Introduction

This white paper provides clinicians with practical guidance on the implementation of *Staphylococcus aureus* infection prevention measures for neonatal intensive care unit (NICU) patients. Except where otherwise specified, “*S. aureus*” refers to both methicillin-resistant *S. aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA). The phrase “parents or family members” refers to all visitors that have physical contact with infants in the NICU.

*S. aureus* is a clinically important pathogen among NICU infants. Neonates may acquire *S. aureus* as part of their normal developing microbiota; yet, colonization predisposes to invasive infection.1,2 Estimated incidence of *S. aureus* infection is up to 45 per 10,000 hospitalized infants.3-5 In a typical NICU, exposure to the NICU environment, including indirect transmission from other critically ill infants, healthcare personnel, parents and/or family members may exacerbate the burden of *S. aureus* colonization and infection.6,7 Despite decreasing device utilization rates within the NICU, *S. aureus* remains a frequent cause of healthcare-associated and device-associated infections.8 *S. aureus* is also a commonly identified pathogen among hospitalized neonates during infection clusters or outbreaks.8,9 Most available literature report on *S. aureus* prevention in the context of outbreak control; few data exist on this topic in endemic NICU settings.

Intended use

The Society for Healthcare Epidemiology of America (SHEA) intends for this document to serve as a companion to the Centers for Disease Control and Prevention (CDC) Healthcare Infection Control Practices Advisory Committee (HICPAC) Recommendations for Prevention and Control of Infections in Neonatal Intensive Care Unit Patients and to provide practical, expert opinion and/or evidence-based answers to frequently asked questions on *S. aureus* detection and prevention in the NICU. The published literature does not contain sufficient high-quality studies to meet Grading of Recommendations Assessment, Development and Evaluation (GRADE) standards and therefore were not included in the HICPAC guideline.10

No guideline, expert guidance, or white paper can anticipate all situations. This document is meant to serve as an adjunct to individual judgment by qualified professionals. In general, these recommendations apply to non-outbreak settings. Healthcare personnel may implement additional measures during an outbreak or other special clinical scenarios. Further details and references are included in the HICPAC Recommendations for Prevention and Control of Infections in Neonatal Intensive Care Unit Patients: *Staphylococcus aureus*.

Methods

This document was developed by a collaborative panel of pediatric and pathogen-specific experts, members of the HICPAC guideline-writing panel, and the SHEA Pediatric Leadership Council, to identify practical questions anticipated from practitioners and infection prevention professionals.

Unlike the SHEA expert guidance format, this document is not based on a systematic literature search; instead, for the selected topic areas, the authors provide practical approaches in question-and-answer format. Answers are based on consensus expert opinion within the context of the literature search conducted for the HICPAC document and supplemented by other published information retrieved by the authors.

This document is part of a SHEA white paper series that includes the “SHEA neonatal intensive care unit (NICU) white paper series: Practical approaches to *Clostridioides difficile* prevention,” published in August 2018.11 SHEA convened a group of experts in pediatrics and neonatology, called the NICU Advisory Panel (see the Acknowledgments section), to oversee the full white paper series. The NICU Advisory Panel members serve as representatives for the following organizations: SHEA, the American Hospital Association (AHA), the American Academy of Pediatrics (AAP), the Association for Professionals in Infection Control and Epidemiology (APIC), the Infectious Diseases Society of America (IDSA), The Joint Commission, the National Association of Neonatal Nurses (NANN), the Pediatric Infectious Diseases Society (PIDS), and the Vermont Oxford Network (VON). This document was reviewed by the NICU Advisory Panel, the SHEA Guidelines Committee, and the...
SHEA Publications Committee. It was endorsed by the Society for Healthcare Epidemiology (SHEA), the Association for Professionals in Infection Control and Epidemiology (APIC), the Infectious Diseases Society of America (IDSA), The Joint Commission, the National Association of Neonatal Nurses (NANN), the Pediatric Infectious Diseases Society (PIDS), and the Vermont Oxford Network (VON).

