Evid Based Dent Prac, 4 (1), Mar 2004, 52-58
Good Meta-analyses...

• Should not mix results of “unlike” formulations
  – Compositions are NOT simply related due to drug type and concentration.
    • Excipients play an important and often critical role
    • Formulations with secondary actives should be excluded
    • Formulations should not be “pharmacy made”
  – Use studies with same dose of ALL drugs
  – Same study duration
So RCT or Observational?

• RCT preferred by FDA
  – Drug vs. Placebo

• Clinicians want Drug A vs Drug B

• RCT vs. Observational:
  – Benson et. al.\textsuperscript{2} “We found little evidence that estimates of treatment effects in observational studies reported after 1984 are either consistently larger than or qualitatively different from those obtained in RCTs”
    • Studied 136 reports of 19 treatments (1985-1998)

Benson et al., NEJM 2000 342 (25), 1878-86
What’s Current and What’s New in Infection Prevention?

- SSI
- BSI
- VAP
- Horizontal Spread
Guidelines used:

• SHEA/IDSA Practice Recommendation
  – ICHE, Oct. 2008 Vol. 29 suppl 1
  – Burden & recommendations referenced herein
  – Evidence:
    • A = good evidence to support a recommendation
    • B = moderate evidence to support a recommendation
    • C = poor evidence to support a recommendation
    • I = Evidence from ≥1 properly randomized controlled trial
    • II = Evidence from ≥1 well designed but not randomized trial
      – (time series, cohort or case controlled analytic study, dramatic results of uncontrolled)
    • III = Evidence from KOLs, clinical experience, etc.
Preventing SSI

- Burden
  - SSIs occur in 2-5% of patients undergoing surgery in the US
  - SSI adds 7-10 addl post op days
  - SSI pts have 2-11X risk of death
  - Cost $3000-$29000/inf patient

- Current Guidelines
  - Surgical scrub (2-5 min soap or alcohol) (AII)
  - Skin prep- clean/wash w/ appropriate antiseptic (AII)
  - Antimicrobial prophylaxis at appropriate time (AI)
  - Surgical technique (tissue care/dead space) (AIII)
  - Minimize operative time (AIII)
  - Theatre ventilation (C-I)
  - Traffic (B-II)
  - Environmental surfaces cleaned with disinfectant (B-III)
  - Surgical equipment sterilization per guidelines (B-I)
Causes of SSI

- Risk for SSI = \( \text{Microbial load} \times \text{Virulence} \times \text{pt. immune status} \)

- Microbial load from:
  - Patient skin flora
  - Clinician skin flora
  - Nasal Colonization

4. ICHE 1999 20(4) 247-278
What’s New in SSI?

• Nasal Decolonization/Patient Bathing\(^5\)
  – BODE et al. studied nasal decolonization with mupirocin + CHG (Hibiscrub\(^\text{TM}\))
  – RCT Trial, SA carriers
    • 6771 pts screened
      – 504 in treatment  17 infections  (3.4%), LOS= 12.2 days
      – 413 in placebo  32 infections  (7.7%), LOS= 14 days

5. Bode et. al. NEJM, 2010, 362(1), 9-17
Bode et al. Results

Table 2. Relative Risk of Hospital-Acquired *Staphylococcus aureus* Infection and Characteristics of Infections (Intention-to-Treat Analysis).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mupirocin-Chlorhexidine (N = 504)</th>
<th>Placebo (N = 413)</th>
<th>Relative Risk (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S. aureus infection</strong></td>
<td>17 (3.4)</td>
<td>32 (7.7)</td>
<td>0.42 (0.23–0.75)</td>
</tr>
<tr>
<td><strong>Source of infection</strong>†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endogenous</td>
<td>12 (2.4)</td>
<td>25 (6.1)</td>
<td>0.39 (0.20–0.77)</td>
</tr>
<tr>
<td>Exogenous</td>
<td>4 (0.8)</td>
<td>6 (1.5)</td>
<td>0.55 (0.16–1.92)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td></td>
</tr>
<tr>
<td><strong>Localization of infection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep surgical site‡</td>
<td>4 (0.9)</td>
<td>16 (4.4)</td>
<td>0.21 (0.07–0.62)</td>
</tr>
<tr>
<td>Superficial surgical site‡</td>
<td>7 (1.6)</td>
<td>13 (3.5)</td>
<td>0.45 (0.18–1.11)</td>
</tr>
<tr>
<td>Lower respiratory tract</td>
<td>2 (0.4)</td>
<td>2 (0.5)</td>
<td>0.82 (0.12–5.78)</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>1 (0.2)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bacteremia</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Soft tissue</td>
<td>2 (0.4)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Mupirocin Resistance

Conclusions:
1. No isolates resistant to Mupirocin or Exp. Antiseptic were detected before serial passage.
2. Emergence of resistance to Mupirocin was detected following serial passage.
3. No Emergence of resistance to Exp Antiseptic was detected following serial passage.

