

# Neurodevelopmental Outcome in Children With Congenital Heart Disease: A Work in Progress

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When I began my residency in 1977, treatment of children with congenital heart defects was evolving in the context of an inspiring collaboration between pediatric cardiology, cardiac surgery, and cardiac anesthesia. In the ensuing decades, thousands of infants were saved by novel imaging, new operations, and refined supportive methods. The impact on these children was, in many instances, not only lifesaving but even miraculous.

A similar phenomenon was occurring nationally and internationally, and advances in diagnosis, treatment, surgical interventions, and support techniques changed faster than in perhaps any other pediatric field.

By the mid-1980s, many previously fatal congenital cardiac lesions had become operable, and survival rates had improved. In addition, new surgical techniques were developed to repair even the most complex lesions during early infancy rather than in 2 stages (ie, first palliative, then later reparative surgery), and morbidity and mortality declined. Dazzling progress in the sophistication of surgical repair is illustrated nowhere better than by the transition of surgery for dextrotransposition of the great arteries from atrial switch surgery (eg, Mustard or Senning procedure) and then the 2-stage arterial switch operation to the primary arterial switch operation. Pushing the field toward earlier age at repair was an article by Newburger et al<sup>1</sup> describing decrements in developmental outcomes in children who remained cyanotic past the age of 2. Newburger's

findings also sounded a warning that management decisions should weigh not only mortality but the kind of life each child would lead. Cardiologists who followed these new survivors of complex congenital heart disease began to realize that with only anecdotal observations of individual patients, complex relationships between interventions and neurodevelopmental outcome could not be discerned.

As a junior faculty member in developmental-behavioral pediatrics, I was invited by Jane Newburger, MD, author of the first cardiac development study, to become part of a team to study the developmental outcomes in the first randomized clinical trial of deep hypothermic circulatory arrest versus low-flow bypass in the arterial switch operation for dextrotransposition of the great arteries.<sup>2</sup> Cardiac surgeons had been using different techniques of vital organ support and were committed to their particular approach, but investigators at Boston Children's Hospital were willing to subject their beliefs to rigorous scrutiny. This trial gave us much new knowledge about the limits of deep hypothermic circulatory arrest and changed the conduct of infant cardiac surgery. Additionally, the trial ushered in a new era of randomized clinical trials and detailed retrospective studies aimed at improving neurodevelopmental outcomes. Future studies would examine the effects of hematocrit levels and pH management,<sup>3-5</sup> among other support techniques, and studies used

these data to shine new light on previously unrecognized harbingers of worse neurodevelopmental outcomes, such as postsurgical seizures.<sup>6</sup>

As a consequence, cardiac surgeons and cardiologists have continued to study the developmental consequences of emerging techniques for treating severe congenital heart disease. Leaders and trainees at national centers developed a subspecialty interest in developmental outcomes. Gaynor et al's<sup>7</sup> article in *Pediatrics* is one of the outcomes of this early work, and the sophistication of the statistical analyses comes from years of effort in this area, but it also highlights some of the challenges of studying outcomes over time in a changing field and with evolving and new developmental tests. With all the caveats listed in the article, the take-home message is that we continue to advance in what we can repair, and developmental outcomes continue to improve, albeit slowly, every year. However, the developmental quotients are still below the population norms, and children with repaired congenital heart disease remain a high-risk group for neurodevelopmental problems.

Many questions remain unanswered. First, what is the impact of anesthesia on the developing brain, and how does it change as the child gets older? Multiple studies by anesthesiologists

are in progress to answer this question, and findings will need to be integrated in multivariate analysis of factors affecting developmental outcomes. Since the 1980s, studies have identified genetic differences that cause both congenital heart disease and developmental disorders, complicating studies of the impact of treatment on developmental outcomes for children with congenital heart disease.

The interdisciplinary effort among cardiac surgeons, cardiologists, anesthesiologists, neuropsychologists, developmental-behavioral pediatricians, neurologists, psychiatrists, biostatisticians, nurses, and parents, all working toward the goals of saving lives and improving outcomes, is a model for other areas of medicine and a tribute to how collaboration can change lives. There is still a long way to go. Pediatricians need to keep in mind that children with congenital heart disease who need surgical repair are at significant risk of neurodevelopmental issues and should be monitored closely and receive early intervention when indicated to maximize function.<sup>8</sup>

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