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## Rapid Growth in Infancy Linked to Cardiovascular and Metabolic Risk Factors Later in Life CME

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CME Released: 06/12/2009; Valid for credit through 06/12/2010

June 12, 2009 — Important determinants of cardiovascular disease and type 2 diabetes **mellitus** in adulthood are increased in infants who gain weight rapidly early in life, a new study has shown [1]. **Increased weight gain relative to height in early infancy is associated with reduced insulin sensitivity and serum high-density lipoprotein (HDL)-cholesterol levels, as well as increased waist circumference and serum triglyceride levels, report investigators.**

"Rapid weight gain in the first three months of life," write Dr Ralph Leunissen (Erasmus Medical Center, Rotterdam, the Netherlands) and colleagues in the June 3, 2009 issue of the *Journal of the American Medical Association*, "is more detrimental than slow weight gain. More studies are required to investigate which factors determine rapid weight gain in early infancy, because those results might lead to interventions that could decrease the risk for development of cardiovascular disease and type 2 diabetes later in life."

The data on birth weight and growth early in life is mixed. Some studies have shown that low birth weight is associated with cardiovascular disease and type 2 diabetes later in life, while others suggested that rapid growth patterns in infancy and childhood were an important determinant of risk later in life. Other data have shown that poor growth early in life, followed by catch-up growth after age two, is related to an increased risk of cardiovascular disease later in life.

In this study, Leunissen and colleagues wanted to determine which period in the first year of life is related to determinants of cardiovascular risk. They collected observational data from 217 participants aged 18 to 24 years participating in the Programming Factors for Growth and Metabolism (PROGRAM) study. These individuals were included in the study because of their short length at birth and normal stature later in life or because of their normal size at birth and short stature later in life. Of these 217 subjects, 84 were small and 129 were normal size at birth.

Weight gain in the first three months was inversely associated with insulin sensitivity and HDL-cholesterol levels. There were positive associations between weight gain during these months and waist circumference, acute insulin response, ratio of total cholesterol to HDL cholesterol, and triglyceride levels. Acute insulin response was positively associated with weight gain in months 3 to 6 after birth, but no other association was observed, including in months 6 to 9 and 9 months to one year.

A subgroup analysis was performed in 87 subjects who gained weight rapidly in the first year to assess possible relationships between the "tempo" of weight gain and determinants of cardiovascular disease and type 2 diabetes. Individuals who gained weight rapidly during the first three months had more body fat, central adiposity, and reduced insulin sensitivity in early adulthood than those with slower growth. Rapid weight gain was defined as  $\geq 0.67$  standard deviation from the mean.

"This indicates that having a low birth weight for gestational age is not directly related with an unfavorable cardiovascular and metabolic profile, but increased weight gain during early childhood is," write Leunissen and colleagues, adding that the tempo of weight gain might even be more important than the timing.

The group said that the reasons for the increased cardiovascular risk are unknown, but that nutrient-enriched diets that contribute to rapid weight gain might have adverse effects of cardiovascular risk factors later in life. Formula-fed infants, for example, grow at a faster rate than breast-fed infants but are more likely to be overweight later in life. Their study, however, is limited, in that there are no **nutritional** data available. Future studies need to confirm these findings and to determine which factors determine weight gain, as well as to investigate associations with parental factors, such as genetics and maternal health during pregnancy.

## References

1. Leunissen RW, Kerkhof GF, Stijnen T, Koelega-Hokken A. Timing and tempo of first-year rapid growth in relation to cardiovascular and metabolic risk profile in early adulthood. *JAMA* 2009; 301: **2234-2242**.

## Clinical Context

Growth in early childhood appears to be linked with a subsequent risk for measures of cardiovascular disease and type 2 diabetes. Data from the **Helsinki** Birth Cohort Study showed that slow weight gain before age 2 years with subsequent catch-up growth in childhood was associated with an increased risk for cardiovascular disease and type 2 diabetes, as reported by **Kajantie** and colleagues in the April 2008 issue of the *International Journal of Epidemiology* and Eriksson and colleagues in the December 2006 issue of *Diabetologia*.

