NICU Infection Prevention Guideline Update

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HICPAC
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Overview

- Stakeholder Engagement
- Key Questions
- Search Strategies
- Abstract Review
- Inclusion Criteria
Stakeholders

- American Academy of Pediatrics
- Society for Healthcare Epidemiology of America
- Association for Professionals in Infection Control
- Vermont Oxford Network
- National Association of Neonatal Nurses (NANN)
Guideline Team

- **Core Writing Group**
  - Alexis Elward
  - Martha Iwamoto
  - Craig Umscheid
  - Amanda Paschke
  - Gretchen Kuntz
  - Michael Brady

- **Expert Reviewers**
Stakeholder Engagement

- Conference calls with core writing group and expert reviewer group
- Key Questions reviewed
- Broad list of potential topics generated
- Initial literature searches performed
  - Existing or developing guidelines addressing topics
  - Adequate literature to include as key question
- Key Questions triaged and consolidated
# Key Questions: Viral Infections

<table>
<thead>
<tr>
<th>Viral Infections</th>
<th>Revised Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial Questions</strong></td>
<td><strong>Revised Questions</strong></td>
</tr>
<tr>
<td>What are the best methods for control of respiratory viral pathogens in the NICU?</td>
<td>What are the most effective methods of prevention and control of viral respiratory illnesses in the NICU?</td>
</tr>
<tr>
<td>What are the best pathogen specific prevention measures of RSV, Pertussis, VZV?</td>
<td>What are the most effective methods for preventing transmission of RSV, Pertussis and VZV in the NICU?</td>
</tr>
<tr>
<td>Should transmission-based precautions be modified for patients in isolettes?</td>
<td></td>
</tr>
<tr>
<td>What are the best diagnostic modalities for detection of an outbreak of respiratory viral pathogens in the NICU?</td>
<td>What is the most effective diagnostic approach to identifying respiratory viral outbreaks in the NICU?</td>
</tr>
</tbody>
</table>
### Key Questions: Central Line Associated Bloodstream Infections (CLABSI)

<table>
<thead>
<tr>
<th>CLABSI</th>
<th>Initial Questions</th>
<th>Revised Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>What are the best strategies to prevent CLABSI in NICU patients?</td>
<td>What are the <em>most effective</em> strategies to prevent CLABSI in the NICU?</td>
</tr>
</tbody>
</table>
### Key Questions: Methicillin Resistant Staphylococcus aureus (MRSA)

<table>
<thead>
<tr>
<th>MRSA</th>
<th>Initial Questions</th>
<th>Revised Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial Questions</strong></td>
<td>What are the risk factors for MRSA and MSSA colonization in NICU patients?</td>
<td>What are the risk factors for MRSA colonization in NICU patients?</td>
</tr>
<tr>
<td></td>
<td>What are the most effective strategies to identify MRSA and MSSA colonization in NICU patients?</td>
<td>What are the most effective strategies to screen for MRSA colonization in NICU patients?</td>
</tr>
<tr>
<td></td>
<td>Does screening of MRSA colonization result in fewer MRSA infections?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>What are the most effective measures to prevent hospital-acquired infection or colonization with MRSA and MSSA?</td>
<td>What are the most effective measures to prevent hospital-acquired infection or colonization with MRSA?</td>
</tr>
<tr>
<td>Invasive fungal disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Initial questions</strong></td>
<td><strong>Revised Questions</strong></td>
<td></td>
</tr>
<tr>
<td>What are the risk factors for invasive candidal infections?</td>
<td>No change</td>
<td></td>
</tr>
<tr>
<td>What are the most effective prevention strategies to prevent colonization or invasive infection with Candida?</td>
<td>What are the <strong>most effective strategies to prevent invasive infection with Candida</strong>?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>What are the most effective strategies to prevent colonization with Candida?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Does prevention of Candidal colonization result in fewer invasive Candidal Infections?</td>
<td></td>
</tr>
<tr>
<td>What are the best diagnostic modalities for detection of invasive fungal infection in NICU patients?</td>
<td>What are the <strong>most effective methods of identifying invasive fungal infections</strong> (Candida, Aspergillus, Zygomycoses, Pichia, Malassezia) in NICU patients?</td>
<td></td>
</tr>
</tbody>
</table>
### Key Questions: *Clostridium difficile*

