Pediatric hypertension update
Joseph T. Flynn

Introduction
The field of pediatric hypertension is undergoing numerous changes, the majority of which are related to the childhood obesity epidemic. It appears that not only is the number of children and adolescents with hypertension increasing, but actual blood pressure (BP) levels may be increasing as well. New data are emerging on the extent of hypertensive target-organ damage in the young. In order to avert an epidemic of young adults with early cardiovascular disease, changes to the approach to high BP in the young may be needed. This study will summarize these developments in the field of pediatric hypertension, pointing out steps that could potentially be taken to reduce the future burden of adult cardiovascular disease.

Epidemiologic aspects
Evidence has been mounting over the past decade that the actual incidence of hypertension in children and adolescents has been increasing, at least in the United States. This is evidenced by data from BP screening studies conducted in healthy children, usually in school-based settings. As summarized in Table 1, the percentage of children and adolescents identified in such studies as having elevated or hypertensive-level BP has increased from approximately 1-2% in studies conducted in the mid-1970s, to 3-5% in studies conducted in the early 2000s [1-7]. One caveat related to the data presented in Table 1 is the number of screening visits performed before categorization of the child or adolescent as hypertensive – some studies that included a greater number of screenings reported a lower prevalence of hypertension, although this was not the case for some of the most recent studies. As pointed out by Falkner [11], the lack of an effect of a greater number of screening visits in the most recent studies may relate to better, more stable normative data than were used in earlier screening studies.

An especially important study is a recent review of BP data in 8-17-year-old children from the National Health and Nutrition Examination Survey (NHANES) and other related population-based studies conducted in the United States from 1963 to 2002, which clearly demonstrated an increase in the prevalence of high BP in children [7], counteracting earlier suggestions that the prevalence of childhood hypertension has remained stable over time [12]. The most recent survey data indicate that the prevalence of prehypertension has now reached 10% and the prevalence of hypertension nearly 4%. A significant strength of this analysis was the application of current BP criteria for hypertension and prehypertension in childhood to all of the data in the various surveys included, thereby eliminating one the problems affecting prior analyses [11]. Of note, this study also demonstrated that the recent trends in high BP have had a much greater

Purpose of review
The field of childhood hypertension has been changing rapidly since publication of the most recent consensus guidelines contained in the 2004 ‘Fourth Report’.

Recent findings
Several epidemiologic studies have indicated that the prevalence of hypertension in children and adolescents is on the increase. A major factor behind this increase is the childhood obesity epidemic. There is substantial new information on the frequency of hypertensive target-organ damage in the young, including vascular, cardiac and renal effects. These data have led some authorities to recommend changes in how hypertension is evaluated and managed in the young.

Summary
There has been significant new knowledge gained about many aspects of childhood hypertension over the past 5 years. Clinicians who care for children and adolescents with high blood pressure should familiarize themselves with these new data and incorporate them into their clinical decision-making.

Keywords
adolescents, cardiovascular disease, children, epidemiology, hypertension, obesity

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effect on non-Hispanic blacks and Mexican Americans than on whites [7]. Interestingly, another recent study of prevalence rates of high BP in children of different ethnic and racial groups found that differences in prevalence were seen in boys but not in girls [13].

Other disturbing data on childhood BP were reported in a 2004 analysis of NHANES data [14] that demonstrated that overall BP levels in US children and adolescents have increased over the past decade: systolic BP was found to be 1.4 mmHg higher in 1999–2000 than in 1988–1994, and diastolic BP was found to be 3.3 mmHg higher. This increase in overall BP levels was more pronounced in non-Hispanic black and Mexican American children, particularly in girls. The difference for black children has previously been described [15], but prior studies had generally shown similar BPs for Mexican American children to other ethnic groups [16]. Whereas some of the increase in childhood BP levels was attributed to obesity, particularly among the Mexican American children [14], much of it could not, implying that other, as yet unidentified, forces were at work among American children resulting in the increased BP levels.

There is, however, no argument at this point that the childhood obesity epidemic is playing an important role in both the increase in prevalence of childhood hypertension and the increase in childhood BP levels. As seen in Fig. 1, the prevalence of obesity among American children has more than trebled over the past 30 years, and now approaches 20% in children aged 6–11 years [17]. A similar picture is emerging among younger children as well: in New York City, among 16,000 children (mean age 3.5 years) enrolled in the Head Start Program in 2004, 27% were obese and 15% were overweight [18]. In a recent study, it was projected that the increase in childhood obesity in the United States will result in a significant increase in obesity among 35-year-olds by 2020, which could then translate into a significant increase in adult cardiovascular disease [19].

