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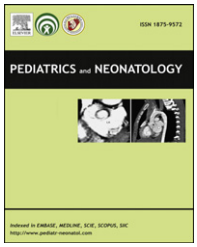

EDITORIAL

Protect the Unprotected: Neonatal Sepsis in Very-Low-Birth-Weight Infants

In the past decade, advances in perinatal care have resulted in the significantly increased survival of preterm infants with very low birth weight (VLBW). However, prolonged stay in the Neonatal Intensive Care Unit (NICU) also leads to increased susceptibility to sepsis. Early- and late-onset neonatal sepsis remain as the leading causes of mortality in VLBW infants. In this issue of the *Pediatrics and Neonatology*, Lim et al[1] reports that approximately 13% of all VLBW infants experience one or more episodes of sepsis before they leave the NICU. In addition to prolonged stays in the NICU, factors such as an immature immune system, the fragility of the skin barrier, the frequent use of invasive procedures, the prolonged use of mechanical ventilation, and total parental nutrition may account for the higher incidence and mortality rate of neonatal sepsis that have been observed in VLBW infants. Clinically, the lack of specific symptoms, signs, and biomarkers make the early diagnosis and prompt treatment of sepsis difficult. The emergence of pathogens with decreased susceptibility to commonly used antibiotics has also made traditional empirical antimicrobial treatments inadequate. In the abovementioned report, nearly 6% of *Escherichia coli* strains are reported as resistant to most cephalosporins and 83% of *Staphylococcus aureus* strains are reported as resistant to oxacillin. These results should be used to guide the use of empirical antibiotics for treating sepsis in VLBW infants.

In the face of these challenges, scientists are actively evaluating several new strategies with the hope of improving the survival of VLBW infants with neonatal sepsis. First of all, rapid and novel diagnostic techniques with higher sensitivities are being tested with some success.[2] For example, procalcitonin and mannose-binding lectin are probably more sensitive and specific for detecting the early stages of bacterial infections than traditional inflammation indicators such as Erythrocyte Sedimentation Rate (ESR) or C-reactive protein (CRP). The amplification and detection of nucleic acids from offending pathogens may also provide additional useful diagnostic information in a timely fashion.[3] The idea of applying proteomics-based techniques for detecting makers of sepsis- or tissue damage-associated molecular patterns also show promising results. Second, in addition to appropriate antimicrobial therapies, nonmedicinal interventions are also important. It has been reported that the majority of sepsis is late-onset and caused by Gram-positive organisms (60.6%), among which 86.5% are coagulase-negative staphylococci. Group B Streptococcus (GBS) is extremely rare in VLBW infants. These results are in accordance with earlier reports,[4] and they suggest that the invasion of skin flora is the major route of infection for most cases of late-onset sepsis in VLBW infants. The importance of strict obedience to aseptic procedures, especially good hand hygiene, cannot be overemphasized.[5] The prompt removal of indwelling catheters is also an important part of the integrated management of sepsis in VLBW infants. Despite the use of appropriate antimicrobial therapies, the morbidity and mortality of sepsis in VLBW infants remain high. The use of certain adjuvant therapies for treating neonatal sepsis has been repeatedly proposed. Since transplacental transfer of maternal protective antibodies does not occur until week 32 of gestation, the infusion of intravenous immunoglobulins (IVIG) may help to control sepsis in this population. However, a recently reported large randomized trial involving 3493 cases concluded that therapy with IVIG has no effect on the clinical outcomes of suspected or proven neonatal sepsis.[6] Studies on other adjuvant therapies, such as colony-stimulating factors, pathogen-specific protective antibodies, probiotics, glutamine supplementation, and lactoferrin, have been tested with mixed results. It is hoped that investigators will finally find adjuvant therapies that are beneficial for treating VLBW infants with sepsis in the future.

In terms of prevention, maternal immunization is an attractive strategy. Some early-stage human studies on maternal immunization with GBS vaccines have shown promising results.[7] However, vaccines against other bacteria are desirable for use in VLBW infants because GBS infection is infrequent in this population. The safety of vaccination during pregnancy is also a concern, especially when the

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vaccines need to be administered during early pregnancy in order to provide timely protection for VLBW infants.

Because they leave their mothers' immunological shield unprepared for the outside world, VLBW infants require special protection. Prompt and appropriate antimicrobial therapy remains the key to the successful treatment of sepsis in these infants. To achieve this goal, maintaining a higher index of suspicion and continuously monitoring local epidemiological factors are crucial. In addition, developing novel therapeutic and preventive strategies are also highly desirable.

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References

1. Lim W, Lien R, Huang Y, et al. Prevalence and pathogen distribution of neonatal sepsis among very low birth weight infants. *Pediatr Neonatol* 2012;**53**:228—34.
2. Srinivasan L, Harris MC. New technologies for the rapid diagnosis of neonatal sepsis. *Curr Opin Pediatr* 2012;**24**:165—71.
3. Pammi M, Flores A, Leeflang M, Versalovic J. Molecular assays in the diagnosis of neonatal sepsis: a systematic review and meta-analysis. *Pediatrics* 2011;**128**:e973—85.
4. Wu JH, Chen CY, Tsao PN, Hsieh WS, Chou HC. Neonatal sepsis: a 6-year analysis in a neonatal care unit in Taiwan. *Pediatr Neonatol* 2009;**50**:88—95.
5. Won SP, Chou HC, Hsieh WS, et al. Handwashing program for the prevention of nosocomial infections in a neonatal intensive care unit. *Infect Control Hosp Epidemiol* 2004;**25**:742—6.
6. Brocklehurst P, Farrell B, King A, et al. Treatment of neonatal sepsis with intravenous immune globulin. *N Engl J Med* 2011; **365**:1201—11.
7. Heath PT. An update on vaccination against group B streptococcus. *Expert Rev Vaccines* 2011;**10**:685—94.