4. Patel, AAC 2005, 49(8), 3187-91
3M™ Skin and Nasal Antiseptic (povidone-iodine solution 5% w/w (0.5% available iodine) USP) Patient Preoperative Skin Preparation

- Rapid antimicrobial activity on skin and nasal tissue in one hour
- Persistent activity
- Acceptable odor and taste
- Easy to apply- two 30 sec swabs/nare
Nasal Study - *in vivo*

Figure 1: 3M Skin and Nasal Antiseptic *S. aureus* Reduction in the Nares Post-prep for Subjects with Baseline Counts of at least 3.7 Log$_{10}$

Results: 3M Skin and Nasal Antiseptic:

- **killed 99.5% of bacteria within 1-hour**
- **maintained 99.5% kill for at least 12-hours post-prep**
Surgical Preop Patient Skin Prep

• Dariouche et. al. study
  – Chloraprep™ vs. Povidone Iodine

• Swenson et. al. Study
  – DuraPrep™ vs. Chloraprep vs. Povidone Iodine/alcohol

• Various other in-vitro studies
  – In-vitro results are not predictive of on-skin performance (TFM)
CHG Alcohol vs. PVP-I
Dariouche et. al. Study

- Randomized Controlled Trial, 6 sites
  - General Surgery:
    - Colorectal, small intestinal, gastroesophageal, biliary, thoracic, gynecologic, or urologic 849 pts
    - 409 in CHG/alcohol (ChloraPrep)
    - 440 in povidone iodine (scrub and paint)

Table 2. Proportion of Patients with Surgical-Site Infection, According to Type of Infection (Intention-to-Treat Population).

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Chlorhexidine–Alcohol (N=409)</th>
<th>Povidone–Iodine (N=440)</th>
<th>Relative Risk (95% CI)*</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any surgical-site infection</td>
<td>39 (9.5)</td>
<td>71 (16.1)</td>
<td>0.59 (0.41–0.85)</td>
<td>0.004</td>
</tr>
<tr>
<td>Superficial incisional infection</td>
<td>17 (4.2)</td>
<td>38 (8.6)</td>
<td>0.48 (0.28–0.84)</td>
<td>0.008</td>
</tr>
<tr>
<td>Deep incisional infection</td>
<td>4 (1.0)</td>
<td>13 (3.0)</td>
<td>0.33 (0.11–1.01)</td>
<td>0.05</td>
</tr>
<tr>
<td>Organ-space infection</td>
<td>18 (4.4)</td>
<td>20 (4.5)</td>
<td>0.97 (0.52–1.80)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Sepsis from surgical-site infection</td>
<td>11 (2.7)</td>
<td>19 (4.3)</td>
<td>0.62 (0.30–1.29)</td>
<td>0.26</td>
</tr>
</tbody>
</table>

* Relative risks are for chlorhexidine–alcohol as compared with povidone–iodine. The 95% confidence intervals were calculated with the use of asymptotic standard-error estimates.
† P values are based on Fisher’s exact test.

6. Dariouche, 2010 NEJM 362(1) 18-26
DuraPrep vs. ChloraPrep vs. Povidone Iodine
Swenson et. al. Study

- Observational Time Series Trial, Single Site
  - All General Surgery:
    - 794 Iodine Povacrylex (DuraPrep)
    - 827 in CHG/alcohol (ChloraPrep)
    - 1514 in povidone iodine (scrub, 70% IPA, paint)

