Divergent Origins of Slow Fetal Growth
Relevance to Adult Cardiovascular Disease

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Barker and Osmond hypothesized nearly 20 years ago that fetal undernutrition leads to permanent alterations in the body’s structure and physiology and increases susceptibility to cardiovascular disease in adult life. Furthermore, they suggested that high blood pressure may be a link between an adverse intrauterine environment and the risk for cardiovascular disease. Since then, numerous epidemiologic studies have assessed the inverse relation between birth weight and blood pressure. Furthermore, experimental studies have supported this inverse association and have demonstrated that the timing, length, and degree of in utero insult, as well as postnatal influences, determine the adult phenotype.

In humans, postnatal influences may also have an important impact on later development of cardiovascular disease in babies who are born small. Accordingly, Barker and colleagues recently suggested that 2 different pathways of childhood growth may precede development of hypertension and adult cardiovascular disease. Early development of more severe hypertension associated with obesity and insulin resistance is more common in individuals who are born small but who experience rapid catch-up growth during childhood. Individuals who are born short and maintain slow growth during childhood and therefore remain short and thin before puberty develop hypertension at a later age. However, these individuals also have a greater risk for stroke as adults.

Interestingly, the increased risk for stroke is more common in individuals with mothers who have a “flat” bony pelvis. Because a flat pelvis is associated with malnutrition during the first year of life, Barker and colleagues proposed that malnutrition during infancy increases the risk for stroke in the next generation. Previous reports also suggest that reduced growth in the female fetus due to undernutrition results in increased blood pressure in the next generation. Thus, findings from these studies suggest that subtle variations in the timing of undernutrition in the mother, whether in utero or during infancy, contributes to cardiovascular disease, including hypertension and/or stroke, in the next generation.

In this issue of Hypertension, Barker and colleagues examined influences that affect prenatal and postnatal growth and the development of hypertension in individuals with divergent postnatal patterns of growth. Hypertension that is severe and/or diagnosed early was associated with being small at birth followed by rapid catch-up growth (Figure). This pattern of fetal and childhood growth was likely due to fetal undernutrition, as indicated by a strong association with decreased placental size, and was associated with poor living conditions after birth, suggesting increased vulnerability to postnatal stress. However, newly diagnosed hypertension and risk of stroke were associated with slow growth in utero and throughout childhood. This pattern of fetal and childhood growth was more strongly associated with mothers who had small pelvic bones, a likely consequence of vitamin D deficiency and rickets during their infancy. Thus, these findings suggest that the reduced fetal and childhood growth observed in these individuals originates from influences that occur early in the lives of their mothers. Thus, slow fetal growth, whether occurring as a result of malnutrition during fetal development or occurring as a result of malnutrition of the mother during her infancy, is associated with adult cardiovascular disease.

In conclusion, fetal undernutrition leads to permanent alterations in the regulatory systems involved in the long-term control of arterial pressure. The severity of hypertension can be exacerbated by postnatal insults. Current studies are beginning to elucidate the role of prenatal and postnatal undernutrition and adverse effects that persist from the previous generation on adult cardiovascular disease. Although undernutrition in the female fetus may lead to development of hypertension in the next generation, as reported by Barker et al in this issue of Hypertension, deficiency during infancy of an essential nutrient, such as vitamin D, leads to permanent alterations in the metabolism of the mother that slow fetal and childhood growth and increase the risk for stroke in the next generation. The obvious implication is that proper nutrition during fetal life and childhood may be critical for the cardiovascular health of the individual and her offspring.

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Divergent origins of slow fetal growth lead to different vulnerabilities to postnatal insult, severity of hypertension, and adult disease. As elucidated by Barker and colleagues, slow fetal growth may originate from undernutrition during fetal life or from influences originating during the mother’s infancy. Divergent origins of slow fetal growth lead to alterations in metabolism and vulnerability to postnatal insult. Slow growth during childhood associated with slow fetal growth originating from maternal influences precedes later development of hypertension and stroke. However, slow fetal growth due to fetal undernutrition followed by accelerated growth during childhood is associated with obesity, insulin resistance, and the early development of more severe hypertension.

Disclosures

None.

References

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