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Nosocomial Infection in Neonates
Inevitable or Preventable?

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In the neonatal intensive care unit population the nosocomial infection rate is highest in the lowest-birth-weight infants. It is this group of infants who require the most therapeutic interventions to support them leading to frequent invasive procedures and the longest exposure to the hospital environment. However, infection rates vary from one unit to another, suggesting that there are differences in either how infection rates are determined or the care provided in the various units. This article will describe nosocomial infections and rates in the neonatal intensive care unit and identify strategies of care to minimize the risks of nosocomial infection in low-birth-weight infants. **Key words:** *low-birth-weight preterm infants*, *nosocomial infection*, *risk factors*, *strategies to minimize risks*

As smaller and less mature infants are being cared for in neonatal intensive care units (NICUs), neonatal nosocomial infection (NI) rates are increasing with an incidence inversely proportionatal to the gestational ages of the infants populating the NICUs.[1–4] Considering that the smallest, least- mature infants often require the most invasive procedures, have sensitive and immature skin that does not provide a strong barrier against environmental organisms, and immune systems that are marginally responsive to infection from any portal of entry, high-infection rates seem inevitable; but are they? Because neonatal NIs are known causes of morbidity and mortality in all neonates, but particularly in the smallest, most immature infants,[1–5] it is important to determine whether the infection risk is inherent to the infant or can be affected by the environment and treatment received in the NICU. The *purpose* of this article is to review the literature to determine strategies available to protect the smallest and most vulnerable intensive care patients from NIs. This review will first describe NIs and discuss differences in reported NI rates. It will then identify strategies to minimize NIs on the basis of NI risk factors.

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NOSOCOMIAL INFECTIONS

Definition

Nosocomial infection is defined as an infection occurring at any site, which was acquired during a hospitalization and results from inoculation with an organism that was not present or incubating in a patient at the time of admission.[3,6] This definition is easily applied to pediatric and adult populations that are admitted from home, but neonates have a unique preadmission environment that can be protective or provide exposure to a host of maternal microbes. To help determine whether a neonatal infection is perinatally acquired or nosocomial in origin, neonatal infections have been divided into early- and late-onset infections on the basis of the timing of the presentation of symptoms and causative organism.[5–8]

An early onset or perinatally acquired infection often presents at delivery or becomes evident by day 3 of life.[6] The Centers for Disease Control and Prevention studied the epidemiology of neonatal NIs and developed the National Nosocomial Infections Surveillance (NNIS) system to benchmark NI-rate data for patients in

the NICU. When tracked using NNIS standardized protocols, 89% of the infants with perinatally acquired infections presented with symptoms in the first 48 hours of life.[7]

The consortium formed by the National Institute of Child Health and Human Development (NICHD) Neonatal Research Network defines *late onset, nosocomially acquired infections* as those occurring after the first 3 days, or 72 hours, of life.[5]

Types of nosocomial infection

In addition to the timing of onset, the NNIS determined there are causative organisms, particularly Group B *Streptococci* or *Eschericheria coli* that are most likely acquired perinatally but do not always cause disease or present with symptoms within the identified time constraints.[7] The infant may be inoculated with these organisms in utero or during deliveries but not present with an infection, often late-onset meningitis, until after the first week of life.[8] This late-onset phenomenon often complicates the categorization of neonatal NIs.

Nosocomial infections include bloodstream infections, ventilator-acquired pneumonia, urinary tract infections, meningitis, secondary skin infections, and abscesses after skin breakdown or an invasive procedure, and eye, ear, nose, or throat infections.[1,4,9] Causative organisms can be bacterial, viral, or fungal in origin.[1,7,9] Technically, even *Candida* diaper dermatitis is a NI as it was acquired during the hospital stay and was not perinatally transmitted.