### Table 4: Surgical-Site Infections (SSIs) and Wound Classifications, by Preparation Solution Actually Received

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of SSIs</th>
<th>No. of surgical procedures</th>
<th>Povidone-iodine (n = 1,514 procedures)</th>
<th>Chlorhexidine (n = 827 procedures)</th>
<th>Iodine povacrylex (n = 794 procedures)</th>
<th>P²</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All¹</td>
<td>178</td>
<td>...</td>
<td>72 (4.8)</td>
<td>68 (8.2)</td>
<td>38 (4.8)</td>
<td>.001</td>
</tr>
<tr>
<td>Superficial</td>
<td>120</td>
<td>...</td>
<td>49 (3.2)</td>
<td>45 (5.4)</td>
<td>26 (3.3)</td>
<td>.019</td>
</tr>
<tr>
<td>Deep</td>
<td>11</td>
<td>...</td>
<td>6 (0.4)</td>
<td>4 (0.5)</td>
<td>1 (0.1)</td>
<td>.49</td>
</tr>
<tr>
<td>Organ/space</td>
<td>49</td>
<td>...</td>
<td>18 (1.2)</td>
<td>19 (2.3)</td>
<td>12 (1.5)</td>
<td>.12</td>
</tr>
<tr>
<td>Wound classification</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clean</td>
<td></td>
<td>1,154</td>
<td>6/714 (0.84)</td>
<td>5/224 (2.2)</td>
<td>3/216 (1.4)</td>
<td>.21</td>
</tr>
<tr>
<td>Clean-contaminated</td>
<td></td>
<td>1,409</td>
<td>44/541 (8.1)</td>
<td>46/454 (10.1)</td>
<td>27/414 (6.5)</td>
<td>.15</td>
</tr>
<tr>
<td>Contaminated</td>
<td></td>
<td>204</td>
<td>9/82 (11.0)</td>
<td>5/65 (7.7)</td>
<td>6/57 (10.5)</td>
<td>.78</td>
</tr>
<tr>
<td>Dirty</td>
<td></td>
<td>278</td>
<td>13/150 (8.7)</td>
<td>12/77 (15.6)</td>
<td>2/51 (3.9)</td>
<td>.076</td>
</tr>
</tbody>
</table>

**Note:** Data are no. (%) or proportion (%) of surgical procedures, unless otherwise indicated. Data were not available on all surgical procedures.

* For pairwise comparison with chlorhexidine.

b Of the 182 SSIs in the study, 4 involved surgical procedures that did not use any of the defined preparation solutions, so the total here is 178.

7. Swenson et. al. ICHE 2009 30(10), 964-970
Preventing CLABSI

• Burden
  – Risk of CLABSI in ICU is high
  – Risk in Non-ICU is substantial & most occur outside ICU
  – Cost $3700-$29000 per episode

• Risk Factors:
  – Prolonged hospitalization before catheterization
  – Prolonged duration of catheterization
  – Heavy microbial colonization at site
  – Heavy microbial colonization at hub
  – IJ catheterization
  – Neutropenia
  – Premature birth
  – Substandard catheter care (over/under care)
Preventing CLABSI

- **Current Guidelines**
  - Educate HCW involved on CVC care CLABSI (A-II)
  - Use catheter checklist (Aseptic technique) (B-II)
  - Hand Hygiene prior to insertion/manipulation (B-II)
    - Soap or alcohol
  - Avoid femoral vein (use subclavian) (A-I)
  - Use all inclusive cart or kit (B-II)
  - Max Barrier Precautions for CVC insertion (A-I)
  - Use Chlorhexidine prep in patients older than 2 mo. (A-I)
    - Alcohol with [CHG] >0.5%
  - Disinfect hubs (clean w/ 70% alcohol) (B-II)
  - Remove nonessential catheters (A-II)
  - Perform site care with CHG every 5-7 days or more (A-I)
  - Replace Admin sets not used for blood/blood prod/lipids (A-II)
    - Less than 96 hrs
  - Perform CLASI surveillance (A-I)
  - Use antimicrobial ointments for hemodialysis cath sites (A-I)
    - Use PVP-I r polysporin NOT mupirocin
For High Rate CLABSI

• Current Guidelines
  – Bath patients daily (B-II)
  – Use antimicrobial CVCs for adults (A-I)
    • CH-Silver sulf or minocycline/rifampin
  – Chlorhexidine sponge dressings (>2mo) (B-I)
  – Antimicrobial locks for CVCs (A-I)
What’s hot in fighting BSI?

