Birth Weight as a Predictor of Future Hypertension

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According to the concept of “fetal programming,” intrauterine conditions that impair fetal growth can program the fetus to express hypertension, as well as other chronic diseases, in later life. A model for the development of hypertension that includes the effect of the intrauterine environment on fetal growth as a mechanistic pathway contributes a new dimension in causality and is of great interest. Experimental studies that apply maneuvers to impose fetal undernutrition in animal models have developed data that support this concept. The evidence developed from epidemiologic investigations on humans is less conclusive. Overall, there tends to be a small but consistent relationship of lower birth weight with higher blood pressure (BP). For each kilogram increase in birth weight, the systolic BP is 1 to 2 mm Hg lower. Am J Hypertens 2002;15:43S–45S © 2002 American Journal of Hypertension, Ltd.

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There are a number of challenges to the birth weight hypothesis as a major contributor to the development of hypertension, including the consistently positive relationship of body weight with blood pressure (BP) throughout childhood and adulthood, and the multiple factors involved in birth weight outcome of pregnancy. However, the concept of fetal programming has resulted in important information and new insights concerning factors in early life that contribute to chronic disease in later life.

Primary hypertension is a multifactorial disorder that results from an interaction of genetic and environmental factors. This process is operational at a young age. Although specific genetic mechanisms are being identified, the risk factors for cardiovascular disease have been described, along with evidence on the benefits of risk factor modification. A growing body of reports on the concept of “fetal programming,” which holds that intrauterine conditions that impair fetal growth can program the fetus to express hypertension in later life, holds that intrauterine conditions that impair fetal growth can program the fetus to express hypertension in later life.1 The concept stems from observations by Barker et al1,2 on an association of higher death rates from coronary heart disease and stroke in adults who had lower weights at birth. Drawing from birth records of 64- to 71-year-old men in the United Kingdom, this group of investigators reported that systolic BP was higher in those with lower birth weight.1,2 The concept that the effect of the intrauterine environment on fetal growth may determine future hypertension contributes a new dimension in causality and is of great interest.

Since the original reports many epidemiologic studies have addressed this issue. An inverse relationship between birth weight and BP have been reported in children in Europe and elsewhere.3,4 An examination of birth records and BP measurements at age10 years in 9921 children in Great Britain detected an inverse relationship between systolic BP and birth weight, despite a direct relationship of systolic BP with current weight. On dividing the sample into three birth weight strata, systolic BP decreased by 0.38 mm Hg in boys and by 1.32 mm Hg in girls from the lowest to the highest birth weight group. In a similar examination of records on 36-year-old adults, an inverse relationship of birth weight with systolic BP was stronger, again despite a direct relationship of BP with current weight. However, an analysis of data including weight, height, and BP at age 17 and birth weight by Seidman et al,5 detected only a weak association of birth weight with current BP and noted that birth weight had little effect on BP compared to the large effect of current weight. Whincup et al,6 using a regression model predicting systolic BP at ages 9 to 11 years on birth weight, found a regression coefficient for birth weight of −2.80 mm Hg/kg of birth weight. A similar study by Taylor et al7 reported a regression coefficient of −1.48 mm Hg/kg birth weight. Other studies have reported a weak or no relationship of birth weight with BP in adolescents or adults. Huxley et al8 conducted a review of all published studies that examined an effect of birth weight on BP and found that overall, there appears to be a small but consistent inverse relationship of birth weight with later BP, with a 1-kg increase in birth weight correlating with a 1- to 2-mm Hg decrease in systolic BP.
Despite the large cohort sizes in many of the epidemiologic studies, such investigations continue to be limited by the small numbers of subjects having low birth weights (<2.5 kg), and the limited scope of the newborn data. Donker et al 9 reported on children enrolled in the Bogalusa Heart Study. Two separate cohorts, which included 117 low birth weight (<2.5 kg) infants in a total sample of 1446, were merged. The subjects were examined in childhood, and the data were analyzed as two groups: birth weight < 2.5 kg and birth weight > 2.5 kg. Regardless of birth weight group, no correlation of birth weight and BP was identified, except a weak negative correlation with diastolic BP in black males. A strong correlation was identified between current body mass index and current BP in black and white subjects, both boys and girls, thus supporting the dominant effect of body size and growth on BP in children.

