Principles of Infection Prevention in the Nursery

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Standard Precautions

Standard precautions (Box 1) are a set of actions that are required of every health-care provider for every patient, regardless of circumstances. Standard precautions include the use of personal protective equipment (PPE) such as eye shielding, masks, gowns, or gloves when in contact with body fluids (or when at risk for exposure). For example, when changing a wet diaper, gloves should be used to prevent contact with urine or feces.

Hand hygiene. Hand hygiene before and after patient contact is an important aspect of standard precautions. The positive effects of hand hygiene have been clear since the 1840s, when Ignaz Semmelweis demonstrated that handwashing

Box 1 Standard Precautions for All Healthcare Settings, Including the Nursery and the Neonatal Intensive Care Unit

1. Perform hand hygiene before and after every patient contact.
2. Use personal protective equipment (gloves, gowns, and/or masks) when in contact with body fluids (or when at risk for body fluid exposure).
3. Use and dispose of sharps safely.
4. Perform routine environmental cleaning.
5. Clean and process shared medical equipment between patients.
6. Follow respiratory hygiene and cough etiquette.
7. Use aseptic technique.
8. Handle and dispose of waste and soiled linen safely.

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dramatically reduced the incidence and mortality of childbed fever (i.e., puerperal sepsis) in Vienna's Allgemeines Krankenhaus maternity ward [1]. Hand hygiene is incredibly effective in prevention of horizontal transmission between patients, but perfect compliance is difficult to achieve and maintain [2, 3]. NICU-specific studies have shown significant reduction in sepsis and pneumonia as hand hygiene compliance improves [4]. Therefore, every individual entering the NICU—whether nursery provider, consultant, technician, or family visitor—should perform thorough handwashing before and after every patient contact. Efforts to support hand hygiene, such as "secret shoppers," written and verbal education and feedback, administrative support, family empowerment, and a culture of giving and accepting feedback are all strategies that have been used to improve hand hygiene compliance [5]. Of note, gloves are not a substitute for proper hand hygiene, and some studies suggest that hand hygiene compliance worsens when routine glove use is promoted [6]. Designing nurseries so that gel dispensers or sinks are readily available at entry to the unit as well as in every care area is an important step in improving hand hygiene compliance [7].

Respiratory etiquette. Respiratory etiquette involves covering coughs or sneezes, ideally with the proximal arm to avoid contaminating hands. However, respiratory etiquette also involves not introducing respiratory viruses to the unit in the first place. Respiratory viruses are a common cause of infection in the NICU setting (see chapter "Respiratory Viruses in the Neonatal Intensive Care Unit"). Visitors to the NICU should disclose active symptoms of illness and avoid visiting when symptomatic. Prior to entry, staff should inquire regarding active symptoms of infection such as cough, congestion, rhinorrhea, and fever [8]. Similarly, staff should avoid coming to work when actively sick with potentially transmissible infections, and administrators should ensure that staff members do not feel pressured to do so [9].

PPE. Gloves, gowns, masks, and other PPE should be worn as indicated by standard or transmission-based precautions (see section "Transmission-Based Precautions" below) by all healthcare personnel. However, the evidence is unclear as to whether family visitors should wear PPE. PPE can interfere with family bonding and prevent skin-to-skin kangaroo care and breastfeeding and is viewed negatively by many families [10]. According to the most recent recommendations by the Society for Healthcare Epidemiology in America, decisions regarding PPE for visitors should be based on the severity of the organism of concern, the healthcare status of the visitor, and the healthcare setting [11]. For example, the benefit of PPE for visitors for an infant with suspected varicella or parvovirus will vary based on immune status, pregnancy, et cetera. A NICU with an active outbreak may enforce PPE use, while a NICU with no ongoing transmission may be more relaxed. Research into the benefits and adverse consequences of visitor PPE use are needed to better inform these policies. Regardless of a given nursery's approach to visitor PPE, hand hygiene compliance should be paramount for all visitors.

Transmission-Based Precautions

Transmission-based precautions (Table 1) are used for certain infections when transmission is not completely interrupted using standard precautions alone. When used in addition to standard precautions, transmission-based precautions can reduce the risk for horizontal transmission and outbreaks (see chapter "Outbreak Control in the Nursery").

