In this volume of *The Journal*, Medina et al describe molecular changes occurring in the left ventricle of pediatric patients implanted with an LVAD, specifically involving the beta-adrenergic receptor expression, phosphorylation pathways and gene program, thereby shedding light on potential mechanisms, which may translate to novel medical therapies tailored to children with heart failure.

Although, the study was conducted in a relatively small group of patients, it is a testament to the need of pediatric data, based on which one can design treatments for children instead of extrapolating adult data. This research can lead to similar studies in larger cohorts with the translational goal of identifying biomarkers of myocardial recovery. The ultimate goal is to develop novel medical therapies, leading to cardiac function recovery and the ability to separate from mechanical circulatory support.

Article page 184 ▶

## Low rate of viral respiratory infections in infants in the NICU

**— Sarah S. Long, MD**

Outbreaks of respiratory tract viral infections in neonatal intensive care units (NICUs) have been reported over the years, frequently with serious consequences in these highly vulnerable infants. Acquisition of respiratory viruses without typical manifestations of infection but with nonspecific worsening of neonatal cardiorespiratory, neurologic, or sepsis symptoms also has been suggested. Seeking evidence of viral respiratory tract infection when premature infants in the NICU have setbacks has become common practice. Some neonatologists have advocated for use of palivizumab in NICUs during the season of respiratory syncytial virus circulation even though the American Academy of Pediatrics has not condoned this use.

It is painstaking, hard work to prove the negative. Caserta et al, from the University of Rochester Medical Center, have done just that in a study reported in this month's volume of *The Journal*. They enrolled 93 preterm and 96 term infants into a prospective, longitudinal study over 2 years, obtaining nose/throat swabs within 7 days of birth, weekly while hospitalized, and then monthly to 4 months after hospital discharge. Using molecular techniques they sought detection of 16 viral respiratory pathogens. They gathered data from medical records and parent interviews while infants were hospitalized and at monthly outpatient visits. They also reviewed the hospital course of all preterm infants who underwent evaluation for late-onset sepsis and correlated this with the infants' weekly viral detections. Infection prevention practices in the Rochester NICU were robust: isolation of infants with suspected viral infection, restriction of children under 14 years of age from visiting in winter months, restriction of unvaccinated and ill family members and staff, mandating influenza vaccine or mask for all healthcare personnel, and more. They found only 4 infants with NICU-acquired viral infections among 618 specimens collected; 2 had recognized clinical symptoms. Upon NICU discharge, preterm infants rapidly acquired respiratory viruses, at rates similar to term infants in the community.

Bottom lines: (1) Acquisition of respiratory viruses in a NICU with strict infection prevention strategies is extremely low and does not appear to be a cause of nonspecific symptoms; and (2) implementation of strict infection prevention practices in the NICU trumps use of monoclonal antibody, and achieves better and broader efficacy.

Article page 53 ▶

## Oxygen saturation targets: The wrinkle in the pulse oximeter calibration software provides another wrinkle

**— Clyde J. Wright, MD**

We had hoped to have the answer to the following question by now: where should we target our oxygen saturation goals for premature neonates born at <28 weeks of gestational age? The hope was that data gathered from 5 trials – Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), Benefits of Oxygen Saturation Targeting (BOOST II) (consisting of three separate trials: UK, Australia, and New Zealand), and Canadian Oxygen Trial (COT) would definitely guide practice. But that data has not. One potential complicating factor has been the question of how to deal with an "anomaly" in the pulse oximeter calibration software, discovered while BOOST II and COT were still ongoing, but SUPPORT was completed. In brief, is has been argued that the oximeter software—once corrected—led to better separation in achieved saturations between babies randomized to 85%-89% and 91%-95%. It has also been argued

that with this better separation in treatment groups, the increased mortality in babies randomized to 85%-89% becomes clearer. However, this interpretation of the study results has been questioned.

In this volume of *The Journal,* Whyte et al asked whether the revised oximeter calibration software did in fact allow for a "cleaner" separation in the BOOST II treatment groups. Why is this study important? BOOST II consisted of three separate trials: UK, Australia, and New Zealand. When BOOST II reported that the revised software allowed for "greater separation," they analyzed data from subjects randomized in all three trials both before and after the oximeter software change. Looking at the babies enrolled after the software change, a cleaner separation of achieved pulse oximeter readings was achieved. However, the New Zealand trial had completed their enrollment prior to the software change, and thus could not contribute any data to the postsoftware change group. Thus, Whyte et al ask whether data from subjects enrolled pre- and postsoftware change from just the UK and Australia trials support the hypothesis that the revised software results in a cleaner separation in treatment groups, thus potentially explaining the clearer signal for increased mortality in babies randomized to the 85%-89% in BOOST II after the software change. Their conclusion is riveting. The data presented here challenge our interpretation of these trials, and forces thoughtful discussion about how to move forward with oxygen saturation target goals in the neonatal intensive care unit.

Article page 382 ▶

## Early life linear growth but not weight gain, impacts adult human capital

— **Julia Steinberger, MD, MS**

The general consensus in the child development literature, originating from growth restricted infants, is that the earlier the infants move onto a positive growth trajectory, the better their growth and developmental outcome will be (*Semin Perinatol* 2010;34:207-10; *Early Hum Dev* 2015;91:491-7). Nevertheless, rapid catch-up growth, in terms of weight, has been linked with adult risk of obesity, metabolic syndrome, and cardiovascular disease (*J Pediatr* 2000;137:36-41; *Curr Opin Clin Nutr Metab Care* 2010;13:294–9). In this volume of *The Journal,* Horta et al take an in-depth look at the associations of birth weight, nutritional status, linear growth, and relative weight gain in early childhood with adult (30 years of age) IQ, schooling, and income measures of human capital in Brazil. The findings show that promotion of intrauterine growth and linear growth in the first 4 years of life is associated with improved adult IQ, schooling, and income at 30 years of age. Weight gain in excess of that expected for linear growth did not improve human capital. This report sends an important message regarding efforts targeted to achieve rapid weight gain in infancy/early childhood in low and middle-income countries, and in general, in infants with growth restrictions. While these efforts may have short-term benefits, including reduction in morbidity and mortality due to infectious diseases, the long-term consequences may be negative. Thus, the emphasis should be on rapid catch-up linear growth and weight gain commensurate, but not in excess of linear growth.

Article page 85 ▶

## Lactated Ringers versus normal saline in children with sepsis

— **Philip Toltzis, MD**

The report by Weiss et al in this volume of *The Journal* employed a large administrative database to investigate whether lactated Ringers is superior to normal saline in resuscitating children with sepsis. There is growing awareness that this question is important, as experimental and adult human data suggest that the supraphysiologic content of chloride in normal saline promotes renal injury and exacerbates the systemic inflammatory response. The clinical relevance of these findings in adult intensive care units is uncertain and results in nonrandomized studies have been mixed, but they support the preferential use of balanced salt solutions. Recognizing that at baseline, critically ill children are typically more physiologically intact than their adult counterparts, Weiss et al used the Premier Healthcare Database, including data from hundreds of geographically diverse American hospitals, to test this hypothesis in pediatrics. Specifically, they measured the incidence of mortality and acute kidney injury in children with sepsis infused with normal saline with those who had received at least some infusion by lactated Ringers. After applying extensive and sophisticated strategies to