The increase in childhood obesity is not limited to the United States. Significant increases in childhood body mass index (BMI) have been documented in several European countries, including Poland [20] and Italy. Among a randomly selected sample of children and adolescents in Catanzaro, Italy, 18% of the children were classified as being at risk for overweight (BMI percentile 85–94%) and another 11% were classified as obese (BMI percentile ≥95%) [21]. Obese children in this sample were more likely to have elevated systolic or diastolic BP than nonobese children, and BMI was a significant predictor of elevated BP. Lesser developed countries are experiencing significant increases in childhood obesity as well. Anthropometric data obtained in 23,459 children in the Seychelles demonstrated an increase in the prevalence of obesity from 2.1 to 5.2% in boys and from 3.1 to 6.2% in girls between 1998 and 2004, with analogous increases in the percentage of children at risk of overweight [22]. Decreased physical activity, which has been closely linked to the childhood obesity epidemic in North America, was present even in this developing country and was associated with excess weight.

Childhood obesity has many significant health consequences, among them impaired glucose tolerance, dyslipidemia, elevated BP, hepatic disease, orthopedic

<table>
<thead>
<tr>
<th>Study location</th>
<th>Year</th>
<th>Number screened</th>
<th>Age (years)</th>
<th>Number of screenings</th>
<th>Normative criteria</th>
<th>Prevalence of HTN</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>New York, New York</td>
<td>1974</td>
<td>3537</td>
<td>14–19</td>
<td>2</td>
<td>140/90</td>
<td>1.2% SHTN, 2.4% DHTN</td>
<td>[1]</td>
</tr>
<tr>
<td>Dallas, Texas</td>
<td>1979</td>
<td>10,641</td>
<td>14</td>
<td>3</td>
<td>95th percentile</td>
<td>1.2% SHTN, 0.4% DHTN</td>
<td>[2]</td>
</tr>
<tr>
<td>Minneapolis, Minnesota</td>
<td>1989</td>
<td>14,668</td>
<td>10–15</td>
<td>1</td>
<td>1987 TF</td>
<td>4.2%</td>
<td>[3]</td>
</tr>
<tr>
<td>Minneapolis, Minnesota</td>
<td>2001</td>
<td>14,668</td>
<td>10–15</td>
<td>2</td>
<td>1996 WG</td>
<td>0.8% SHTN, 0.4% DHTN</td>
<td>[4]</td>
</tr>
<tr>
<td>Houston, Texas</td>
<td>2004</td>
<td>5102</td>
<td>12–16</td>
<td>3</td>
<td>1998 WG</td>
<td>4.5%</td>
<td>[5]</td>
</tr>
</tbody>
</table>

Figure 1 Percentage of children and adolescents with BMI at least 95th percentile for age and sex in NHANES surveys since 1963

Adapted from reference [17].
problems and psychosocial disorders. From a cardiovascular standpoint, numerous studies over the years have firmly established the link between increased BMI in childhood and the development of elevated BP. Recent school screening studies conducted in the United States over the past several years provide ample evidence of this effect, most notably in Houston, Texas, where the prevalence of hypertension in adolescents has been shown to be as high as 10% among those with a BMI greater than or equal to the 97th percentile [5,6]. Strong associations between overweight and elevated BP have also recently been reported in sixth-graders in Seminole County, Florida [23], and in even younger children in Anadarko, Oklahoma [24]. In another Italian study, the prevalence of prehypertension was nearly 12 times that in a control group of normal-weight children and prehypertension was associated with insulin resistance [25*]. An additional finding in the American studies cited earlier is a higher prevalence of both overweight and elevated BP among minority children (including Native Americans, African Americans, and those of Hispanic ethnicity) than among white children. This has significant public health implications given the excess prevalence of hypertension-related sequelae such as kidney disease in minority adults [26,27].

**Adverse effects of elevated blood pressure**

The sequelae of long-standing hypertension in adults are well known, and include coronary artery disease, stroke, kidney damage and increased mortality [28*]. In children, however, there are few data available on the natural history of primary hypertension, making it impossible to predict the long-term outcome of an untreated hypertensive adolescent or school-aged child. The one exception to this statement is a recent small study from Iceland demonstrating a correlation between childhood systolic BP and the development of coronary artery disease in adulthood [29*]. Therefore, it is necessary to look at surrogate markers such as hypertensive target-organ damage, or study pediatric populations with secondary hypertension, in order to gain insights into the effects of long-standing hypertension in the young.

Hypertensive target-organ damage can be divided into several broad categories, among them vascular changes, cardiac damage and renal effects. All of these can be seen in hypertensive children and adolescents to varying extents. There are even reports of target-organ effects of high BP in pediatric patients with prehypertension and white coat hypertension (WCH), implying that any level of BP elevation at an early age may be detrimental.

