

Editorial

Large Infection Problems in Small Patients Merit a Renewed Emphasis on Prevention

Nalini Singh, MD, MPH

One who maintains one's hygiene through cleanliness derives ten bodily benefits, whereas, one who is moderate in one's diet gets only six benefits.—Vidur (from the *Vedas*, 1500 BC)

Advances in neonatal care have improved the survival of immature, very low birth weight (VLBW) infants. These infants (< 1,500 g) experience a disproportionate share of healthcare-associated infections (approximately 75%) compared with other newborns in the neonatal intensive care unit (NICU).^{1,2} The number of sepsis episodes increases with decreasing birth weight. Complications related to prematurity and late-onset sepsis are associated with increased morbidity and mortality and higher healthcare costs. These infants have a significantly longer hospital stay (79 vs 60 days; $P < .001$) and higher mortality rate (18% vs 7%; $P < .001$).³ This issue of *Infection Control and Hospital Epidemiology* contains multiple important articles focusing on infections, their consequences, and/or their prevention among NICU patients.⁴⁻⁸

In high-risk infants, there may be an increase in the incidence of healthcare-associated infections due to multidrug-resistant gram-negative organisms.^{9,10} In a multicenter study from the Neonatal Research Network of the National Institute of Child Health and Human Development, among 5,447 patients, the increased use of intrapartum antimicrobials for the prevention of group B streptococcal disease was associated with a decrease in the incidence of early-onset (< 3 days) group B streptococcal sepsis (from 5.9 to 1.7 per 1,000 live births) but an increase in sepsis with ampicillin-resistant *Escherichia coli* isolates (from 3.2 to 6.8 per 1,000 live births).¹¹ The mortality rate

also is higher for VLBW infants with infections due to gram-negative organisms (36%; odds ratio for gram-negative vs other organisms, 3.5; $P < .001$).³ Three of the articles in this issue of *Infection Control and Hospital Epidemiology* deal with outbreaks of *Serratia marcescens* infections among NICU patients.^{4,6}

High-risk infants acquire gram-negative infections either endogenously or exogenously. The major endogenous reservoir for many organisms, such as Enterobacteriaceae and *Candida*, is the large intestine of the patient.¹² Exogenously, *S. marcescens* has been acquired through the contaminated hands of healthcare workers or through contaminated soap, equipment, or milk.¹³⁻¹⁸ *S. marcescens*, a member of the Enterobacteriaceae family, is responsible for outbreaks in NICUs that are difficult to control due to persistent gastrointestinal colonization.^{19,22} In a point-prevalence survey of 29 NICUs in the United States, it caused only 5% of healthcare-associated infections.¹ The clinical spectrum of disease varies from colonization, ophthalmic infections such as conjunctivitis, and endophthalmitis to invasive infections such as bacteremia, meningitis, and cerebral abscess.²³⁻³⁴

Intestinal colonization along with selective pressure exerted by the widespread use of antimicrobial agents plays an important role in healthcare-associated infections and colonization among VLBW infants.^{10,12,35} These infants are prime targets for the spread of pathogens of healthcare-associated infections because of lack of bowel control, close proximity of patients, and frequent patient movements within the NICU to accommodate staffing needs. Any breach in infection control practices can lead to horizontal spread via the hands of healthcare workers, or through the use of shared, contaminated equipment.

Dr. Singh is Professor of Pediatrics, Epidemiology and Global Health, The George Washington University, Children's National Medical Center, Washington, DC.

Address correspondence to Nalini Singh, MD, MPH, Children's National Medical Center, 111 Michigan Avenue NW, Washington, DC 20010. The author thanks Sumathi Nambiar, MD, and Rachel Temple, RN, for reviewing the manuscript and offering helpful suggestions.

Studies in this issue of *Infection Control and Hospital Epidemiology* by Milisavljevic et al.,⁴ Sarvikivi et al.,⁵ and Lai et al.⁶ illustrate (1) the ability of *S. marcescens* to cause sporadic outbreaks in populations of vulnerable infants hospitalized in NICUs over months to years; (2) protean clinical manifestations ranging from simple colonization to conjunctivitis and sepsis; (3) resistance to various antimicrobial agents, thereby limiting the therapeutic options of clinicians; (4) use of molecular epidemiologic tools such as pulsed-field gel electrophoresis to confirm clonal outbreaks of *S. marcescens*; (5) the need for aggressive infection control measures to limit spread of the organisms (performing active surveillance cultures, cohorting infected or colonized patients, assessing staffing, performing environmental cultures, enforcing hand hygiene, and installing alcohol-based hand gels in locations convenient to the staff); and (6) similar risk factors for these infections such as low gestational age, low birth weight, and frequency of invasive procedures.