<table>
<thead>
<tr>
<th>Other</th>
<th>Initial Questions</th>
<th>Revised Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>What are the most effective strategies for <em>C. difficile</em> testing in NICU patients?</strong></td>
<td><strong>What are the most effective strategies for <em>C. difficile</em> testing in NICU patients?</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>When should testing for <em>C. difficile</em> be performed in NICU patients?</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>What is the significance of a positive <em>C. difficile</em> test in a NICU patient?</strong></td>
</tr>
<tr>
<td></td>
<td><strong>What is the most effective way to perform hand hygiene to prevent infection in NICU patients?</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>What is the optimal architectural design for NICU to prevent infection transmission?</strong></td>
<td></td>
</tr>
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</table>
Search Strategies
Databases

- MEDLINE
- Cochrane Library
- Excerpta Medica Database (EMBASE)
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- National Guideline Clearinghouse
- Professional Societies: SHEA, IDSA, APIC, HICPAC, AAP
Respiratory Viruses and RSV

<table>
<thead>
<tr>
<th>#</th>
<th>Search History</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>exp Intensive Care Units, Neonatal/ or exp Intensive Care, Neonatal/</td>
<td>10481</td>
</tr>
<tr>
<td>2</td>
<td>Infant, Newborn/</td>
<td>440263</td>
</tr>
<tr>
<td>3</td>
<td>1 or 2</td>
<td>440999</td>
</tr>
<tr>
<td>4</td>
<td>exp Respiratory Tract Infections/</td>
<td>249278</td>
</tr>
<tr>
<td>5</td>
<td>exp Virus Diseases/</td>
<td>614076</td>
</tr>
<tr>
<td>6</td>
<td>4 and 5</td>
<td>54452</td>
</tr>
<tr>
<td>7</td>
<td>exp Respiratory Syncytial Virus Infections/ or exp Respiratory Syncytial Viruses/</td>
<td>7292</td>
</tr>
<tr>
<td>8</td>
<td>6 or 7</td>
<td>59287</td>
</tr>
<tr>
<td>9</td>
<td>3 and 8</td>
<td>3846</td>
</tr>
<tr>
<td>10</td>
<td>exp Infection Control/</td>
<td>43521</td>
</tr>
<tr>
<td>11</td>
<td>exp Cross Infection/</td>
<td>39370</td>
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<tr>
<td>12</td>
<td>exp Communicable Disease Control/</td>
<td>207284</td>
</tr>
<tr>
<td>13</td>
<td>10 or 11 or 12</td>
<td>236787</td>
</tr>
<tr>
<td>14</td>
<td>9 and 13</td>
<td>432</td>
</tr>
<tr>
<td>15</td>
<td>limit 14 to (english language and humans)</td>
<td>341</td>
</tr>
</tbody>
</table>

Medline results only shown, same search strategy for other databases
Study Selection Agreement
Among Reviewers
Sampling Strategy

- Screening of titles and abstracts
  - Single author – 100%
  - Two authors – 20% sample

- Inter-reviewer comparison of 20% sample using kappa statistic

- Calculating change agreement
  - Formula for calculating kappa
    \[(\text{Observed agreement} - \text{agreement expected by chance}) / (100\% - \text{agreement expected by chance})\]
Measures of Observer Variability (Kappa Statistic)

Table 1: Qualitative classification of kappa values as degree of agreement beyond chance

<table>
<thead>
<tr>
<th>Kappa value</th>
<th>Degree of agreement beyond chance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>0–0.2</td>
<td>Slight</td>
</tr>
<tr>
<td>0.2–0.4</td>
<td>Fair</td>
</tr>
<tr>
<td>0.4–0.6</td>
<td>Moderate</td>
</tr>
<tr>
<td>0.6–0.8</td>
<td>Substantial</td>
</tr>
<tr>
<td>0.8–1.0</td>
<td>Almost perfect</td>
</tr>
</tbody>
</table>