Bloodstream infections, frequently with coagulase negative *Staphylococci* and associated with central venous lines,[1–4,6,9] are reported to be the most common NI with an incidence as high as 78% of the total NIs reported.[10] The next most common site varies among NICUs but is often in either the respiratory[1,4,9] or urinary tract.[10]

Impact of nosocomial infection

Nosocomial infections are associated with significant morbidity and increased mortality and impact the healthcare system. The site of infection determines the type of morbidity. Meningitis, for example, may result in multiple major morbidities including hearing loss, visual impairment, seizure disorder, cerebral palsy, learning disabilities, and mental retardation.[11,12] Any combination of these morbidities changes the infant's life potential. Follow-up care with a multidisciplinary team becomes a lifetime commitment for the family.

Ventilator-acquired pneumonia predisposes the infant to chronic lung changes from the impact of the inflammatory response, supplemental oxygen, and the ventilatory support required to manage the infant through the infectious process.[13] As a result, the infant may have a longer hospital stay, require home oxygen, and need follow-up care with a pulmonologist to manage the long-term sequelae of a nosocomial pneumonia.

Nosocomial infections contribute to increased mortality rates. Systemic infections presenting with septic shock, hypotension, decreased tissue perfusion, profound acidosis, and end-organ failure can lead to death. Mortality rates are reported to be from 13% to 50% in infants who develop an NI, specifically those with bloodstream infections and meningitis.[8] The NICHD Neonatal Research Network reported the mortality rate for infants with any NI to be 18% as compared with an overall NICU infant mortality rate of 7%.[5]

Nosocomial infections also impact the healthcare system. Nosocomial infections increase the use of medical resources and the cost of healthcare. An infant with an NI has a median NICU stay of 88 days compared with a median hospital stay of 32 days for an infant without an NI.[9] An increased number of hospital days alone will increase the cost of the infant's care. Add the cost of diagnostic tests, respiratory and nutritional support, medications, and nursing care to the daily cost of a NICU bed for each additional hospital day, and the cost of a caring for an infant with a NI increases substantially over the cost of his care had he remained infection-free.[5] In the United States, it is estimated that NIs increase the overall cost of healthcare by $3.5 billion a year.[14]

For example, an infant who developed nosocomial meningitis and has major postinfection morbidities will require additional health services and expenditure of dollars on healthcare throughout a lifetime. Although the cost of coordinating and providing out-patient services for children with special healthcare needs is not separated by causative diagnosis, the cost of providing home healthcare for infants and children with chronic physical, neurodevelopmental, or behavioral, and emotional morbidities resulting from NIs does contribute to the annual cost of home care.

In the year 2000, there were approximately 500 000 children using home healthcare services at an estimated annual cost of $5.3 billion[15] or approximately $10 000 per child per year. However, money was not evenly divided among the children but paid out based on required services that varied from home parenteral nutrition and central line care to tracheostomy care and mechanical ventilation. Oxygen-dependent children with tracheostomies have a mean annual home care cost of $63 650.[16] Antonelli and Antonelli[17] reported the cost of coordinating services for a child with special healthcare needs to range from $22 809 to $33 048, depending on the number of major morbidities and organ systems affected.[17]

Hospital stay days and healthcare dollars are the hard, easily measurable costs of NI. The cost to the infant and family is immeasurable in terms of the loss of individual potential, impact on family resources, and unfulfilled dreams that cannot be measured with a positive blood culture or by additional days in the hospital.

Incidence of nosocomial infection

There is a wide variation in the reported incidence of NI rates between NICUs. In the United States, NI rates vary from 6% to greater than 40%.[1,5,6,9,18] Internationally, the incidence has been reported to be as high as 69%.[19] This discrepancy in NI rates could be due to differences in defining, identifying, and reporting NIs.

There are differences in reporting NI, particularly the timing of onset. There appears to be no clear-cut delineation for the optimal cutoff time for identification of an infection as perinatally acquired or nosocomial in origin. As previously discussed, NNIS identified 48 hours[7] and the NICHD Neonatal Research Network uses 3 days[5] as the cutoff for perinatally acquired infections. However, neonatal textbooks determine 5 to 7 days[8,20] to be the cutoff time for perinatally acquired infections with late-onset NIs occurring after that.