• **CHG Prep**
  Chaiyakunpruk, Ann Intern Med 2002; 136:792-801
  Dariouche, 2010 NEJM 362(1) 18-26

• **CHG at site**
  – Biopatch
    Maki, 40th ICAAC Abstract 2000
  – Tegaderm CHG
    Maki, 2008 Abstract SHEA 2008
    Bashir, 2008 Abstract IDSA/ICAAC
**Table 1. Characteristics of Studies Comparing Chlorhexidine Gluconate Solutions with Povidone-Iodine Solutions for Vascular Catheter-Site Care**

<table>
<thead>
<tr>
<th>Study (Reference), Year</th>
<th>Antiseptic CHG Solution</th>
<th>Patient Population</th>
<th>Catheters and Patients, n/n</th>
<th>Mean Catheter Duration, d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>CHG Group</td>
<td>Povidone-Iodine Group†</td>
</tr>
<tr>
<td>Maki et al. (7), 1991</td>
<td>2% aqueous</td>
<td>ICU</td>
<td>214/214</td>
<td>227/227</td>
</tr>
<tr>
<td>Sheehan et al. (9), 1993</td>
<td>2% aqueous</td>
<td>ICU</td>
<td>169/94</td>
<td>177/95</td>
</tr>
<tr>
<td>Meffre et al. (10), 1995‡</td>
<td>0.5% alcohol</td>
<td>Any hospital unit</td>
<td>568/568</td>
<td>549/549</td>
</tr>
<tr>
<td>Minoz et al. (11), 1996</td>
<td>Biseprine§</td>
<td>ICU</td>
<td>170/NA</td>
<td>145/NA</td>
</tr>
<tr>
<td>Legras et al. (12), 1997</td>
<td>0.5% alcohol</td>
<td>ICU</td>
<td>208/88</td>
<td>249/102</td>
</tr>
<tr>
<td>LeBlanc and Cobett (13), 1999</td>
<td>0.5% alcohol</td>
<td>Any hospital unit</td>
<td>83/83</td>
<td>161/161</td>
</tr>
<tr>
<td>Humar et al. (14), 2000</td>
<td>0.5% alcohol</td>
<td>ICU</td>
<td>193/193</td>
<td>181/181</td>
</tr>
<tr>
<td>Knasinski and Maki, 2000†</td>
<td>1% alcohol</td>
<td>Any hospital unit</td>
<td>349/349</td>
<td>500/500</td>
</tr>
</tbody>
</table>

* CFU = colony-forming unit; CHG = chlorhexidine gluconate; ICU = intensive care unit; NA = not available.
† All studies used 10% povidone-iodine solution.
‡ Author provided additional information.
§ Biseprine (Nicholas, Gaillard, France) consists of 0.25% CHG, 0.025% benzalkonium chloride, and 4% benzyl alcohol.
‖ Required one of the following symptoms: fever, erythema, heat at the site, pain.
Table 2. Results of Studies Comparing Chlorhexidine Gluconate Solutions with Povidone-Iodine Solutions for Vascular Catheter-Site Care*

<table>
<thead>
<tr>
<th>Study (Reference), Year</th>
<th>Catheter Colonization</th>
<th>Catheter-Related Bloodstream Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Proportion of Positive Cultures</td>
<td>RR (95% CI) Using CHG Solution†</td>
</tr>
<tr>
<td></td>
<td>CHG Group</td>
<td>Povidone-Iodine Group</td>
</tr>
<tr>
<td>Maki et al. (7), 1991</td>
<td>5/214 (2.3)</td>
<td>21/227 (9.2)</td>
</tr>
<tr>
<td>Sheehan et al. (9), 1993</td>
<td>3/169 (1.8)</td>
<td>12/177 (6.8)</td>
</tr>
<tr>
<td>Meffre et al. (10), 1995†</td>
<td>9/568 (1.6)</td>
<td>22/549 (4.0)</td>
</tr>
<tr>
<td>Mizo et al. (11), 1996</td>
<td>12/170 (7.1)</td>
<td>24/145 (16.6)</td>
</tr>
<tr>
<td>Legras et al. (12), 1997</td>
<td>19/208 (9.1)</td>
<td>31/249 (12.4)</td>
</tr>
<tr>
<td>LeBlanc and Cobett (13), 1999†</td>
<td>6/83 (7.2)</td>
<td>23/161 (14.4)</td>
</tr>
<tr>
<td>Humar et al. (14), 2000</td>
<td>36/116 (31.0)</td>
<td>27/116 (23.3)</td>
</tr>
<tr>
<td>Knasinski and Maki, 2000‡</td>
<td>33/349 (9.5)</td>
<td>127/500 (25.4)</td>
</tr>
<tr>
<td>All studies</td>
<td>0.49 (0.31–0.71)</td>
<td>0.43 (0.33–0.55)</td>
</tr>
</tbody>
</table>

