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Letter to the Editor: Preterm Birth Weight and Insulin Resistance at Adolescence

In the September issue of *GGH* (Vol 19, No 3) you reviewed an interesting publication by Singhal et al¹ who studied the relation between infant feeding, early growth and insulin resistance at age 13-16 years in individuals with a birth weight below 1,850 grams (which the authors labeled preterm). In their study, insulin resistance was not associated with birth weight but with growth in the first two weeks of postnatal life; thus, they concluded that Barker's hypothesis "can be reinterpreted as a postnatal event". In our opinion, their data should be interpreted more cautiously, for the following reasons.

The first point is that selection bias is quite likely. The application of birth weight instead of gestational age as inclusion criterion (< 1,850 grams) suggests that severely growth-retarded individuals born at term are also included. Another point of our concern is that in both experimental groups there were considerable numbers lost to follow-up (65-68%).

Secondly, conclusions with respect to insulin resistance in later life were drawn from a population aged 13-16 years. In this age period there is a wide variation in pubertal stages, and during pubertal development insulin sensitivity is decreased.² Moreover, girls born small for gestational age have a tendency towards early and rapid progression of puberty,³ and hyperandrogenism,⁴ which is accompanied by decreased insulin sensitivity. It is likely that many infants in the experimental groups had a low weight for gestational age at term; thus, it is conceivable that they may have shown abnormalities in pubertal onset and tempo, as well as in androgen metabolism.

Thirdly, although an earlier study of this research group (in the same population at age 7.5-8 years) suggested that suboptimal nutrition, which may result in poor early postnatal growth, adversely affects neurodevelopmental outcomes, little emphasis is put on the possible beneficial effects of nutrient-enriched preterm formulas.⁵ This suggests that discouraging early postnatal catch-up growth by restricted food intake in infants with a birth weight below 1,850 grams is hard to justify.

The last and major point is that Singhal and colleagues have extrapolated their findings in individuals born preterm to conclusions about the general population. The first two postnatal weeks of the experimental groups took place halfway into the third trimester. In our opinion it cannot be automatically assumed that postnatal growth taking place at an age that is normally spent *in utero*, can be considered equivalent to postnatal growth of a term infant.

In conclusion, this interesting study has shown that slow early postnatal growth of preterm infants is associated with low insulin resistance at adolescence. In our view it is uncertain whether these effects persist into adulthood and whether early postnatal catch-up growth predisposes to insulin resistance only in preterm infants or also in those born at term.

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Martijn JJ Finken, MD; Anne Margriet Euser, MSc; Friedo W. Dekker, PhD; Jan Maarten Wit, MD PhD
*Leiden University Medical Center
Leiden, The Netherlands*

Response: *The comments of Dr. Finken and colleagues are welcome as they point to several possible methodologic and interpretive flaws in the work of Singhal et al. Although we do not know the exact number of small for gestational age neonates included in the cohort of subjects reported, it is likely that the majority were preterm and appropriate for gestational age. If there is a potential way in which to prevent the development of insulin resistance and the dysmetabolic syndrome, it should be explored. However, clearly, one would not want to jeopardize optimal neural development under any circumstances.*

Allen W. Root, MD