The importance of examining newborn variables in addition to birth weight only is supported by a recent report by Siewert-Delle et al. 10 In their study, a sample of Swedish men aged 49 years (n = 430) were examined and the BP and anthropometric data were related to data found in birth records. They detected no correlation of adult BP with birth weight. They did, however, detect a significant inverse correlation of adult BP with gestational age (which was computed from the maternal report of last menstrual period) in the entire sample (P = .04). Furthermore, the correlation of gestational age with adult BP was stronger (P = .001) in the small (n = 44) group having a gestational age < 38 weeks. In this group, after adjustment for birth weight, an increase by 1 week of gestation was associated with a decrease in adult systolic BP of 7.2 mm Hg. In this study, the contribution of birth parameters to adult BP emerged from the portion of the cohort having a gestational age < 38 weeks.

The relationship between birth weight and BP is described in newborns having birth weights that are relatively small for the duration of gestation, as opposed to infants born prematurely. Premature infants having birth weight appropriate for gestational age theoretically would not be at risk. Infants considered to be at risk for later high BP may have a birth weight within the range of normal birth weights but may be described as “thin.”

Birth weight is a measure of total fetal growth including length, muscle mass, fat mass, and head size. Differing conditions can result in different types of intrauterine growth retardation. According to Barker 11, the gestational timing of nutritional impairment results in different risk pathways for diseases in later life, and these variations can be further distinguished by the size of the placenta relative to the size of the fetus. A limitation of this concept is that it tends to minimize the very strong effect of postnatal environmental factors on BP and subsequent cardiovascular disease. Another criticism is the absence of an altered adult mortality pattern in twins despite frequent discordant birth weights. In addition, fetal and infant anthropometrics are not simply related to maternal and infant nutrition but are multifactorial and include race, 12 sociodemographic variables, 13 maternal systemic disease, and maternal smoking and substance abuse. 14 Explanations for the “programming” effect of intrauterine undernutrition are speculative, but do have substantial support from experimental work. For example, offspring of female rats subjected to low protein diets had higher BP at age 9 weeks compared to offspring of control fed rats. 15 Experimental maneuvers that dampen placental–fetal blood flow attenuate fetal nephronogenesis with a subsequent reduction in total nephron number. The reduced nephron number, then subjected to hyperfiltration injury, may be a pathway for a renal origin of hypertension. 16 Hinchliffe et al 17 proposed that the undernourished fetus becomes a low birth weight newborn whose kidneys have a reduced number of nephrons, and it is this fetal pathology that sets the stage for adult hypertension. However, at present there are no data to demonstrate that “thin” newborns, within the normal range of birth weight for gestational age, have a reduction in nephron number, or other aberrant organ structure. Theoretically, the concept proposed by Hinchliffe could be applied to infants born prematurely, thus having a restriction of intrauterine exposure for fetal development.

The major challenge to the low birth weight–high BP hypothesis is the large body of epidemiologic data on BP and body size. In adults, 18 children, 19 and newborn infants, 20 a direct relationship between weight and BP is consistently demonstrated. The direct correlation of weight with BP in the newborn period is consistently observed from very low birth weight newborns 20 to normal full-term infants. 21 In addition to the consistent strong relationship of BP with body size and growth throughout childhood, the phenomenon of BP tracking has also been established. 22, 23 Data from childhood epidemiologic studies demonstrate that children in the higher range of the BP distribution at a given age continue to have higher BP as they grow and age. It has also been documented that elevated BP in childhood is associated with hypertension in early adulthood. 23 An analysis of the available United States data on BP in children and adolescence determined that height and weight are strong direct correlates of BP.

Excessive weight (obesity) contributes to higher BP and the development of hypertension. 24 Overall, however, the reports on the relationship of birth weight to later BP continue to detect a small but significant effect of low birth weight on higher BP in later life. An alternative concept that integrates these two seemingly discrepant observations may be the relationship of birth weight with subsequent growth. The interaction of the intrauterine environment with genetic factors may “program” the developing fetus with organ development determined to accommodate its total “programmed” body mass. Subsequent excessive growth, or obesity, that overrides the programmed body size imposes excessive demands on organ function and contributes to later hypertension and cardiovascular disease. The insights gained from the birth weight–BP con-
cept serve to amplify the importance of obstetric issues known to have an adverse effect on birth weight, including poverty, maternal hypertension, and maternal smoking and substance abuse. The potential greater impact of obesity at the lower ranges of birth weight also augment the importance of obesity prevention in childhood.

References