Long-term Outcome of Preterm Infants and the Role of Neuroimaging

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• Prematurity • Outcome • Follow-up
• Neuroimaging • Plasticity

A recent report of the Institute of Medicine defines preterm birth as one of the major public health problems of this decade.[1] With preterm birth come preterm survivors—more every year—and as survival rates increase, the next great imperative for perinatal medicine is to understand and prevent the serious adverse neurodevelopmental outcomes of preterm birth. Neonatology as a field of medicine is recently organized, with the first Neonatal Intensive Care Unit in the United States opening in 1965 at Yale University School of Medicine and with the American Academy of Pediatrics recognizing Neonatology as a subspecialty field in 1975. Exogenous surfactant was first described as a therapy for Respiratory Distress Syndrome in 1980,[2] and surfactant replacement therapy was first recognized in a policy statement by the American Academy of Pediatrics in 1999.[3] Antenatal steroid use was formalized in a National Institutes of Health consensus statement in 1994, and recognized by the American College of Obstetricians and Gynecologists shortly thereafter.[4] These therapies have revolutionized survival rates for very preterm neonates, but many have questioned the neurodevelopmental cost. An understanding of both changing patterns of survival and emerging long-term neurodevelopmental disability is necessary to address outcome in the prematurely born.

TRENDS IN PREVALENCE, MORTALITY, AND MORBIDITY

From 1965 through the early 1990s, survival statistics improved annually, with steadily decreasing mortality at every gestational age (GA) and birth weight (BW) point.[1] Progress since the 1990s to the present is less clear. A review for the National Institute of

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Child Health and Human Development (NICHD) Neonatal Research Network in 2007 found that the infant mortality rate rose between 2001 and 2002, from 6.8 per 1000 live births to 7.0 per 1000 live births, for the first time in 4 decades, whereas the survival of very low birth weight (VLBW) infants changed ''almost imperceptibly'' between 1997 and 2002.[5] At the same time, the overall incidence for premature birth is slowly increasing, mostly in the late preterm infant but also in the very and extremely low birth weight (ELBW) infant: from 1.2% in 1980 to 1.5% in 2006.[6] These data are particularly useful because they consolidate standardized information across multiple level-III perinatal centers.

That the incidence of neurodevelopmental disability in preterm populations has been reported to change little over time is a phenomenon documented in several reviews.[1] Taken together, then, the coincidence of increasing incidence of VLBW and ELBW infants (501–1500 g)—the same infants at highest risk for neurodevelopmental impairment—with the lack of progress in overall morbidity of these infants suggests that increasing numbers of impaired infants are surviving every year. In 2005, Wilson-Costello and colleagues[7] concluded just that; in their single perinatal center, whereas overall survival increased in the 1990s compared with the 1980s, the risk for significant neurodevelopmental impairment also increased. This study concludes that the absolute numbers of ELBW (500–999 g) survivors is increasing in both the unimpaired and impaired groups.

These and other epidemiologic studies are difficult to compare because of differences between institutional practices, definitions (particularly comparing BW categories with weeks of gestation when describing prematurity), patient populations, and follow-up parameters, but the overall trend in the United States seems to be toward an increasing number of premature births, with increasing survival rates that perhaps outpace improvements in morbidity, such that increasing numbers of both impaired and intact premature infants are surviving every year. It is therefore possible that overall survival is increasing at the expense of intact survival, although this, too, is impossible to know until the most current generation of survivors reaches follow-up age.

Whether or not increasing incidence of impaired survival is the case, the next imperative in neonatology is to better understand the pathophysiology of preterm birth, the role of neurologic injury on neurodevelopmental impairment, and the potential for recovery in the injured preterm brain. This review attempts to report the current understanding of neurodevelopmental outcome of premature infants in the postsurfactant/antenatal steroid era, and to describe current practices of monitoring the developing brain.

PRESENT STATUS OF OUTCOME DATA

Outcome for surviving infants is defined by various neurodevelopmental impairments and by general measures of health, including chronic respiratory diseases, growth parameters, and recurrent infections. This review focuses on the neurodevelopmental dysfunctions. These disabilities, including cerebral palsy, mental retardation, and visual and hearing deficits, exist on a spectrum ranging from mild involvement (including learning disability, language disability, attention deficit-hyperactivity disorder and coordination, behavior, and social-emotional disorders) to profound impairment.[1] This spectrum of deficits represents the sequelae of that injury to the developing brain associated with preterm birth.

The group of premature infants born since 1995, the postsurfactant/antenatal steroid era, is just now reaching adolescence. Little data yet exist describing this