In addition to the control measures outlined above, Lai et al.⁶ also banned artificial fingernails among their staff. Whether artificial fingernails are responsible for the transmission of pathogens of healthcare-associated infections is unknown.³⁶ However, healthcare workers who wear them are more likely to harbor gram-negative pathogens before and after washing their hands, and they have been implicated in other outbreaks involving *Pseudomonas aeruginosa*.³⁷⁻⁴⁰ Healthcare workers should be discouraged from wearing long or artificial fingernails when caring for high-risk patients.

Overcrowding and understaffing are common themes in these outbreaks of *S. marcescens* and in previously published studies.^{41,42} Currently, healthcare is an "industry" with a corporate culture and hospitals continue to admit patients to remain financially solvent despite staffing problems. Front-line healthcare workers are facing, on a daily basis, the challenges of managing increasingly complex patients, who require intensive support. Meticulous hand hygiene is one of the many tasks they need to perform while caring for multiple patients. Noncompliance with this practice has the potential to spread the pathogens of healthcare-associated infections from person to person.

Enhanced infection control measures are needed when epidemiologically significant organisms are detected by either active surveillance or clinical cultures. *S. marcescens* is an organism of epidemiologic significance due to its ability to not only cause invasive infection in neonates and outbreaks, but also acquire resistance to antimicrobial agents frequently used in NICUs.^{10,43-45} Various DNA-based molecular typing methods are available and should be integrated into the investigation of an outbreak. Many have been used in "real time" to allow NICUs to remain open while genetically distinct strains are being identified.⁴⁶⁻⁵¹

Another important article in this issue of *Infection Control and Hospital Epidemiology* found that administration of inadequate empiric antimicrobial therapy was associated with worse outcomes among NICU patients with

bloodstream infection, as previously demonstrated in multiple studies of adult patients.⁷ In a cohort of 229 patients, 45 neonates had 90 episodes of bloodstream infection. Only 14% of these episodes occurred in the first 7 days of life and 86% occurred after this period. Isolation of coagulase-negative staphylococci in blood cultures may reflect either a true infection or a contaminant. A limitation noted by the authors of this study was that a single positive blood culture from an indwelling catheter was considered to represent a bloodstream infection even when a coagulase-negative staphylococci was grown. Neonates with *Candida* species sepsis were more likely to die as a result of not receiving appropriate antimicrobial treatment within 48 hours of performing a blood culture. Empiric antifungal therapy for at-risk VLBW neonates was proposed previously based on a clinical predictive model that had a sensitivity of 85% and a specificity of 47%⁵²; empiric antifungal treatment was recommended if neonates had a gestational age below 25 weeks, thrombocytopenia, or a history of third-generation cephalosporin or carbapenem therapy in the 7 days before obtaining blood for culture.

Although routine infection control practices may seem too simple to address the complexity of the issue at hand, their faithful application has been shown to be effective. In this issue of *Infection Control and Hospital Epidemiology*, Won et al. found that a multifaceted motivational approach for improving compliance with hand hygiene using both positive and negative reinforcement strategies was associated with a significant reduction in healthcare-associated infections among NICU patients, especially respiratory tract infections.⁸ The healthcare community is encouraged to once again return to basics while using molecular typing as needed to confirm apparent outbreaks. It is important to remember that infection control is everyone's responsibility.

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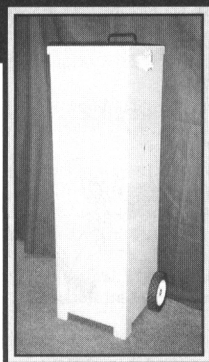
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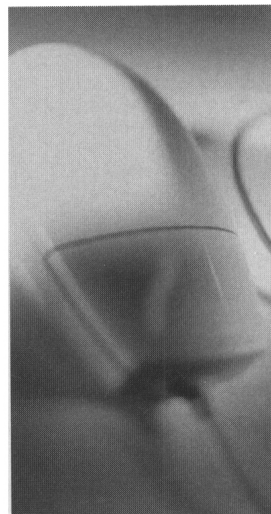


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