Authors
The authors include current and past members of the SHEA Guidelines Committee and the SHEA Pediatric Leadership Council. Ms. Berg served as the representative from APIC. All authors served as volunteers. The authors are directly involved or provide an advisory role, at their respective institutions, in the development of policies pertaining to pediatric and/or neonatal infection prevention in the NICU.

The NICU Advisory Panel (see the Acknowledgments section), a collaborative group of pediatric and pathogen-specific experts convened by SHEA, provided oversight and review of the draft document. The NICU Advisory Panel includes representatives from SHEA, AHA, AAP, APIC, IDSA, The Joint Commission, NANN, PIDS, and VON.

Practical approaches: Questions and Answers

**Question 1:** Should family members and visitors wear personal protective equipment (PPE) when visiting an infant on contact precautions for MRSA?

**Answer 1:**

1. Family members and visitors should perform proper hand hygiene upon entering and exiting the NICU, and before and after each contact with the infant(s).
2. Healthcare personnel may choose not to require family members and visitors to use PPE for infants with MRSA colonization.

Some NICUs require parents and visitors to wear PPE (ie, donning of gowns and gloves) if their infant has been placed on contact precautions (eg, for MRSA colonization). Although some studies have shown that prevention bundles, including universal gown and gloving of healthcare personnel, can reduce the horizontal transmission of organisms, no compelling evidence exists to support gloving of healthcare personnel, can reduce the horizontal transmission of organisms. Although some studies have shown that prevention bundles, including universal gown and gloving of healthcare personnel, can reduce the horizontal transmission of organisms.

**Question 2:** If a parent is known to have MRSA infection or colonization, should healthcare personnel place infants on contact precautions, encourage skin-to-skin bonding, and/or institute breastfeeding restrictions?

**Answer 2:**

1. Contact precautions are not necessary for infants of MRSA-colonized or infected parents.
2. Healthcare personnel should emphasize hand hygiene to prevent transfer of organisms and consistently model the practice to parents and family members.
3. Healthcare personnel should encourage and promote skin-to-skin care and breastfeeding while taking into consideration the location of the parent’s MRSA lesion, ability to contain drainage, and likelihood of infant’s contact with the lesion.
4. Parents known to be colonized with MRSA do not need to wear gowns or gloves while caring for their infant.
5. As long as drainage is contained, the site of infection is covered and strict hand hygiene practices are followed, healthcare personnel should not require parents known to have active MRSA infection(s) to wear gowns or gloves while caring for their infant(s).
6. Units should strongly consider routine screening of infant(s) (eg, weekly) whose parent has an active MRSA infection.

Managing the care of infants with an MRSA-colonized or -infected parent varies. Such infants may be at increased risk of acquiring MRSA compared to other infants. There are case reports of transmission of MRSA from parent to infant, however, the risk is reduced with appropriate and frequent hand hygiene. A recent trial suggested that decolonizing parents may reduce the risk of parent-to-child *S. aureus* transmission, but further studies are needed to confirm this finding and to assess the impact on preventing infections in neonates. Empiric contact precautions are not necessary for infants with a parent known to have MRSA infection because no data suggest that this practice reduces MRSA transmission in the NICU. Specifically, any benefit of reducing transmission has not been shown to outweigh the potential unintended consequences of preemptive contact precautions. Units should strongly consider routine screening of infants (eg, weekly or biweekly) whose parent has a recent MRSA infection.

Measures to prevent MRSA transmission should not interfere with parental bonding. Healthcare personnel should encourage and promote skin-to-skin care and breastfeeding for MRSA-colonized and infected parents (see Question 1). The benefits of breastfeeding likely outweigh the risks of transmission of MRSA to noncolonized infants. If a parent has an active MRSA infection on the neck or chest (for skin-to-skin care); breast (for breastfeeding); or the hands (for all contact), the parent should ensure that the lesion is fully covered and should avoid any direct contact of the infant with the infected area until the lesion is healed.
Contact precautions only apply to patients with MRSA. Standard precautions are indicated for MSSA. Finally, adherence to hand hygiene practices is the critical element needed to prevent MRSA transmission. Parental infection prevention education should be a routine part of the NICU plan of care.