Most reports used a positive culture, whether blood, spinal fluid, or urine, to determine a NI.[1,5,6,9,18,19] However, NIs in infants who have a positive blood culture and a central venous line are reported either as a percentage of the patient population or as the number of positive blood cultures per catheter days, making it difficult to compare one study's results to another.

Some studies included infants with clinical symptoms of infections who had negative cultures, especially suspected bloodstream infections with a systemic impact.[21] Clinical symptoms of infection include temperature instability, respiratory distress, lethargy, hypotension and hypoperfusion, feeding intolerance, and metabolic acidosis.[8,20] These symptoms are nonspecific and may indicate a problem other than infection. As a result, suspected infections based on clinical presentation without a positive culture were often not included in reports of NI, nor were pneumonia and necrotizing enterocolitis because of the subjective nature of the diagnostic criteria.[10] Consequently, when comparing reported NI rates from one unit to another, it is important to determine whether or not clinically suspected infections with negative cultures are included in the report and which method, percentage, or NIs per catheter days, was used to determine the incidence of NI.

STRATEGIES TO MINIMIZE RISK

To identify strategies to minimize the risk of NIs, it is necessary to understand the risk factors associated with increased NI rates.

Risk factors

Risk factors are varied and multifactorial. Table 1 shows risk factors related to prematurity, NICU therapies, and unit design and culture.

Low-birth weight and decreasing gestational age are associated with increased NI rates. Infants with a birth weight of 1500 g or less are 2.69 times more likely to acquire an NI than infants who are born at a higher weight.[9] Prematurity by itself is a risk factor for NI because preterm infants are immune

Table 1. Risk factors predisposing an infant to nosocomial infection

Risk factor	Infection site(s)	
Prematurity/low-birth-weight	Skin, airway, respiratory tract bloodstream, spinal fluid, GU tract, and GI tract	Out of our control
Central line	Bloodstream	Controllable
Endotracheal tube	Respiratory tract	Controllable
Multiple venipunctures or heelsticks	Skin and bloodstream	Controllable
Prolonged NPO	GI tract	Controllable
Parenteral nutrition	Bloodstream	
Indwelling urinary catheters	GU tract	Controllable
Antibiotic exposure	Skin, airway, respiratory tract, bloodstream, GU tract, and GI tract	Controllable
Unit design/culture	Skin, airway, respiratory tract bloodstream, spinal fluid, GU tract, and GI tract	Controllable

Abbreviations: GI, gastrointestinal; GU, genitourinary; NPO, nil per os (nothing by mouth).

compromised and have increased susceptibility to infection due to an immature immune system, inefficient neutrophil function,[20,22,23] and lack of antigen type-specific antibodies to pathogens in their environment.[20]

In addition to the inability to mount a mature immune response, preterm infants are exposed to a multitude of therapies during their NICU stay that places them at risk for acquiring an infection. Neonatal intensive care unit therapies that provide a portal of entry for pathogens include intubation and ventilation, central venous catheters and parenteral nutrition, peripheral intravenous lines, venipuncture or heelstick blood draws and indwelling urinary catheters.[22] Of the therapeutic interventions used in the NICU, the use of central venous catheters is most frequently associated with NI.[24] Other identified NI risk factors change the flora in the infant and/or the environment and include prolonged, nil per os (nothing by mouth) and frequent or prophylactic use of antibiotics.[24]

Unit design and unit culture also impact the NI rate. Overcrowded nurseries with a minimal number of sinks or lack of alternative methods of hand cleansing are at risk for increased NI rates due to the direct transmission of pathogens from the hands of the healthcare provider to the infant.[24,25] Units with long-established practices and an unwillingness to change approaches to care or to utilize protocols based on continuous quality improvement (CQI) processes have a limited ability to impact the NI rate.[24–26]