Contact precautions. Contact precautions (gown and gloves) are used to prevent transmission of infectious agents that are spread by direct or indirect contact with the patient or the patient's environment [12]. A single-patient room is preferred for infants in contact precautions; if one is not available, cohorting can be used (i.e., placing patients with the same colonization or infection in the same room) [13]. As much space as possible should be left between beds to reduce the opportunities for horizontal transmission between infants [12].

Droplet precautions. Droplet precautions (mask) are used to prevent transmission of pathogens that spread through infected droplets, which can be spread by expulsion during coughing or sneezing or by close contact with respiratory secretions. Droplet precautions are often used in combination with contact precautions, as most agents that can be spread by droplet can also be spread by indirect contact with droplets that land on nearby surfaces [12].

Table 1 Transmission-based precautions and common indications in the nursery setting

Precautions[a]	Equipment	Example pathogens
Contact	Gown and gloves	Methicillin-resistant staphylococci ESBL-producing gram negatives Vancomycin-resistant enterococci Herpes simplex virus Respiratory syncytial virus[b] Parainfluenza[b]
Droplet	Surgical mask	Influenza Rhinovirus Parvovirus Pertussis
Airborne	N95 mask Negative-pressure room with HEPA filter	Varicella Tuberculosis

[a]In addition to standard precautions

[b]Respiratory syncytial virus and parainfluenza require contact precautions rather than droplet. However, as part of standard precautions, surgical mask should be worn if contact with respiratory secretions is likely (e.g., if patient coughing or sneezing)Note that cytomegalovirus infection requires only standard precautions, since it is transmitted by body fluids (saliva, urine, etc.), and gloves should be worn for all potential body fluid contact as per standard precautions. Exclusion of pregnant caregivers is not specifically recommended (as it is for rubella or varicella nonimmune pregnant healthcare providers)A comprehensive list of pathogens and their recommended isolation precautions can be found in Appendix A of reference [12]

Airborne precautions. Airborne precautions (N95 mask, negative pressure room with HEPA filter) prevent transmission of pathogens by airborne particles. In contrast to droplets, which have a range of 3–6 ft before landing, airborne infections can remain suspended in air for long periods of time and can cover tremendous distances. Specialized negative pressure rooms prevent infectious airborne particles from spreading. Healthcare personnel should wear an N95 respirator when inside the negative pressure room [12, 14].

Surveillance Cultures

As opposed to clinical cultures, which are obtained when infection is suspected, surveillance cultures can be used to periodically ascertain whether or not infants are colonized with certain pathogens (Table 2) [15]. In clinical practice, surveillance cultures are usually used for two purposes—first, to determine whether specific transmission-based precautions are needed for a given infant (e.g., if the infant is found to be colonized with methicillin-resistant *Staphylococcus aureus* [MRSA], they are then placed in contact precautions) and second, to determine whether a given infant requires different empiric antibiotic treatment when infection is suspected (e.g., if an infant is colonized with an extended-spectrum beta-lactamase (ESBL)-producing gram-negative organism, they may need empiric carbapenem therapy). Conversely, surveillance cultures can support antibiotic stewardship—if an infant is known to be MRSA negative on surveillance cultures, then vancomycin can be safely withheld in most circumstances [16]. Examples of specific surveillance approaches are shown below.

MRSA. *S. aureus* is one of the more common causes of late-onset sepsis (see chapter "Late-Onset Sepsis") and causes significant morbidity and mortality. Approximately 25% of staphylococcal infections in US nurseries are due to MRSA

Table 2 Approach to surveillance cultures for common multidrug-resistant organisms encountered in the neonatal intensive care unit

	MRSA	ESBL	VRE
Source	Axilla and/or groin	Rectum	Rectum
Interventions	1. Contact precautions 2. Include vancomycin in empiric antibiotic therapy 3. Consider decolonization (nasal mupirocin and chlorhexidine bathing)	1. Contract precautions 2. Consider including meropenem in empiric antibiotic therapy	1. Contact precautions 2. Consider including linezolid in empiric antibiotic therapy
Evidence grade	A1	C2	C2