**Question 3:** In cases of multiple gestations with discordant MRSA status (eg, one twin with MRSA colonization and the other twin without MRSA colonization), should healthcare personnel place discordant multiples on contact precautions, permit skin-to-skin care with parents, and/or institute breastfeeding restrictions?

**Answer 3:**
1. Contact isolation should be used for MRSA-colonized infants.19 Healthcare personnel should also consider use of contact precautions for the noncolonized infant(s) among discordant multiples.
2. Healthcare personnel should encourage skin-to-skin care to promote parent–infant bonding, while emphasizing hand hygiene to prevent organism transfer to the noncolonized infant.
3. Healthcare personnel may consider having parents perform skin-to-skin care with the noncolonized infant prior to performing skin-to-skin care with the MRSA-colonized infant.
4. Healthcare personnel should encourage breastfeeding regardless of an infant’s MRSA status.
5. Units should strongly consider routine screening of noncolonized infants (eg, weekly, biweekly) with MRSA-colonized or infected siblings in the NICU.

Managing the care of multiple gestation infants with discordant MRSA status varies across institutions. There are case reports of transmission between siblings18,20; therefore, compared with other infants in the NICU, noncolonized infants who have MRSA-colonized siblings may be at increased risk of acquiring MRSA. Units should consider use of contact precautions empirically for the noncolonized neonate while acknowledging that the benefit of reducing transmission has not been shown to outweigh the potential unintended consequences of empirical contact precautions (eg, reduced interaction with healthcare personnel). Units should strongly consider routine screening of the noncolonized neonate to detect colonization (eg, weekly, biweekly). Management of MRSA-discordant infants should be based on the following principles: (1) contact precautions to prevent transmission should not interfere with parental bonding and skin-to-skin care; (2) the benefits of breastfeeding outweigh the low risk of MRSA transmission to noncolonized infants; (3) adherence to hand hygiene practices is critical to preventing S. aureus transmission; and (4) parental education about infection prevention should be incorporated into the routine plan of care. Parents should be informed about their possible role in the spread of MRSA between siblings and monitored to ensure hand hygiene compliance; however, healthcare personnel do not need to have parents clean their skin in between skin-to-skin care for infants with discordant MRSA status. Because standard precautions are indicated for MSSA, the preceding recommendations do not apply to infants colonized with MSSA.

**Question 4:** How long should healthcare personnel maintain contact precautions for MRSA-colonized neonates and what are reasonable criteria for discontinuation of contact precautions?

**Answer 4:**
1. Healthcare personnel should strongly consider continuing contact precautions for the duration of hospitalization in high-risk groups who are likely to remain MRSA-colonized, for example, infants with invasive (endotracheal tube) or noninvasive (nasal prongs) ventilation, a tracheostomy, or a draining/open wound.

Some infants may remain MRSA-colonized for long periods, even infants that undergo treatment with topical antibiotics/antiseptics (decolonization). Invasive devices, such as endotracheal or tracheostomy tubes, are reservoirs for MRSA and may promote persistent colonization.2,21,22 Because these infants may be ongoing reservoirs for MRSA transmission, units should consider continuing contact precautions for these infants while these devices remain in place. Other devices may serve as reservoirs for MRSA, such as gastrostomy tubes, but few data exist describing the natural history of colonization in infants with these devices. Infants with a history of MRSA-infected wounds may remain persistently colonized long after the wound has healed. However, certain infants’ colonization status may change over time, such as after extubation or wound healing.