* CHG = chlorhexidine gluconate; RR = risk ratio.
† Risk ratio for use of chlorhexidine gluconate versus povidone-iodine.
‡ Author provided additional information.
Efficacy of Chlorhexidine-Impregnated Sponge (Biopatch) for the Prevention of Intravascular Catheter Related Infection - A Prospective, Randomized, Controlled, Multicenter Study*

- Transparent dressing vs. Transparent Dressing + CHG sponge (Biopatch)
- CVC, Pulmonary arterial, Peripheral arterial catheters
- No information on skin prep used etc.

<table>
<thead>
<tr>
<th>Group</th>
<th># colonized</th>
<th># catheters</th>
<th>% colonized</th>
<th>RR</th>
<th>CRBSI</th>
<th>%</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transparent Dressing</td>
<td>216</td>
<td>736</td>
<td>29</td>
<td></td>
<td>24</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>Transparent Dressing + Biopatch</td>
<td>109</td>
<td>665</td>
<td>16</td>
<td>0.62</td>
<td>8</td>
<td>1.2</td>
<td>0.38</td>
</tr>
</tbody>
</table>

Maki et. al., 40th ICAAC Abstract 2000
A Novel Integrated Chlorhexidine Impregnated Transparent Dressing for Prevention of Vascular Catheter Related Bloodstream Infection: A prospective Comparative Study in Healthy Volunteers*

**Suppression of Regrowth Following 1 min Prep with 70% IPA**

**Flora Reduction on Unprepped Skin**

**FIGURE 5.** Suppression of regrowth on prepped subclavian sites with the two CHG-impregnated dressings in healthy volunteers. At day 7, the new integrated CHG transparent dressing showed significantly lower regrowth post prep compared to the control (p<0.0001). At day 10, both CHG dressings showed significantly lower regrowth (p<0.0003). There was a statistically significant difference between the new integrated CHG-impregnated transparent dressing and the CHG-impregnated sponge dressing at day 7 (Δ log10 cfu 0.80, P<0.02).

**FIGURE 6.** In Vivo time kill of normal flora on unprepped skin with the two CHG-impregnated dressings in healthy volunteers. The likelihood-based repeated measures analysis, which included both dressing and time in the model, showed the new integrated CHG-impregnated transparent dressing to be significantly more effective than the CHG-impregnated sponge dressing in reducing floral counts on unprepped skin across all time points (P=0.008).

Maki, 2008 Abstract SHEA 2008
Suppression of Regrowth of Normal Skin Flora under Chlorhexidine Gluconate Dressings Applied to CHG Prepped Skin*

- ChloraPrep™ prepped skin
- Regrowth on back under Tegaderm CHG, Biopatch, Tegaderm
- N=30

* Bashir, 2008 Abstract IDSA/ICAAC
Tegaderm™ CHG

- Proven to be as effective as, or better, at reducing skin flora on healthy volunteers for up to 10 days than BIOPATCH{1}.

- Proven to be more effective at preventing re-growth on healthy volunteers at 7 days than BIOPATCH{1}.

- Transparent, allowing continuous visualization of insertion site.

- Integrated design of dressing and CHG gel pad reduces application steps and minimizes potential for application error.

- As easy-to-use and easy-to-train as a Tegaderm™ dressing.

Preventing VAP

- **Burden**
  - 1-4 cases/1000 ventilator days in ICU
  - Rates can exceed 10 cases/1000 in neonatal and surg
  - Mortality >10%
  - Cost $35,000 per episode

- **Note: Definition of VAP varies**
  - See National Healthcare Safety Network which requires
    - Clinical- vented w/in 48 hrs of onset (Fever, leukopenia, altered mental status)
    - Radiographic (infiltrate, consolidation, cavitation)
    - Microbiological (pleural fluid culture, LRT culture, BAL

1. Restrepo ICHE 2010 31(5):509-515
Preventing VAP

• Current Guidelines
  – Educate HCW who care for vented patients (A-II)
  – Surveillance (Direct observation for best practices) (B-III)
  – Surveillance of high risk patients (A-II)
  – Sterilization & maintenance of respiratory circuits (A-II)
  – Semi-recumbent position (B-II)
  – Regular antiseptic oral care (A-I)
  – Promote noninvasive ventilation (B-III)

