EDITORIALS

Determinants of Risk for Childhood Obesity

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The body-fat content of a healthy full-term infant rises sharply from 10 to 14% at birth to 25 to 30% at 6 months of age,[1] with a consequent 30% increase in the body-mass index (BMI). The accrual of body fat during infancy correlates with, and may be required for, normal linear growth, brain development, and cognitive function.[2] After peaking at 6 to 12 months of age, the BMI normally declines to a nadir at 5 to 6 years of age and then "rebounds," rising progressively throughout late childhood and adolescence.

Numerous studies have shown that an early or exaggerated "adiposity rebound" portends an increased risk of obesity in later childhood and adolescence.[3] An early rebound is also associated with earlier menarche in girls[4] and higher risks of obesity, glucose intolerance, and the metabolic syndrome in adulthood.[5,6] However, whether an early or exaggerated adiposity rebound is a *cause* of future obesity, a *consequence* of intrauterine or perinatal programming or infant feeding practices, a *reflection* of genetic determinants that govern childhood energy intake and expenditure, or a combination thereof is unknown. And, until now, whether the timing and magnitude of adiposity rebound uniquely predict subsequent weight gain in childhood and adulthood has not been known.

To identify developmental windows that may be critical for the establishment and maintenance of childhood obesity, Geserick et al.[7] examined the trajectories of weight gain and adiposity in more than 50,000 healthy German infants, children, and adolescents. Major strengths of their study, the results of which are reported in this issue of the *Journal*,[7] include its longitudinal, population-based design and the combination of retrospective and prospective analyses.

Their findings are new and important. First, an overwhelming majority of normal-weight adolescents had a normal BMI at 1 to 2 years of age that remained within the normal range throughout childhood. Second, although children who were large for gestational age at birth had higher rates of overweight and obesity throughout childhood and adolescence than children who had an appropriate birth weight or were small for gestational age, nearly 75% of obese adolescents had had a normal BMI during the first 2 years of life. However, approximately half of obese adolescents had become overweight or obese by 5 years of age. Third, the most powerful predictor of obesity in adolescence was an increase in the BMI standard-deviation score between the ages of 2 and 6 years; obese teenagers had had early and exaggerated adiposity rebounds and steady increases in BMI standard-deviation scores thereafter. Few overweight or obese children were underweight in adolescence, and few underweight children became obese teenagers.

The authors found that rates of obesity were higher among children of overweight or obese mothers than among children whose mothers were not overweight or obese, a finding that is consistent with results of previous investigations.[8] Other factors that contribute to childhood obesity were not examined; these include paternal overweight and obesity, intrauterine exposure to maternal diabetes, a history of maternal smoking, and formula feeding as compared with breastfeeding.[8] Conversely, parental educational level and family income correlate inversely with the

risk of obesity in childhood and adulthood, at least in the developed world.[8] In that regard, we do not know whether the findings of the current study can be extrapolated to children in other countries, whose timing and magnitude of changes in BMI may differ from those of German children. Generalizability would be particularly relevant for children in the developing world, where intrauterine growth restriction and postnatal stunting are commonly associated with excessive catch-up weight gain but not linear growth.[9]

The current study was not designed to determine whether exaggerated weight gain in early childhood is a cause of subsequent obesity or a marker of previous, inherent, or future risk of obesity. Nevertheless, the identification of a critical window for predicting childhood weight gain provides an opportunity for intervention to prevent obesity in children at risk. The finding that the risk of adolescent obesity manifests by 3 to 5 years of age suggests that nutritional counseling should be considered when exaggerated weight gain persists or emerges after 2 years of age; it would be of value to test the efficacy of early dietary intervention in an appropriate trial. Counseling could be applied preemptively for families in which the parents are overweight, particularly if there is a history of maternal diabetes or smoking.

We are now witness to an evolving epidemic of childhood obesity in the United States and other westernized countries, along with the emergence in young people of serious complications, including insulin resistance, type 2 diabetes mellitus, hyperlipidemia, hypertension, and fatty liver disease.[8] It is an ominous sign that the number of American children with the most severe and recalcitrant forms of obesity has increased progressively during the past 10 years.[8,10] One hopes that interventions tailored to high-risk children at an early age can help to prevent or limit excess weight gain before obesity becomes irreversible.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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COMMANDER HF — A Trial and an Answer

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Patients with heart failure and a reduced left ventricular ejection fraction are at high risk for complications and death, despite the proven benefits of established medications and devices. Several newer medications that have been tested in this context have not yielded positive results or have even caused harm. Therefore, the search continues for additional therapeutic avenues to improve the fate of patients who have this highly prevalent condition.

COMMANDER HF (A Study to Assess the Effectiveness and Safety of Rivaroxaban in Reduc-