Infants with anticipated prolonged NICU stays can be periodically reassessed to determine whether they have persistent colonization or whether they can be cleared from contact precautions. A number of factors leads some units to consider removing infants from contact precautions: (1) infants’ transient colonization; (2) potential negative consequences of contact precautions in reducing interaction with healthcare personnel, parent bonding, and increasing healthcare costs; and (3) the physical layout of the NICU (eg, private room vs. open bay). If units choose to remove infants with prior MRSA colonization from contact precautions, then the unit should define clear criteria for removal. Healthcare personnel should be aware that MRSA colonization can be intermittently missed using standard methods. As such, to document the absence of MRSA, collecting a minimum of 2 consecutive nares cultures at least a week apart increases the likelihood that the child is no longer colonized with MRSA.17,23 Units may consider screening infants who are not on antibiotics with activity against MRSA and do not have actively draining lesions or clinical symptoms of an MRSA infection for removal of contact precautions. When an infant with a known history of MRSA colonization or infection is readmitted to the NICU, clinicians should strongly consider using contact precautions and determine whether retesting for continued MRSA carriage is warranted. These recommendations do not apply to MSSA-colonized infants because MSSA-colonized infants are not routinely placed on contact precautions.

**Question 5:** Should healthcare personnel consider active surveillance cultures of hospitalized neonates for S. aureus and if so, what are the best strategies?

**Answer 5:**
1. No specific standard protocol exists for frequency of S. aureus surveillance testing, specific population(s) to test, or duration of active surveillance.
2. For MRSA
   a. Healthcare personnel should consider routine active surveillance when the results can inform infection prevention and control measures (eg, patient cohorting, contact precautions, and/or decolonization) and/or clinical management decisions (ie, antibiotic selection if subsequent invasive disease occurs).
   b. In specific situations, healthcare personnel should perform active surveillance to inform additional infection prevention strategies when (1) an outbreak has been identified; (2) healthcare-associated transmission is ongoing and deemed of clinical importance; or (3) an individual patient may be at higher risk for colonization or infection (eg, prior to surgery, multiple gestation with differing MRSA colonization status, parent known to be a carrier or otherwise infected with MRSA, or outborn newborns from settings of higher prevalence).

3. For MSSA
   a. Routine active surveillance has no clear benefit unless units use surveillance results to inform infection prevention and control measures (eg, decolonization).
   b. In specific situations, healthcare personnel should consider performing active surveillance to inform additional infection prevention strategies (1) when an outbreak has been identified and (2) when there is a need to identify individual patients who may be at higher risk for infection (eg, low birth weight or prior to surgery).

4. Units should use culture-based or molecular methods for S. aureus surveillance, with anterior nares being the preferred site to sample. If multiple sites are sampled, units should consider performing a composite culture of all swabs.

5. Units should institute contact precautions for infants with positive MRSA test results. See Question 4 regarding duration of contact precautions.

6. Healthcare personnel should not routinely perform S. aureus testing of equipment and/or other environmental surfaces.

Nearly all studies that include data supporting the use of active surveillance cultures are observational in design. Typically, the studies include colonization as an outcome, and in some studies, active disease.24 Overall, although higher rates may be noted in outborn infants, MRSA colonization among NICU infants in the United States is between 0 and 4%.2 Although the anterior nares are the most frequent site for identification of S. aureus colonization, the addition of the umbilical, rectal, perirectal, or axillary sites may increase sensitivity.25 Patient samples can be cultured on blood agar and/or chromogenic selective agar for identification of S. aureus; however, molecular-based methods may improve sensitivity and rapid identification.26 Whether sampling additional sites and using more sensitive molecular-based methods is cost-effective and reduces MRSA infections remains unknown.

In the outbreak setting, active surveillance for S. aureus is most useful when combined with other infection prevention and control measures such as contact precautions and targeted decolonization.24 In the outbreak setting, some facilities perform active surveillance on all new admissions, only outborn infants (MRSA only), on infants with bed spaces geographically close to infected babies, and/or all babies resident in the NICU at the time of surveillance. Active surveillance protocols vary. Repeated surveillance screening on a weekly or biweekly basis may be useful to confirm or exclude ongoing transmission, but if it is used as an isolated intervention, its effectiveness in preventing MRSA infections is uncertain.