• Special measures for high rates
  – ET tube with inline subglottic suction (B-II)
  – Continuously monitor bed incline (B-III)

• Process measures
  – Hand Hygiene prior to patient contact
  – Daily sedation interruptions
  – Compliance with regular antiseptic oral care
  – Compliance with semirecumbent position
IHI VAP Bundle*

1. Elevate Head of the Bed, 30-45 degrees
2. Daily sedation interruption and assessment to extubate
3. Use Peptic Ulcer Disease Prophylaxis
4. Deep Venous Thrombosis Prophylaxis
5. Daily Oral Care with Chlorhexidine

*5 million Lives Campaign, How to Guide: Prevent Ventilator Associated Pneumonia, IHI.org
What’s New to Prevent VAP?

– VAP- CHG rinses reduce LRTI 50%
  • 2 Meta-analyses:
    – Chan et. al. BMJ 2007; On-line First 1-11
    – Kola et. al. JHI 2007; 66:207-216

– Silver ET tubes
  • Kollef et. al. JAMA 2008; 300(7):805-813

– Subglottic suction
  • Meta-analysis:
Efficacy of Chlorhexidine in preventing lower respiratory tract infections. Meta-analysis of randomized trials*

- 7 RCTs for CHG rinse effect on LRTI
  - 0.12%(3), 0.2%(3) and 2%(1) CHG products
  - vs. placebo, usual care or comparator product
  - RR=0.56  CI: 0.44-0.72

<table>
<thead>
<tr>
<th>Study</th>
<th>CHX n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeRiso 1996</td>
<td>3/173</td>
<td>9/180</td>
<td>0.35 [0.10, 1.26]</td>
<td>5.73</td>
<td></td>
</tr>
<tr>
<td>Fourrier 2000</td>
<td>5/30</td>
<td>18/30</td>
<td>0.28 [0.12, 0.65]</td>
<td>11.69</td>
<td></td>
</tr>
<tr>
<td>Houston 2002</td>
<td>4/270</td>
<td>9/291</td>
<td>0.48 [0.15, 1.54]</td>
<td>5.63</td>
<td></td>
</tr>
<tr>
<td>Grap 2004</td>
<td>4/7</td>
<td>3/5</td>
<td>0.95 [0.36, 2.49]</td>
<td>2.27</td>
<td></td>
</tr>
<tr>
<td>Fourrier 2005</td>
<td>14/114</td>
<td>17/114</td>
<td>0.82 [0.43, 1.59]</td>
<td>11.04</td>
<td></td>
</tr>
<tr>
<td>Koemann 2006</td>
<td>13/127</td>
<td>23/130</td>
<td>0.58 [0.31, 1.09]</td>
<td>14.76</td>
<td></td>
</tr>
<tr>
<td>Segers 2006</td>
<td>45/485</td>
<td>74/469</td>
<td>0.59 [0.42, 0.83]</td>
<td>48.87</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1206</td>
<td>1219</td>
<td>0.56 [0.44, 0.72]</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1 Forrest plot of the meta-analysis (fixed effects model). The diamond indicates summary relative risk (RR) and 95% confidence interval (CI). CHX, chlorhexidine; n, number of LRTI events; N, number of participants.

Kola et. al. JHI 2007; 66:207-216
Silver Coated Endotracheal Tubes and Incidence of Ventilator-Associated Pneumonia: NASCENT Randomized Trial

- 9417 pts screened, 2003 enrolled, 1509 intubated >24 hrs
- 54 centers in North America
- 2002-2006

Table 2. Incidence of Microbiologically Confirmed Ventilator-Associated Pneumonia (VAP)^4

<table>
<thead>
<tr>
<th></th>
<th>Evaluable Patients With VAP, No./Total (%) [95% CI]</th>
<th>RR Reduction, % [95% CI]</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAP at any time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intubated &gt;=24 h</td>
<td>37/765 (4.8) [3.4-6.6]</td>
<td>50/743 (6.7) [5.7-7.7]</td>
<td>.36</td>
</tr>
<tr>
<td>All intubated</td>
<td>37/968 (3.8) [2.7-5.2]</td>
<td>50/934 (5.8) [4.4-7.5]</td>
<td>.34</td>
</tr>
<tr>
<td>VAP within 10 d of intubation</td>
<td>27/766 (3.5) [2.3-5.1]</td>
<td>50/743 (6.7) [5.0-8.8]</td>
<td>.47</td>
</tr>
<tr>
<td>All intubated</td>
<td>27/968 (2.8) [1.9-4.0]</td>
<td>50/934 (5.2) [3.9-6.8]</td>
<td>.46</td>
</tr>
</tbody>
</table>

