Editorial Commentary

Hypertension, Growth, and Skeletal Maturation in the Young
A New Look at an Old Idea

Joseph T. Flynn

Traditionally, most cases of hypertension in children and adolescents have been attributed to secondary causes, with renal and cardiac disorders being the most common, at least in preadolescent children. However, most hypertensive adolescents have no identifiable underlying cause for their hypertension, perhaps with the exception of obese adolescents, in whom the hypertension is likely attributable to the same renal, central, and hormonal mechanisms present in hypertensive obese adults.1 But what causes hypertension in youth with no underlying renal or other systemic disease and who are not obese? The answer to this question would likely provide significant insight into the pathophysiology of “essential” hypertension in adults as well.

In this issue of Hypertension, Pludowski et al2 present intriguing data supporting the hypothesis that hypertension in the young is a disorder of maturation. Using dual x-ray absorptiometry to assess bone age, they demonstrate that hypertensive children and adolescents manifest advanced skeletal maturation compared with matched, normotensive control subjects. Advanced bone age was an independent predictor of blood pressure (BP) status in children with normal BP, prehypertension, and stages 1 and 2 hypertension. Significantly, the investigators matched not only for sex and age, but also for body mass index, thereby avoiding the confounding effects of obesity, which is known to be associated with accelerated skeletal growth in children.3

These data reinvigorate a line of investigation from several decades ago, when the phenomenon of pediatric hypertension was first being recognized, and mechanisms of hypertension in the young were first being examined. As summarized by Ingelfinger,4 early investigators interested in childhood primary hypertension focused on multiple possible underlying factors, including altered hemodynamic regulation, abnormalities of the renin-angiotensin system, and other hormonal perturbations that had already been demonstrated in adults with hypertension. At the same time, epidemiologists interested in childhood hypertension were recognizing that normative values for childhood BP based on age only might result in misclassification of BP because of differences in maturation among children of comparable ages.5 It was, therefore, suggested that height as an index of maturation should be considered when classifying a child’s or an adolescent’s BP as normal or elevated, an approach that was adopted by the Working Group on High Blood Pressure in Children and Adolescents in 1996 and that remains a cornerstone of current consensus recommendations for evaluating childhood BP.

At approximately the same time, investigators associated with the Philadelphia Blood Pressure Project analyzed data including bone age on a sample of children (all black) followed longitudinally into adolescence and found those children who had the highest levels of BP at 7 years of age achieved adult levels of BP earlier than those who had the lowest levels of BP at age 7 and had advanced bone age in adolescence compared with those with the lowest levels of BP at 7 years of age.6 In other words, advanced skeletal maturation in children with high BP was demonstrated to be associated with higher BP in early adolescence. Although drawn from different data, these findings reinforced the conclusions drawn by epidemiologists5 that growth and maturation should be considered when assessing BP in the young.

It was Lever and Harrap7 who eventually summarized multiple lines of evidence, including the bone age data from the Philadelphia Blood Pressure Project, to advance the hypothesis that, in childhood, the development of primary hypertension is likely tied to other growth-promoting processes and suggested 3 possible endocrinologic mechanisms, among them insulin resistance. This is an especially interesting suggestion given the evidence for insulin resistance as one possible underlying mechanism in lean hypertensive patients.8 Seen in this context, it is unfortunate that Pludowski et al2 did not assess pertinent metabolic and hormonal parameters in their study population. However, as Lever and Harrap7 clearly stated, the preponderance of evidence available at the time (and one could argue, available today) did not favor any single mechanism but clearly pointed toward growth-promoting processes in general as being related to the development of hypertension in the pediatric age group. They specifically stated that, optimally, mechanistic studies of primary hypertension should be conducted in children to capitalize on the relationship between maturation and BP and to avoid the many confounding factors associated with aging.7

So what additional research has been conducted to explore growth-related mechanisms in the development of primary
hypertension? Much work has focused on the relationship between vascular growth and the perpetuation of hypertension, the second half of the thesis by Lever and Harrap, but few new data have emerged focusing on somatic growth/maturation and BP. Thus, the study of Pludowski et al² adds significant information to that known to Lever and Harrap, specifically by demonstrating that the same phenomenon of advanced skeletal maturation can be demonstrated in hypertensive youth from multiple racial backgrounds (as noted above, the Philadelphia data were obtained in black children). Although the clinical utility of demonstrating advanced skeletal maturation in hypertensive children is likely to be nil, these data could be used as justification for the reopening of an important, potentially fruitful line of research with important implications for understanding the pathogenesis of hypertension in adults.

Hypertension in the young is increasing in prevalence, with much of the increase being fueled by the increase in childhood obesity. Although significant cardiovascular complications of high BP infrequently develop in children and adolescents, the long-term prognosis for the development of adult cardiovascular disease is worrisome. Advances in understanding the epidemiology of childhood hypertension and in testing the efficacy of antihypertensive medications in the pediatric age group have not been accompanied by commensurate advances in understanding the mechanisms responsible for the development of hypertension in the first place.

Re-examining early mechanistic hypotheses as Pludowski et al² have done is not only appropriate but also necessary given current trends.

Disclosures
None.

References
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