Slow Prenatal Growth and Accelerated Postnatal Growth
Critical Influences on Adult Blood Pressure

Barbara T. Alexander, Norma B. Ojeda

I

t is well established that birth weight has a significant and
inverse relationship with systolic blood pressure. Rapid
weight gain in early infancy after slow fetal growth promotes
higher blood pressure and increased cardiovascular risk in
later life. Accelerated weight gain during childhood also
enhances the risk of elevated blood pressure associated with
low birth weight. However, the exact contribution of weight
gain during “distinct” periods of early life on later blood
pressure and whether accelerated postnatal growth independent
of birth weight is critical to a later increase in blood
pressure remain unclear. In the current issue of Hypertension, Ben-Shlomo et al. used multiple measures of growth from
birth to 5 years with an approach that modeled changes in
growth velocity rather than anthropometry in relation to adult
blood pressure. Use of this approach to model growth trajectories allowed them to investigate the inherent complexities of discrete periods of early growth on later blood
pressure. In this study they demonstrated that rapid increases
in postnatal weight in the first 6 months of life were critical to
elevated adult systolic and diastolic blood pressure. Importantly, this finding was independent of fetal growth. In
addition, an inverse association between birth weight and blood pressure was noted, and weight gain in childhood was
positively associated with systolic blood pressure. Although several studies have noted an inverse relationship between
birth weight and diastolic blood pressure, the prediction of
diastolic blood pressure by immediate postnatal weight gain
is novel. An increase in diastolic blood pressure in childhood is a significant predictor of cardiovascular risk. Therefore,
this study by Ben-Shlomo et al. highlights the contribution of
early accelerated growth on adult blood pressure and cardio-
vascular risk and indicates that growth during both the prenatal and postnatal periods is a critical determinant for
adult blood pressure.

Because the postnatal period is more amenable for inter-
vention, this study emphasizes the importance of investiga-
tion into the consequences of accelerated growth in early postnatal life. During development, compensatory growth can occur after a period of nutritional deficit. Accelerated post-
natal growth after slow fetal growth may reflect an effort to
obtain approximately normal weight. Moreover, rapid early
catch-up growth is associated with short-term benefits in
small newborns. However, accelerated fetal growth may also
reflect excess growth and the development of obesity. In a
well-nourished cohort, catch-up growth between birth and 2
years was associated with greater body mass index and central fat distribution at 5 years of age in low birth weight children relative to other children. Another study noted that
rapid weight gain in the first 6 months of life was a critical
period of development associated with a risk of later obesity.
Body weight is directly correlated with blood pressure, and
excessive weight gain during any stage of childhood or
adolescence is associated with an increase in adult blood
pressure. Therefore, based on the vulnerability of children
small at birth to develop excessive weight gain and the
observation that accelerated weight gain during infancy and
childhood in individuals born small leads to a further
increase in later blood pressure, weight gain during early
life may have important health implications for hypertension
and cardiovascular risk.

The mechanism by which environmental influences in
early life lead to an elevation in blood pressure has not been
clearly elucidated. Obesity is associated with increased plasma leptin concentrations, and a chronic increase in
circulating leptin leads to a marked increase in blood pres-
sure. The long-term actions of leptin in the regulation of
blood pressure are not clearly understood but are suggested to
involve interactions with hypothalamic neuropeptides critical to appetite, energy homeostasis, and sympathetic nervous system outflow. Experimental studies indicate that prenatal
undernutrition followed by postnatal nutritional excess leads to
increased circulating levels of leptin, leptin resistance, and
dysregulation of hypothalamic neuropeptides. Thus, a
mismatch of adverse nutritional influences during prenatal
and postnatal life may lead to long-term consequences on
blood pressure through the developmental programming of
the hypothalamic pathway and leptin resistance. Environmental
influences during critical periods of development lead to
changes in gene expression that do not involve modification
of the basic DNA sequence, a process referred to as “epige-
etics.” Thus, epigenetic modifications that occur in re-
sponse to an insult during a critical period of development
may be important determinants for adult blood pressure by
altering the expression of genes critical to the hypothalamic
regulation of appetite and energy homeostasis.

The concept of early events programming disease in later
life began with population studies first proposed by Fors
dahl and later Barker and Osmond. Forsdahl initiated the
theory that an adverse stimulus during childhood and ade
cency to Barbara T. Alexander, Department of Physiology, University of Mississippi Medical Center, 2500 North State St, Jackson, MS 39216-4505. E-mail balexander@physiology.umsmed.edu

Hypertension is available at http://hyper.ahajournals.org

DOI: 10.1161/HYPERTENSIONAHA.108.115485
cience could lead to an increased risk for cardiovascular disease in adulthood; Barker and Osmond advanced the concept to suggest that increased cardiovascular risk may originate during prenatal life. New insight from the study by Ben-Shlomo et al indicates both the prenatal and the immediate postnatal periods as sensitive windows for the developmental programming of blood pressure. This study provides additional support for the fetal origins hypothesis and the accelerated postnatal growth hypothesis and demonstrates the importance of research into the mechanisms linking early growth and adult blood pressure.

Sources of Funding
B.T.A. is supported by grants from the National Institutes of Health (HL074927, HL51971, and MD002725).

Disclosures
None.

References
Slow Prenatal Growth and Accelerated Postnatal Growth. Critical Influences on Adult Blood Pressure
Barbara T. Alexander and Norma B. Ojeda

Hypertension. published online September 2, 2008;
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2008 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/early/2008/09/02/HYPERTENSIONAHA.108.115485.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/