Figure 2. Kaplan-Meier Analyses of Occurrence of Microbiologically Confirmed Ventilator-Associated Pneumonia (VAP) in Patients Intubated for 24 Hours or Longer

Kollef et al. JAMA 2008; 300(7):805-813
Subglotic Secretion drainage for preventing ventilator-associated pneumonia: a meta-analysis

• 5 Studies with a total of 896 patients
  – Rigorous pneumonia definition

• Results:
  – RR = 0.51  CI: 0.37-0.71
  – Less time on vent by 2 days; CI: 1.7-2.3 days
  – Decreased LOS by 3 days; CI: 2.1-3.9 days
  – Delayed pneumonia onset by 6.8 days, CI: 5.5-8.1 days

Meets new IHI bundle recommendation
Peridex is an effective oral rinse supported by more than 20 years of clinical proof in reducing gingivitis.
Provides antimicrobial activity during oral rinsing.
Does not cause bacterial resistance.
3M 24hr Oral Care Kit
with Peridex™ (chlorhexidine gluconate 0.12% oral rinse)

• 3M will be launching soon a complete 24hr oral care kit
Preventing “Horizontal Spread”
(...of MRSA/C. diff etc.)

• Current Guidelines:
  – Conduct a risk assessment (baseline) B-III
  – Implement a monitoring program A-III
    » See flow chart
  – Compliance with CDC/WHO Hand Hygiene A-II
  – **Isolate** carriers and use contact precautions A-II
  – **Clean/disinfect** equipment/environment B-III/B-II
  – Educate about MRSA/CDI B-III
    • Risk factors, routes of transmission, outcomes, prevention
  – Implement lab based alert system for new case B-III
    • Colonization or infection
  – Implement alert system for readmits/transfers B-III
  – Educate patients and families about MRSA/CDI B-III
  – Measure compliance with CDC/WHO HH &
  – Contact precautions B-III
Environmental Contamination
Environmental Contamination

• Is there a problem?
  – MRSA can survive 5-50 days on surfaces\textsuperscript{1}
  – C. Diff. can survive on environmental surfaces for up to 70 days!\textsuperscript{2}

TABLE 2. Effect of inoculum size on survival of CNS on fabrics and plastic

<table>
<thead>
<tr>
<th>Isolate</th>
<th>Inoculum (CFU)</th>
<th>Survival (no. of days) on:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cotton</td>
</tr>
<tr>
<td>1</td>
<td>$9 \times 10^2$</td>
<td>5</td>
</tr>
<tr>
<td>1</td>
<td>$9 \times 10^4$</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>$6 \times 10^2$</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>$1 \times 10^5$</td>
<td>21</td>
</tr>
</tbody>
</table>

Neely, J Clin Micro, 38:724-726, 2000
C. difficile on Patients

Frequency of *Clostridium difficile* contamination of skin sites of 27 patients with *C. difficile*–associated disease (CDAD)

Bobulsky CID 2008; 46: 447-50
C. difficile transfer...

Typical illustration of acquisition of *C. difficile* on sterile gloves after contact with a CDAD-affected patient’s groin. The larger yellow colonies outlining the fingers are *C. difficile*. Of note, the patient had showered 1 h before collection of the culture specimen.

Bobulsky CID 2008; 46: 447-50
Patient Room Analysis…

- The medical devices entering are clean and sterile
- The pharmaceuticals entering are clean
- The food entering the room is safe
- But what about the room?

<table>
<thead>
<tr>
<th></th>
<th>MRSA</th>
<th>VRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior + pt</td>
<td>3.9%</td>
<td>4.5%</td>
</tr>
<tr>
<td>Prior - pt</td>
<td>2.9</td>
<td>2.8</td>
</tr>
<tr>
<td>P value</td>
<td>0.04</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Acquisition of Antibiotic Resistant Organisms in ICUs

Huang Arch Int Med. 2006;166:1945-1951
Process Check: Monitoring Room Cleanliness

- **Fluorescent markings (Dr. Philip Carling)**
  - Simple and easy to access
  - Will only access cleaning efficiency at predetermined locations
  - Predetermined marked locations

- **ATP (e.g. 3M Cleantrace™)**
  - Can measure ATP on almost any surface
    - Swab and measure
  - Direct evidence of cleanliness but may not correlate with CFU
  - Requires an instrument to read fluorescence
"One or more of the hospitals cleaned 10 of the 14 objects without any oversights during the study, whereas at least one hospital failed ever to clean one or more of the seven objects, which were cleaned less than 80% of the time."