Increased carotid intimal–medial thickness (cIMT), which is well established as a surrogate marker for atherosclerosis in adults [30], has also been found in children and adolescents with primary hypertension [31–33], and is a potential early marker of hypertensive vascular damage, especially in those with additional cardiovascular risk factors [34*]. Although early studies of cIMT in hypertensive youth were complicated by the effects of obesity [31], a more recent study that controlled for BMI demonstrated a definitive relationship between elevated BP itself and increased cIMT in young patients [32]. These vascular changes, which may or may not represent subclinical atherosclerosis [35], could potentially be explained by the so-called Folkow hypothesis, which posits that elevated BP of any cause leads to thickening of the medial layer of resistance vessels, which in turn perpetuates the hypertension [36]. Along these lines, recent studies have demonstrated impaired endothelial function and increased vascular stiffness in obese adolescents that are associated with ambulatory BP parameters [37**].

Additional evidence of vascular effects of elevated BP in the young comes from a recent study of retinal vessel caliber in children aged 6–8 years in Singapore and Sydney [38]. In this study, there was a significant association between retinal arteriolar caliber and systolic BP, with children in the highest BP quartile having narrower vessels than those in the lowest BP quartile. Of note, it is well known from population-based studies that narrower retinal arterioles are linked with the future development of hypertension [39,40]. These data build upon earlier work by Daniels et al. [41] examining the prevalence of hypertension-related retinal changes in children, and provide additional evidence of BP-related vascular damage in the young.

Whereas the vascular effects of high BP are concerning, they are difficult to assess clinically because of technique issues associated with measuring cIMT, and the subtlety of retinal changes, which typically require examination by a pediatric ophthalmologist to detect. A more commonly assessed target-organ effect of high BP is left ventricular hypertrophy (LVH), which was first demonstrated to occur in hypertensive youth by Laird and Fidler [42], who also demonstrated the superiority of echocardiography over other diagnostic methods. Since then, LVH has been repeatedly shown to occur in a significant proportion of hypertensive children and adolescents, with reported prevalences ranging between 20 and 41% depending upon the diagnostic criteria utilized [43–46].

That the development of LVH in the young may not be related to the severity of BP elevation is especially interesting. There are single-center data that have demonstrated a correlation between the severity of BP elevation and the likelihood of developing LVH [44,45], but a larger, multicenter study failed to demonstrate any definite relationship between LVH and specific parameters of BP elevation [46]. These conflicting data underscore the
need to perform echocardiography at the diagnosis of hypertension and periodically thereafter in children and adolescents, as recommended in 2004 by the National High Blood Pressure Education Program Working Group [8]. Emerging data on LVH in children with WCH [47,48] add further weight to this recommendation.

An additional target-organ effect of elevated BP recently demonstrated in the young is impaired cognitive function [49]. Whereas long-standing hypertension has long been recognized as a risk factor for the development of cognitive impairment and even dementia in the elderly [50], this study based upon NHANES data demonstrated that children and adolescents with elevated BP (>90th percentile) had poorer performance on selected cognitive tests than normotensive children. A follow-up study from the same investigators in a small group of children with primary hypertension demonstrated other behavioral abnormalities in hypertensive children compared with normotensive controls, including lower parental ratings of executive function [51]. These provocative findings, although requiring additional confirmation, add further impetus to consensus recommendations for instituting antihypertensive drug therapy in children and adolescents with persistently elevated BP [8].

Fewer pediatric data are available on the other major target-organ effect of hypertension, namely renal damage. Although hypertension commonly accompanies chronic kidney disease in children [52**], and although changes consistent with hypertensive nephrosclerosis have been described in autopsy specimens from persons aged 14–21 years [53], hypertension alone is rarely if ever the cause of kidney disease in the young. Even microalbuminuria, which is commonly seen in hypertensive adults, is infrequently seen in children with isolated hypertension. One study comparing hypertensive children in a referral clinic with another group identified by school-based screening did not show significant microalbuminuria despite a significant prevalence of LVH [54]. However, a more recent study demonstrated that approximately 58% of hypertensive adolescents had microalbuminuria, with an increased prevalence in stage 2 hypertension compared with stage 1 [55]. Reduction of BP in the latter study with an angiotensin-converting enzyme (ACE) inhibitor was accompanied by a reduction in both microalbuminuria and LVH.

There is also new evidence that modestly elevated BP can lead to reduced glomerular filtration rate (GFR) in the pediatric age group. In an Italian study of nonobese children aged 6–14 years, those with prehypertension had lower GFR and higher levels of urinary protein excretion – both within the normal range, however – than a normotensive control group [56**]. Additionally, those prehypertensive children with the highest BP load on ambulatory BP monitoring had the lowest GFR. However, although all three of these studies suggest that high BP may lead to kidney damage in the young, all are also relatively small single-center studies with many limitations, whose findings need to be confirmed in larger populations.