This observational study used data from the Programming Factors for Growth and Metabolism study, described by Leunissen and colleagues in the September 2008 issue of *Clinical Endocrinology*, to assess whether growth and the rate of weight gain in the first year of life are associated with determinants of cardiovascular disease and type 2 diabetes in early adulthood.

## Study Highlights

- Of 323 invited healthy adults aged 18 to 24 years, 217 adults had data on growth at ages **3, 6, 9**, and 12 months.
  - a Inclusion criteria were white, singleton, gestational age at least 36 weeks, and uncomplicated neonatal course.
  - a Exclusion criteria were serious conditions, treatment known to interfere with growth, dysmorphic features, endocrine or metabolic disorders, or chromosomal defects.
  - a Growth data were obtained from hospital, healthcare center, and general practitioner records.
  - a Of 84 subjects who were small at birth, 9 had short adult stature.
  - a Of 129 subjects of normal birth size, 41 had short adult stature.
- Mean gestational age was 39.3 weeks.
  - a Mean birth length was 47.6 cm and weight was 2.78 kg.
- Adulthood mean age was 20.8 years.
  - a Mean adult height was 1.68 meters, weight was 63.9 kg, and body mass index was 22.5 mg/m<sup>2</sup>.
  - a Analysis was adjusted for gestational age, sex, age, socioeconomic status, and SD score for height growth.
  - a Weight gain in the first 3 months of life was inversely associated with insulin sensitivity and HDL levels in early adulthood.
  - a Weight gain in the first 3 months of life was positively associated with waist circumference, acute insulin response, ratio of total cholesterol to HDL levels, and triglyceride levels in early adulthood.
- After additional adjustment for body fat percentage, weight gain in the first 3 months of life was no longer linked with waist circumference, acute insulin response, and **triglyceride** level.
  - a Weight gain during 3 to 6 months was positively linked to acute insulin response.
- Weight gain during 6 to 9 months and 9 to 12 months was not linked with any outcome measures.
- Of 87 participants who had rapid weight gain in the first year (> 0.67 SD), 65 had rapid weight gain (> 0.5 SD), and 22 had slower weight gain (≤ 0.5 SD) in the first 3 months.
- Rapid weight gain in the first 3 months of life vs slower weight gain in the first year was linked with higher body fat percentage, greater central adiposity, higher ratio of trunk fat to total fat, and reduced insulin sensitivity in early adulthood.
- Adjusting for body fat percentage resulted in no significant link between rapid weight gain in the first 3 months and waist circumference, fat distribution, and insulin sensitivity.
  - a Limitations of the study include lack of nutritional data.

## Clinical Implications

- Weight gain in the first 3 months of life is linked with reduced insulin sensitivity and serum HDL level and greater waist circumference, acute insulin response, ratio of total cholesterol to HDL cholesterol level, and triglyceride level in early adulthood.
- Rapid weight gain in the first 3 months of life is linked with greater body fat percentage and central adiposity and reduced insulin sensitivity in early adulthood.

## CME Test

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Weight gain in which of the following age groups is most likely to be associated with greater central adiposity and triglyceride levels in early adulthood?

- Birth to 3 months
- 3 to 6 months
- 6 to 9 months
- 9 to 12 months
- None of the above

Which of the following characteristics of growth in the first 3 months of life is *most* likely to have a greater link with reduced insulin sensitivity in early adulthood?

- Rapid weight gain
- Slow** weight gain
- Neither rapid nor slow weight gain
- Weight loss

Save and Proceed

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### Target Audience

This article is intended for primary care clinicians, cardiologists, endocrinologists, and other specialists who provide care to patients with cardiovascular disease or type 2 diabetes.

### Goal

The goal of this activity is to provide medical news to primary care clinicians and other healthcare professionals in order to enhance patient care.

### Learning Objectives

Upon completion of this activity, participants will be able to:

- Report which growth period in the first year of life is linked with determinants of cardiovascular disease and type 2 diabetes in early adulthood.
- Describe whether rate of weight gain in the first year of life is linked with determinants of cardiovascular disease and type 2 diabetes in early adulthood.

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