Table 2. Strategies to decrease the nosocomial infection rates

Risk factor	Strategy to minimize impact
Any/all	Handwashing CQI program
Immature skin	Skin care team Identify products and processes to protect skin
Central line	PCVC Team Limit days of catheter in place (early feeds) Catheter insertion and maintenance protocols
NPO	Multidisciplinary team approach to early feedings using a feeding protocol with guidelines for advancing/continuing/discontinuing feedings
Indwelling endotracheal tube	Multidisciplinary team commitment to early extubation/CPAP
Venipuncture/heelsticks	Cluster laboratory results, minimize skin punctures Adequate skin preparation/cleansing
Indwelling urinary catheter	Adequate skin cleansing at insertion Limit days of catheter in place Aseptic technique with care
Unit design/culture	Minimize overcrowding. Provision of alcohol-based alternative hand-cleansing products Utilization of CQI processes to identify risks, strategies to minimize risks, and follow-up effectiveness of strategies

Abbreviations: CQI, continuous quality improvement; PCVC, percutaneous venous catheters; NPO, nil per os (nothing by mouth); CPAP, continuous positive airway pressure.

Strategies to minimize risks

Do the risk factors inevitably lead to NIs or are there strategies that can minimize the impact of identified risks and decrease the NI rate?

Risk factors can be categorized into 2 groups: out-of-control and potentially controllable groups. Once potentially controllable risks are identified, strategies to minimize or eliminate specific risks can be implemented (Table 2).

The NICU team may not be able to control the gestational age or birth weight of the infants admitted to their NICU; however, each individual person and collective group in any unit can work to develop patient care strategies that minimize the NI risk incurred by neonates in their NICU. By comparing low NI rate units with those with higher NI rates, strategies that decrease NI rates have been identified.[18,25–30]

One strategy that is easy to implement and effective in reducing NI rates is hand washing. The initiation of and adherence to a meticulous hand hygiene program has been shown to be the single most effective strategy to reduce NI rates by decreasing direct transfer of hospital pathogens and skin flora to the infant and its environment.[24,28,29,31] Washing hands faithfully both before and after touching the infant is paramount in limiting the transfer of microbes to and from the infant, its environment, and the hands of the caregiver.[25] In addition, eliminating jewelry (rings, watches, bracelets) and artificial nails has been shown to decrease the transfer of bacteria from the caregiver's hands to the infant's environment.[24,27,28]

The success of a hand-washing protocol depends on both the individual's behavior and the unit's commitment to providing the necessary supplies. Having alternative hand-cleansing methods like alcohol-based waterless rubs readily available and conveniently

placed in patient care areas improves compliance with hand-washing protocols as does a unit culture that encourages staff members to remind each other to wash when a breech is about to occur.[25,28,29] In addition to the immediate nursing staff, all healthcare workers and family members who have contact with infants in the unit must be committed to adherence to a strict hand-washing protocol for it to be effective in reducing NI.

A multidisciplinary team approach to care for infants in the NICU potentially can provide a partnership of caregivers dedicated to identifying strategies and practices to decrease NI.[25,28,29] The following are examples of how changes in unit culture using a multidisciplinary team approach can directly impact NI risk factors.