Finally, additional data on the effects of hypertension in the young can be gleaned from populations with secondary hypertension. One such group are patients with repaired coarctation of the aorta. Several early studies of patients postcoarctation repair have documented a high incidence of LVH and sudden cardiac death [57,58]. Another group of patients in which persistent hypertension has significant late sequelae are children with chronic kidney disease. As noted earlier, the majority of children with chronic kidney disease are hypertensive [52**], and many have associated immediate consequences of their hypertension such as LVH [59]. Additionally, cardiovascular disease is now recognized as the leading cause of late morbidity and mortality in adults with childhood-onset chronic kidney disease [60]. However, it must also be recognized that risk factors for development of cardiovascular disease other than elevated BP, such as inflammation, dyslipidemia and disordered calcium–phosphorus metabolism, are almost always present in children with chronic kidney disease [61], making it difficult to determine the specific contribution of hypertension in their long-term outcome.

Should the approach to high blood pressure in children and adolescents be changed?

Given these new data on changes in the epidemiology of childhood hypertension and on the short and long-term effects of elevated BP in the young, questions are beginning to emerge on the best approach to detection and management as well. Current consensus recommendations as embodied in the National High BP Education Program’s Fourth Report [8] remain conservative, emphasizing the need for accurate BP measurement and careful evaluation before clinicians either label a child or adolescent as having hypertension or initiate aggressive treatment with antihypertensive medications. But is this the correct approach given the growing number of youth with high BP and the possibility of hypertensive target-organ damage or future atherosclerosis?

Recently it has been argued that the conservative approach advocated by the Fourth Report should be modified to make the diagnosis of hypertension more straightforward, and to initiate treatment earlier, particularly in children with WCH and prehypertension [62**]. It is perhaps true that the percentile-based diagnostic thresholds published in the Fourth Report are complex. This complexity is perhaps responsible for the significant underdiagnosis of hypertension that has been reported in reviews of pediatric
Electronic medical record data [63] and the failure of general pediatricians to follow consensus recommendations [64]. On the contrary, it is not clear that we yet have enough data to abandon the 95th percentile as the cut-point to diagnose elevated BP in pediatric patients in favor of a more simplified approach as is used in adults [65]. Adoption of the 95th percentile as a cut-point for pediatric BP by Londe and others in the 1970s was based upon a lack of reliable normative data on BP in childhood, as well as a lack of data on the effects of high BP in the young. Both of these issues contributed to adoption of a statistical definition of high BP in children and adolescents instead of a single cut-point as used in adults. Thirty years later, we do have more robust normative data for pediatric BP and also data on intermediate effects of high BP in childhood, so it is appropriate to question old definitions. What remains to be defined is the absolute BP level at which disease begins and that justifies earlier diagnosis.

It is clear, however, that even children and adolescents with either WCH or prehypertension warrant some form of intervention to prevent progression to more significant levels of BP elevation and/or early cardiovascular disease. Analysis of tracking studies confirms that high BP in the young predicts future high BP [66], so it is likely that the child or adolescent with either WCH or prehypertension will go on to develop true hypertension later in life. Additionally, recent data on target-organ effects in children with WCH [32,47,48], and the intriguing data on reduced GFR and proteinuria in children with prehypertension [56], make it clear that modest levels of BP elevation can have significant effects even in childhood. Although there are no pediatric data at present to support pharmacologic treatment of these children [67], ‘therapeutic lifestyle interventions’ (weight loss, dietary changes, exercise) as outlined in the Fourth Report are appropriate and should be initiated, and such children should be monitored on an ongoing basis for possible progression of their BP to higher levels. Given the changes occurring on a population level as a consequence of the childhood obesity epidemic, there is ample justification for adoption of such measures on a much wider scale than previously recommended.

**Conclusion**

As should be evident from the preceding discussion, there have been significant changes in many aspects of childhood hypertension over the past decade. The changes in epidemiology, influence of the obesity epidemic, and growing evidence of early hypertensive target-organ damage have increased the level of interest in childhood hypertension among clinicians, epidemiologists and researchers alike. Although questions have been raised regarding the optimal approach to diagnosis of hypertension in the young, there should be no hesitation in adopting appropriate preventive strategies to avert a future epidemic of adult cardiovascular disease.

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**References and recommended reading**

Papers of particular interest, published within the annual period of review, have been highlighted as:
- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 328–329).


Proconvulsive study demonstrating the effect of elevated BP on renal function and proteinuria.


Editorial commentary calling for changes in the approach to pediatric hypertension.


Small study that reveals inconsistent adherence to consensus recommendations for evaluation of high BP among general pediatrics.


Contrasts earlier studies showing that high childhood BP tracks into adulthood.