

Beta Cell Capacity and Insulin Sensitivity in Prepubertal Children Born Small for Gestational Age

The association between intrauterine growth retardation (IUGR) and the development of type 2 diabetes mellitus (T2DM) in adulthood has been demonstrated in several studies. Veening et al studied beta cell capacity and insulin sensitivity in 28 children born small for gestational age (SGA) and 22 children born appropriate for gestational age (AGA). All were Caucasian, born at term, and pre-pubertal (mean age 9.1 and 9.0 years, respectively). Insulin sensitivity was determined using a hyperinsulinemic-euglycemic clamp, while beta cell capacity was determined using a hyperglycemic clamp combined with arginine infusion. Anthropometric studies were obtained and relationships between catch-up growth, change in BMI, and clamp findings were determined.

Family history of T2DM and hypertension was not different between the two groups and at the time of the studies, mean actual length and BMI were similar in both groups. Insulin sensitivity was significantly lower in the SGA group. However, arginine-stimulated insulin secretion, a measure of beta cell capacity, was similar in both groups. Changes in BMI values between 0 and 1 year, 0 and 2 years, and 2 to 9 years, were categorized into tertiles. In SGA children, insulin sensitivity was significantly lower in those with the highest BMI change between years 2 to 9, compared to those with the smallest BMI change. Insulin secretion was significantly higher in SGA children with the highest BMI change in years 2 to 9, compared to those with the lowest BMI change during those years. No similar changes were seen among the responses in the AGA children.

The authors conclude that insulin sensitivity, but not beta cell capacity, is reduced in children born SGA. Thus, insulin sensitivity is the primary effect promoting the

development of T2DM in later life. But studies have shown that insulin resistance is not by itself sufficient to cause T2DM. SGA children whose BMI was greater during childhood had more insulin resistance. Thus, being overweight is clearly an important factor in the insulin resistance of SGA children and adults. The authors suggest that SGA children with excessive gain in BMI after the second year of life should be screened for the development of T2DM and associated cardiovascular risk factors.

Veening MA, et al. *Diabetes* 2003;52:1756-1760.

Editor's Comment: *This is an important paper. These investigators have performed complex studies in a large group of SGA and AGA children and showed that insulin sensitivity rather than beta cell capacity is abnormal in the SGA children. Since we know that the risk for T2DM is increased among adults who were born SGA, and we know that T2DM requires both insulin resistance and reduced beta cell capacity, this paper implies that reduced beta cell capacity must occur later than 9 years of age. Whether reduced capacity occurs at a later age or is related in some way to increasing BMI remains to be demonstrated. The findings with regard to BMI tertiles support the need for weight control among these individuals. What role exogenous GH administration will pay in this complex metabolic process also remains to be seen. It is clearly very important that careful metabolic studies be performed in children born SGA before and during treatment with exogenous GH. Such studies should be an important part of every database that records the effects of such treatment with these children.*

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