Fig. 1: Two observers independently assess the presence or absence of a finding or outcome. Each observer determines that the finding is present in exactly 50% of the subjects. Their assessments agree in 75% of the cases. The yellow horizontal bar represents potential agreement (100%), and the turquoise bar represents actual agreement. The portion of each coloured bar that lies to the left of the dotted vertical line represents the agreement expected by chance (50%). The observed agreement above chance is half of the possible agreement above chance. The ratio of these 2 numbers is the kappa score.

kappa = 25/50 = 0.5 (moderate agreement)
## Agreement Between Reviewers

<table>
<thead>
<tr>
<th>Key question</th>
<th>Observed agreement</th>
<th>Kappa statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory viral</td>
<td>.84</td>
<td>0.69</td>
</tr>
<tr>
<td>Varicella</td>
<td>.90</td>
<td>0.80</td>
</tr>
<tr>
<td>Pertussis</td>
<td>.83</td>
<td>0.67</td>
</tr>
<tr>
<td>CLABSI</td>
<td>.86</td>
<td>0.71</td>
</tr>
<tr>
<td>MRSA</td>
<td>.88</td>
<td>0.75</td>
</tr>
<tr>
<td>Fungal</td>
<td>.89</td>
<td>0.74</td>
</tr>
<tr>
<td>C. difficile</td>
<td>.78</td>
<td>0.58</td>
</tr>
</tbody>
</table>
Results of the Study Selection Process
Respiratory Viral Infections

Literature search

513 references identified for title and abstract screening

Study selection

207 references selected for full-text review

16 narrative reviews
19 outbreak reports
6 existing guidelines
Varicella

98 references identified for title and abstract screening

32 references selected for full-text review

2 narrative reviews
3 outbreak reports
Pertussis

Literature search

147 references identified for title and abstract screening

Study selection

31 references selected for full-text review

6 outbreak reports
CLABSI

**Literature search**

499 references identified for title and abstract screening

**Study selection**

295 references selected for full-text review

26 narrative reviews
7 existing guidelines
MRSA

Literature search

663 references identified for title and abstract screening

Study selection

346 references selected for full-text review

6 existing guidelines
C. difficile

Literature search

160 references identified for title and abstract screening

Study selection

105 references selected for full-text review
General Inclusion Criteria

Include
- Original data
- Systematic review

Exclude
- Non-U.S. descriptive epidemiology only
- Mixed patient population without NICU or infant subgroup analysis
- Studies that do not include NICU patients or infants
- General hospital-acquired infection surveillance
Respiratory Pathogen Exclusion Criteria

- Immunization
- Non-respiratory viruses in NICU population (Enteroviruses, Herpes Simplex Virus, Cytomegalovirus)
CLABSI Exclusion Criteria

- Treatment only
- Catheter removal for documented infections
- Peripheral IV studies
- Endocarditis
MRSA: Exclusion Criteria

- Molecular epidemiology study, only
- Endocarditis
- Japan MRSA neonatal toxic-shock entity (only reported in Japan, very specific syndrome)
- Case reports of single-site infections (such as case report of periorbital cellulitis)
- Community-acquired or community-onset infections
  - WILL include infections in NICU patients with CA-MRSA strains
- Treatment only
Fungal Infections Exclusion Criteria

- Treatment only
- Pharmacokinetics studies of antifungals in neonates
- Case Reports except for non-Candidal fungal infections
- Case series with n <10
- Vaginitis without infant colonization/infection outcome
- Nonclinical (immunologic) studies
Clostridium difficile Exclusion Criteria

- Molecular biology of Clostridium difficile
- Molecular epidemiology without clinical information
Timeline

- January 2010 Tentative guideline team and key questions
- April 2010 Final guideline team
- June 2010 Key questions finalized
- July 2010 Literature search performed
- **September 2010 Abstract and full text review**
- November 2010 Data extracted into draft evidence tables
- February 2011 Extraction finalized, evidence quality graded using GRADE approach, and narrative summaries drafted
- June 2011 Narrative summaries finalized and recommendations drafted using GRADE approach
- November 2011 Recommendations finalized
Next Steps

- Identify replacement for Amanda Paschke
- Finalize inclusion and exclusion criteria for full text review
- Begin full text review
“The first thing we need is a definition.”
Ben, age 10 years

“Sometimes when babies come out they are not fully done.”
Katie, age 7 years