In the nonoutbreak setting, asymptomatically colonized infants are a known reservoir for transmission and are still at risk for developing infection.2,17,24 Although data on patients in the NICU may be limited, studies report that placement of asymptomatic patients on contact precautions may have potential unintended consequences, such as reduced monitoring by staff.27 Units should balance the decision to perform active surveillance for MRSA with potential risks and associated costs. The costs and logistical requirements for routine S. aureus screening may be substantial, and the clinical value and cost-effectiveness of such approaches in the nonoutbreak setting are not well supported. Whether implementing other interventions, such as contact precautions in addition to performing active surveillance, prevents infections remains unclear. Limited data exist on the use of active MSSA surveillance or contact precautions to prevent infections in the NICU.28,29 Some prospective data show success with routine surveillance of new admissions followed by decolonization with nasal mupirocin to reduce invasive disease.30

Whether environmental contamination contributes to S. aureus acquisition in the NICU remains unclear. No data exist, in any age group, to suggest that environmental culturing provides useful information to prevent S. aureus transmission and infections. In the NICU setting, observational data suggest that those housed in a single room (vs. multibed pods) were less likely to acquire MRSA and MSSA. Thus, single- versus multiple-occupancy room is potentially a marker for environmental and/or staff contamination.31 In adult populations, MRSA colonization (not disease) may be more common in patients who reside in a room of a prior occupant known to have MRSA disease.32

Although healthcare personnel have been implicated as reservoirs propagating NICU MRSA outbreaks, routine healthcare personnel screening is not recommended unless epidemiologic data strongly suggest a possible link to transmission and other standard measures have been unsuccessful at controlling transmission.

**Question 6:** What are potential methods and indications for decolonizing NICU infants colonized with S. aureus?

**Answer 6:**

1. An optimal decolonization regimen for infants has not been determined. Intranasal mupirocin twice daily for 5–7 days is an acceptable method for S. aureus decolonization of infants.
2. Units should not use systemic antimicrobials as a decolonization strategy because this approach has not been studied in this population and it may select for antibiotic resistant organisms and may lead to adverse drug events.
3. Units may choose to perform targeted S. aureus decolonization in specific situations to reduce the risk of infection in colonized infants, for example, (1) when an outbreak has been identified and (2) when a colonized patient may be at higher risk for infection (eg, low birth weight, indwelling devices, or prior to high-risk surgeries).
4. The literature does not definitively determine the effectiveness of universal decolonization (treating all infants regardless of S. aureus colonization status) as a strategy to prevent S. aureus infections in NICUs.

Infants colonized with MRSA have an estimated 22%–28% risk of developing a MRSA infection.2,21,32–34 Infants colonized with MSSA are also at increased risk of infection.30,31 In some

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populations, eradicating *S. aureus* colonization, via decolonization, can reduce the risk of infection.21,28,30,36 Both targeted and universal decolonization strategies have been employed in NICUs, but data are more limited for universal decolonization. Data showing efficacy and safety of *S. aureus* decolonization to reduce infection risk are primarily available from observational studies and a recent randomized trial that was not powered to detect a reduction in *S. aureus* infections.28,30,35-37

Even though decolonization has included treatment with topical antibiotics, topical antisepsics, and rarely, systemic antimicrobials, intranasal mupirocin alone is most commonly used. Intranasal mupirocin is not approved by the US Food and Drug Administration (FDA) for this indication in neonates, yet numerous studies reporting the use of mupirocin for *S. aureus* decolonization have not identified any clinically relevant adverse effects.28,30,38 Mupirocin can be applied twice daily for 5–7 days, although some centers report treating for longer. Although mupirocin intranasal application is extrapolated from studies in adult patients, no data exist on whether there is additional benefit to applying mupirocin to other body sites that may be colonized (eg, the umbilical stump, intertriginous areas, etc) among neonates. One study found a 5-day course of mupirocin applied to intranasal, periumbilical, and perianal areas to be safe and effective at reducing *S. aureus* colonization among NICU infants.21 Systemic antimicrobials have not been studied as part of decolonization regimens in infants.