Frequency of screening depends on local epidemiology; higher incidence requires more frequent screening. Reported schedules range from monthly to as often as twice weekly during outbreaks. *MRSA* methicillin-resistant *Staphylococcus aureus*, *ESBL* extended-spectrum beta-lactamase-producing gram negatives, *VRE* vancomycin-resistant *Enterococcus* rather than methicillin-susceptible strains [17]. Prematurity and prolonged NICU stay are major risk factors for MRSA colonization [18]. MRSA-colonized infants can be cohorted and decolonized (treated with intranasal mupirocin twice daily for 5 days along with chlorhexidine bathing), which has been shown to reduce the risk of infection and horizontal transmission [19].

ESBL-producing gram negatives. The prevalence of colonization with ESBL-producing gram negatives mirrors the community prevalence; infants born to mothers who are colonized are at increased risk. Most transmission occurs within the first 2–4 weeks after delivery but may occur at any point during the NICU stay [20]. Surveillance rectal or skin swabs to detect ESBL-producing gram negatives have been used during outbreaks [21]. However, data regarding the use of routine surveillance for ESBL producers is lacking. Given that colonization with a given organism is a risk factor for subsequent infection with that organism, and since ESBL-producing organisms usually require carbapenem therapy for treatment, the logical extension is that screening for these organisms could be beneficial. However, the implications for microbiology lab workflow, cost-effectiveness, and impact on infant outcome have not been well studied [22].

Vancomycin-resistant Enterococci (*VRE*). *Enterococcus* species are generally susceptible to ampicillin and/or vancomycin; enterococci that develop resistance to vancomycin are referred to as VRE. As with MRSA and ESBL producers, VRE most commonly colonizes and subsequently infects preterm infants. Vancomycin exposure is an unsurprising risk factor for VRE colonization [23]. Colonized infants should be placed in contract precautions, and linezolid should be considered as part of empiric antibiotic therapy when sepsis is suspected.

Device-Associated Infections

Central line-associated bloodstream infections. Central line-associated bloodstream infections (CLABSIs) are the most common hospital-acquired infection in the NICU and are associated with significant morbidity and mortality [24–26]. Central lines are commonly required for the administration of fluid, nutrition, and medications. The primary risk factors for CLABSIs include prematurity and catheter dwell time. The longer that a central line remains in place, the higher the risk for CLABSI. Each manipulation of the central line—such as infusions, tubing changes, opening or recapping the hub—will increase risk for CLABSI if proper technique is not followed. On average, preterm infants undergo catheter manipulation every 8 h [27]. Intra-abdominal pathology such as necrotizing enterocolitis or bowel perforation usually requires bowel rest and total parenteral nutrition through a central line, which increases catheter dwell time and therefore the risk for CLABSI. Histamine-2 receptor blockers and proton pump inhibitors are also associated with increased risk for necrotizing enterocolitis, sepsis, and CLABSIs [28, 29]. Presumably, this is due to lowered gastric acidity and increased central line requirement if the infant develops necrotizing enterocolitis.

CLABSI reduction can be achieved by combining evidence-based prevention strategies into “bundles.” Bundles focus on avoiding central-line insertion whenever possible, minimizing dwell times, and careful attention to sterile line maintenance (Box 2). Unnecessary line placement can be avoided if specific criteria for insertion are used [30]. Having a dedicated team of providers (i.e., a central line team) who are specially trained in insertion and maintenance of central lines has been associated with decreased risk for CLABSI [31, 32]. Feeding guidelines that emphasize prompt feeding initiation and advancement will help to minimize line days. Bundles that focus on reaching 120 cc/kg/day of enteral feeds and then promptly removing the central line have been shown to reduce CLABSIs [33]. The CLABSI risk per line/day is higher with umbilical venous catheters than with other catheters once dwell times exceed 7–14 days [34, 35]. Therefore, a reasonable strategy is to exchange the umbilical venous catheter for a peripherally inserted central catheter within 7–10 days and to remove the central line as soon as it is no longer needed.