# Room Cleaning Assessment, ATP

<table>
<thead>
<tr>
<th></th>
<th>% Failure</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before cleaning</td>
<td>After cleaning</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Visual</td>
<td>ATP</td>
<td>ACC</td>
<td>Visual</td>
</tr>
<tr>
<td>Hospital A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paediatric</td>
<td>28</td>
<td>94</td>
<td>76</td>
<td>20</td>
</tr>
<tr>
<td>Surgical</td>
<td>27</td>
<td>98</td>
<td>86</td>
<td>15</td>
</tr>
<tr>
<td>Hospital B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paediatric</td>
<td>24</td>
<td>83</td>
<td>80</td>
<td>3</td>
</tr>
<tr>
<td>Surgical</td>
<td>25</td>
<td>92</td>
<td>75</td>
<td>15</td>
</tr>
<tr>
<td>Hospital C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paediatric</td>
<td>19</td>
<td>89</td>
<td>67</td>
<td>7</td>
</tr>
<tr>
<td>Surgical</td>
<td>11</td>
<td>88</td>
<td>75</td>
<td>7</td>
</tr>
<tr>
<td>Hospital D</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paediatric</td>
<td>11</td>
<td>100</td>
<td>81</td>
<td>13</td>
</tr>
<tr>
<td>Surgical</td>
<td>15</td>
<td>100</td>
<td>81</td>
<td>6</td>
</tr>
</tbody>
</table>

ATP, adenosine triphosphate; ACC, aerobic colony counts.
3M Clean-Trace™

• Rapidly detects the presence of organic contamination as ATP
  – 30 seconds!
  – Swab/ click / measure

• Quantitative methodology to monitor cleanliness

It’s as easy as... 1, 2, 3

1. Swab
2. Click
3. Measure
# Clean Monitoring Comparison

<table>
<thead>
<tr>
<th></th>
<th>Visual assessment</th>
<th>Microbiological tests</th>
<th>Fluorescence Monitoring</th>
<th>ATP Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Objective</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sensitive</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Detect product residues</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Test Any where</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Simple</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (need meter)</td>
</tr>
</tbody>
</table>

(Lab required)
Summary

• Keep up to date!
• Implement bundles, modify as necessary
• Meta-analysis is a useful but not “end all” tool
• Look at the data closely
  – Apples to apples?
  – Formulation matters!
• Technology AND Clinician Training
Back Up Slides
Current Guidelines to Prevent CAUTI

• Implement guidelines on catheter use, insertion, and maintenance  A-II
• Ensure only trained dedicated HCWs insert catheters  B-III
• Supplies for aseptic technique available  A-III
• Document ind. for cath, date/time/HCW in/out  A-III
• Trained personnel/technology to support surveillance  A-III
  – ID pt groups/units, risk factors  B-III
  – Use std criteria to ID CAUTI  A-II
  – Collect data on catheter days  A-II
  – Measure use of indwelling catheters  B-II
• Educate HCWs (insert, care, maintenance, CAUTI Prevention (reduction, removal)  A-III
• Insert properly
  – Only when necessary  A-II
  – Consider intermittent or condom  A-I
  – Use proper HH  A-III
  – Insert with aseptic technique and sterile equip  A-III
Current Guidelines to Prevent CAUTI

• Insert properly cont.
  – Use gloves, drape, sponges, sterile or Antiseptic soln to clean meatus, single pack lub A-III
  – Use as small of a catheter as possible B-III

• Appropriate Management of in-dwelling cath
  – Properly secure to prevent movement A-III
  – Sterile, continuous, closed drainage A-I
  – Do not disconnect cath unless irrigate A-I
  – Replace collection bag by aseptic technique B-III
  – Collect urine samples for sample port A-III
  – Collect large vol samples from drainage bag A-III
  – Maintain urine flow A-II
  – Empty bag regularly A-II
  – Keep bag below level of bladder A-II
  – Routine meatal hygiene- antiseptic unnecessary A-I