Some units may choose to include topical antisepsis, most frequently with chlorhexidine gluconate (CHG). NICUs often use CHG for skin antisepsis; however, the FDA notes that these products should be "used with care in premature infants or infants under 2 months of age."39 Despite widespread CHG use in NICUs, adverse events are infrequent.40-43 Concerns about skin irritation and the potential for systemic absorption have led to significant practice variations in CHG use; many NICUs restrict CHG application, especially in preterm infants within the first month of life.44

Healthcare personnel should consider decolonization in the following settings: outbreaks, periods with high rates of *S. aureus* transmission or infection despite other standard infection prevention measures, and the management of colonized infants at high risk of *S. aureus* infection such as preterm, low-birth-weight infants, infants with indwelling devices, and prior to high-risk surgery. When implementing a decolonization program, units must be thoughtful about possible unintended consequences including (1) changes in the microbial ecology in the intensive care unit (ICU), (2) alterations of the individual infant’s microbiota, and (3) selection for antibiotic-resistant and antiseptic-tolerant strains. Commonly, *S. aureus* recolonization occurs following intranasal mupirocin.21,30,45 In settings for which decolonization is implemented, the risk of *S. aureus* disease among colonized infants should outweigh the potential consequences of decolonization noted above. Further studies are needed to determine the safety and efficacy of decolonization in infant populations, who will have the greatest benefit from decolonization, optimal decolonization regimens, and unintended consequences.

**Question 7:** Should NICUs use preemptive contact precautions for patients being screened for MRSA on admission?

**Answer 7:**

1. Units may choose not to use preemptive contact precautions for all NICU infants screened for MRSA at admission.
2. In outbreak settings or in NICUs with ongoing MRSA transmission, units may consider applying preemptive contact precautions for complex patients (eg, with central venous catheters, nonintact skin, or ventilator tubes) while admission *S. aureus* surveillance results are pending.

Preemptive contact precautions entail healthcare personnel wearing PPE while caring for the infant until surveillance culture results are finalized. If healthcare personnel perceive admitted neonates to be at high risk of MRSA colonization, then preemptive contact precautions may reduce the risk of exposure of healthcare personnel to MRSA. Small retrospective studies have suggested that undetected MRSA carriers that are not placed on contact precautions pose a significant risk to other patients within the unit.37 However, if healthcare personnel perceive admitted neonates to be at low risk of MRSA colonization, then preemptive contact precautions are likely not indicated. Some states mandate screening all neonates, even those at low risk of colonization. Therefore, units may choose not to use preemptive contact precautions for all infants admitted to their unit. The average onset of MRSA colonization among NICU infants is ~21–30 days of age; therefore, older infants who are admitted from another NICU or from the community may have a higher likelihood of MRSA colonization compared to newborn NICU admissions.2 Studies also suggest that the risk of multidrug-resistant organism colonization is 5–6 times higher after the first week of life.46 Therefore, preemptive contact precautions might be considered in older infants transferred after age 7 days. Still, in absolute terms, the risk is low and the cost-effectiveness of screening older infants at admission is unknown. For this reason, the authors do not currently recommend routine preemptive contact precautions.

Similarly, use of preemptive contact precautions for infants colonized with MSSA has not been studied. Acquisition of MSSA parallels that of MRSA, with a median time to colonization in the third to fourth week of life.1 For this reason, the yield of surveillance cultures for MSSA in the first week of life is expected to be low. Studies evaluating the use of preemptive contact precautions in the context of optimized hand hygiene among healthcare personnel and routine active surveillance cultures showed little to no impact on transmission.47 One large observational study reported a significant reduction in endemic MRSA transmission with the use of preemptive contact precautions; however, there was also a marked increase in hand hygiene compliance rates during the study period that confounds the results.48 In outbreak settings, units should consider a multimodal approach to mitigating MRSA transmission within the NICU, focused primarily on optimal hand hygiene practices. This approach may also include preemptive contact precautions for select high-risk patients or older newborn infants.

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