Ventilator-associated pneumonia. Ventilator-associated pneumonia (VAP) is defined as new lower respiratory tract infection in a mechanically ventilated infant occurring >48 h after intubation [36]. VAP is a difficult diagnosis to confirm, as the clinical criteria are subjective and the majority of intubated neonates have preexisting, noninfectious lower respiratory tract disease such as respiratory distress syndrome, transient tachypnea of the newborn, or bronchopulmonary dysplasia [37]. The primary risk factor for VAP is intubation. An endotracheal tube allows bacteria to avoid most of the innate defenses of the upper airway and directly communicate with distal airways and alveoli [38]. Another major risk factor for VAP is prematurity and concomitant lung immaturity. The most preterm infants generally require the longest duration of mechanical ventilation and therefore have the highest

Box 2 Evidence-Based Bundles to Prevent Central-Line Associated Bloodstream Infections in the Neonatal Intensive Care Unit

Insertion

- Avoid placement of unnecessary central lines
- Hand hygiene and maximal sterile barrier precautions before catheter insertion
- Povidone-iodine or 2% chlorhexidine skin preparation before insertion

Maintenance

- Disinfect catheter hubs and connectors before accessing ports
- Perform dressing changes *only* if dressing is loose or soiled

Removal

- Remove catheter promptly once no longer required

Box 3 Evidence-Based Bundles to Prevent Ventilator-Associated Pneumonia in the Neonatal Intensive Care Unit

Insertion

- Avoid intubation when possible
- Use sterile tube for intubation

Maintenance

- Elevate head of bed 30° if possible
- Oral care with sterile water or colostrum
- Change breathing circuit only when malfunctioning or visibly soiled
- Closed-circuit suctioning
- Avoid unplanned extubations

Removal

- Avoid oversedation
- Daily evaluation for readiness to extubate

incidence of VAP. As with CLABSI, antacid therapy has been linked to pneumonia and VAP [39–41].

Bundled prevention of VAP care (Box 3) includes careful insertion and maintenance of endotracheal tubes, closed suctioning systems, avoiding unplanned extubations, oral care with sterile water or breast milk, avoiding oversedation, and extubating infants as soon as feasible [42, 43]. In addition, as discussed in chapter "Late-Onset Sepsis," culture of the endotracheal tube should be avoided whenever possible. The upper airway is not sterile, and endotracheal tubes are rapidly colonized [44]. Therefore, bacteria recovered from the endotracheal tube are likely to represent colonization rather than infection, particularly if signs of lower respiratory tract disease are absent. Endotracheal tube cultures should only be considered when both clinical and radiographic evidence of pneumonia are present [45].

Ventricular shunt infection. Infants may require cerebrospinal fluid shunting due to congenital (e.g., aqueductal stenosis, Dandy-Walker malformation) or acquired (e.g., posthemorrhagic or postinfectious) hydrocephalus. Shunting can be accomplished with a ventriculoperitoneal shunt (VPS) or, for infants too small to undergo definitive VPS shunting, a temporizing measure such as a ventricular reservoir, subgaleal shunts, or serial lumbar punctures. Both definitive and temporizing shunts are associated with risk for shunt-associated meningitis or ventriculitis. The risk of shunt infection decreases as the age and size of the child increase [46]. Temporizing measures generally have a higher incidence of infection than VPS. Regardless of the type of shunt, risk is highest within a few weeks of shunt placement or revision and then decreases sharply over time, but never reaches zero [47].

Prevention of shunt infection requires striking a balance between higher-risk temporizing measures that allow growth until the lower-risk VPS is available. Careful insertion and maintenance technique is critical for temporizing measures. The optimal strategy is to standardize the approach to ventricular diversion at a given center, with input from pediatric neurosurgery, neonatology, infectious diseases, and infection prevention. Standardized surgical approaches to VPS placement are associated with lower infection rates [48]. Antibiotic-impregnated shunt catheters or injection of antibiotics into the shunt during placement has also been shown to reduce infection risk [49–51]. Double-gloving—where the neurosurgeon removes the first pair of gloves intraoperatively prior to handling the shunt catheter—also appears to be effective in reducing risk [52].

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