Linear Growth and Neurodevelopmental Outcomes

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KEYWORDS

• Linear growth • Fat-free mass • Inflammation • Outcomes • Neurodevelopment
• Premature infants • Very low birth weight

KEY POINTS

- Premature infants exhibit disproportionate growth characterized by reduced length/height and fat-free mass (FFM), as well as neurodevelopmental delay.
- Growth should no longer be defined as weight gain alone, as increases or stunting in other metrics are associated with lasting effects on neurodevelopment.
- Brain maturation is characterized by critical periods of growth, each with specific nutrient needs.
- Protein status plays an important role in FFM accretion, neurogenesis, and neuronal differentiation.
- Early inflammation and illness have a long-term negative influence on linear growth and in FFM gains, as well as on later neurodevelopment.

INTRODUCTION

Despite recent improvements in nutritional support, premature infants continue to exhibit disproportionate growth (characterized by reduced length/height and fat-free mass [FFM], and increased relative adiposity), as well as neurodevelopmental delay. Recent literature suggests that some of the same factors (eg, nutritional and inflammatory) are responsible for both outcomes, by directly and negatively affecting both developing neurons and white matter, and suppressing the growth hormone (GH)/insulin-like growth factor 1 (IGF-1) axes. Reduced FFM accretion and linear growth are associated with a risk to the developing brain. To date, neonatal nutritional strategies have been ineffective in preventing failure of linear growth and its attendant risk to cognitive development, in part because of a lack of thorough understanding of what

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causes suppression of linear growth and in part because of an inappropriate emphasis on defining "growth" as weight gain. A potential change in care to improve developmental outcomes might include more careful monitoring of linear growth and body composition (including FFM), accompanied by strategic nutritional and nonnutritional interventions aimed at supporting FFM growth. The latter could include strategies to reduce the duration of illness and the number of inflammatory events.

INCIDENCE OF GROWTH FAILURE IN PREMATURE INFANTS

In 2011, the rate of preterm birth in the United States remained greater than 11%.[1] According to a review from the National Institute of Child Health and Human Development, the rate of growth failure among VLBW preterm infants remains unacceptably high, with 79% weighing less than the 10th percentile at 36 weeks.[2] Hack and colleagues[3] reported that many of these infants remain underweight and short for age (<2 standard deviations [SD]) at 20 months corrected age for prematurity, and that very low birth weight (VLBW) males remain small and short into adulthood.

The prevalence and importance of poor weight gain in preterm infants has been widely cited for decades. Although first described in 1981,[4] the incidence, persistence, and significance of linear-growth failure has only recently reemerged as a topic of importance. This renewed emphasis is particularly important because linear growth and gains in FFM closely index organ growth, and specifically the brain, in other populations. Multiple recently published studies have described prolonged suppression of linear growth in preterm infants beyond 18 to 24 months corrected age for prematurity (**Fig. 1**).[5–7]

In each of these studies, length *z*-scores were more severely depressed and remained lower longer than *z*-scores of weight and head circumference[6,7] and body mass index (kg/m^2).[5,6] This finding is unlike the classic undernutrition anthropometric pattern of growth failure whereby weight is compromised but length and head circumference are spared. The body habitus of excessively suppressed linear growth (ie, the

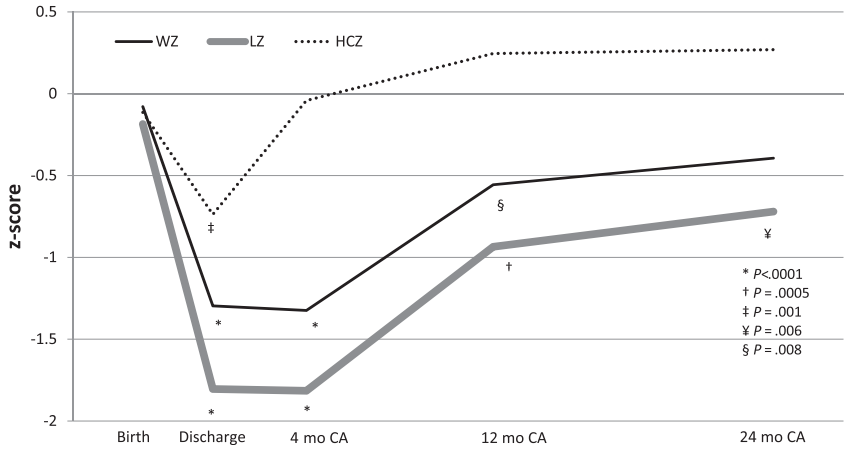

Fig. 1. Growth of very low birth weight preterm infants from birth to 24 months corrected age illustrating persistent linear stunting. *P* values refer to statistical significance of the difference between the mean growth *z*-score at each time point compared with the mean *z*-score at birth. HCZ, head circumference *z*-score; LZ, length *z*-score; WZ, weight *z*-score. (*From* Ramel SE, Demerath EW, Gray HL, et al. The relationship of poor linear growth velocity with neonatal illness and 2 year neurodevelopment in preterm infants. Neonatology 2012;102:21; with permission.)