1. A team commitment to early extubation decreases the number of days an endotracheal tube is in place as a portal for infection.
2. A team commitment to an early feeding protocol increases the number of infants who are successfully fed early. Early feedings minimize changes in the intestinal mucosa that increase the risk of necrotizing enterocolitis and the translocation of intestinal microbes that lead to sepsis in infants who are kept nil per os (nothing by mouth).[32] Early feedings also decrease the need for long-term exposure to parenteral nutrition and central venous lines by shortening the duration of time it takes to advance feedings to volumes that support growth.
3. A team commitment to decreasing the number of skin punctures an infant receives can decrease NI rates.[24,25] Limiting the number of venipunctures and heelsticks can lead to clustered laboratory tests and a reduced number of glucose checks that aids in maintaining skin integrity and decreases the number of entry sites for pathogens.
4. A team commitment to limiting exposure to antibiotics can decrease NI rates. Exposure to broad-spectrum antibiotics changes the pathogens in the community, the hospital, and the NICU. Subsequently, the organisms colonizing the skin and respiratory and gastrointestinal tracts of patients in the hospital may become resistant to frequently prescribed antibiotics.[24,33,34] Limiting the use of prophylactic antibiotics with negative cultures and discontinuing antibiotics after 48 hours have been shown to be effective strategies to decrease NI rates.[19,35] When committed to a strategy that limits antibiotic exposure, a multidisciplinary team can actively decrease the number of antibiotic doses given to every infant with a "rule out sepsis" diagnosis by writing for only 48 hours of antibiotic coverage. Then, instead of having to remember to discontinue antibiotics with negative cultures at 48 hours, the team orders the desired duration of antibiotic treatment if a culture is reported to be positive and the organism is identified.
5. Designating a limited number of specially trained nurses as members of a central line team for both placement and maintenance of percutaneous venous catheters (PCVC) should improve competency of insertion skills and standardization of techniques and in turn reduce NI risk. A PCVC protocol should include a limited number of team members, a system for hub care and tubing changes, and a determination of the entire NICU team to limit the number of times the line is entered for any reason.[24,25] Using this strategy has decreased bloodstream infection rates in infants with central lines.[19,24–26] One unit reports a decrease of nosocomial bloodstream infection rates from 25.4% to 2.2% when compared against itself before and after instituting a comprehensive strategy for the insertion and care of PCVCs.[26] Another unit reported a decrease in the incidence of NI from 69% to 17%, using a multidisciplinary approach.[19]
6. Utilizing a multidisciplinary skin care committee to identify new and more effective skin-protective products adds dimension to the development of a strategy that maintains skin integrity. Protecting skin integrity, one of the body's primary defenses against infection, and eliminating skin breakdown can remove denuded skin as a portal of entry for bacteria.[36]

Many strategies overlap: For example, early feedings will limit the number of days the infant in NICU needs a central line and decrease the use of parenteral nutrition, thus reducing its exposure to the risk of a bloodstream infection resulting from prolonged use of these therapies. Most strategies that reduce NIs require a commitment from the individual nurse and the unit as a whole. The social culture of the NICU must support development of specialized teams, like a PCVC or skin care team, and utilization of a CQI process to track the effectiveness of chosen strategies to determine whether there is a measurable impact on the NI rate.[18] In addition to evaluating outcomes, the entire team must be willing to modify strategies that have been shown to be ineffective, implement changes in practice, and continuously reevaluate NI rates. Units that have initiated a CQI-based approach for developing strategies to minimize the risks of NI have been able

to lower their NI rate and sustain a lower incidence of NIs over time.[18]

CONCLUSION

The risk of NI increases with decreasing birth weight and gestational age and increasing invasive therapies. There are significant morbidities and an increased mortality rate associated with NI. By comparing units with low-infection rates with those with higher-infection rates, strategies to minimize the impact of risk factors have been identified. In addition, units that have instituted infection reduction strategies and compared NI rates before and after a change in practice have identified strategies that decrease NI rates. The most significant impact has been seen after the institution of a strict hand-washing policy and a change in the unit's culture to promote adherence to the policy. Other factors that decrease NI rates include decreasing exposure to invasive procedures with early extubation, limiting parenteral nutrition and central line days, and minimizing skin punctures for laboratory draws, sugar checks, and intravenous fluids. Early feedings and minimizing antibiotic exposure have also been shown to decrease NI. By evaluating the risks of NI in the NICU, adopting a structured strategy that changes unit practices to address those risks, and evaluating the impact of the newly adopted strategies by tracking infection sites and organisms, the incidence of NIs in the neonatal population can be reduced.

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