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Updates on Hypertension and New Guidelines

Pamela S. Singer, MD, MS

Cohen Children's Medical Center, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, 269-01 76th Avenue, New Hyde Park, NY 11040, USA

Keywords

• Blood pressure • Hypertension • Pediatrics • Cardiovascular • Nephrology • Epidemiology

Key points

- Pediatric high blood pressure tracks into adulthood and can be a significant cause of morbidity and mortality; therefore, early recognition is critical for prevention.
- Recently updated practice guidelines provide new normative data for blood pressure in children, using only normal-weight subjects to provide a more accurate assessment of normal pediatric blood pressure values.
- Ambulatory blood pressure monitoring is a crucial diagnostic tool for pediatric hypertension and is the only way to identify white coat and masked hypertension.
- Therapeutic lifestyle modifications, including diet and exercise, are recommended as first-line treatment in most cases of high blood pressure.

GENERAL CONTENT

Epidemiology

Elevated blood pressure (BP) represents a major cause of morbidity and mortality in the United States. An estimated 32% of adults in the United States have hypertension (HTN), with another one-third having pre-HTN [1]. Adult BP has its roots in pediatrics, because children with higher BPs have an increased prevalence of HTN in adulthood [2]. Studies of the prevalence and risk factors for pediatric HTN have relied mainly on large-scale studies, such as National

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E-mail address: psinger@northwell.edu

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Health and Nutrition Examination Survey (NHANES) and the Bogalusa Heart Study [2–7]. Prevalence estimates in these studies generally range from 3% to 5% for HTN, and higher for pre-HTN. Studies using repeated BP measurements have resulted in lower estimates [8,9].

Numerous nonmodifiable risk factors have been associated with pediatric high BP. Boys have been shown to have higher rates of high BP as compared to girls [9], as do Hispanics and non-Hispanic African Americans as compared with whites [7].

Although there has been a general increase in the prevalence of pediatric HTN over time, which has mirrored the increase in pediatric obesity [9,10], a study of NHANES data from 1999 to 2012 actually found a leveling off in prevalence of high BP between the 1999 to 2002 and 2009 to 2012 time periods [3,4].

Obesity has been shown in numerous studies to be a risk factor for elevated BP [11–13]. A study of 2585 pediatric NHANES subjects found average BP was 8 mm Hg higher in obese patients as compared with those who were normal weight [14]. The association between elevated weight and BP could be seen even in young, preadolescent children [15].

In addition to obesity, other medical conditions have been shown to be associated with increased risk of high BP. Specifically, premature infants are at increased risk of high BP, as are those with obstructive sleep apnea. These conditions are in addition to the more classically recognized secondary causes of HTN. Studies have shown an incidence of about 0.2% to 3% for HTN in the neonatal intensive care unit [16,17]. Although previously, umbilical artery catheters have been attributed as a major source of neonatal HTN, much of the elevated BP in this population is now likely due to improved survival of premature babies [17]. Prematurity is associated with decreased nephron mass, upregulation of the renin-angiotensin system, increased catecholamine release, and endothelial dysfunction [18]. In up to 50% of patients, no other clearly identifiable cause of HTN is elucidated [17]. Although outcomes are variable, in most cases, BP due to prematurity can normalize within the first 6 months of life [19]; however, prematurity remains a long-term risk factor for future high BP as well.

Diagnosis

Although data linking pediatric HTN to cardiovascular morbidity and mortality are lacking, HTN is a well-known contributor to adult cardiovascular disease [20] and intermediate markers of damage are visible in children [21]. Children with elevated BP have also been found to perform less well on tests of cognitive function, suggesting potential central nervous system end-organ damage [22]. These findings underscore the importance of early diagnosis of high BP in children, in order to prevent future damage. Despite a 2013 US Preventative Services Task Force guideline stating insufficient evidence to recommend routine BP measurement in asymptomatic children and adolescents [23], the new 2017 high BP clinical practice guidelines continue to recommend

screening at least annually for children ≥3 years of age. Furthermore, children with known risk factors, including obesity, should be screened at all health care encounters, and those under 3 years of age with known risk factors should be screened at well child visits as well [24]. High-risk conditions include prematurity, history of congenital heart disease, patients with known structural or functional renal disease, transplant recipients, those on medications known to raise BP, such as stimulants for attention-deficit/hyperactivity disorder, and those with syndromes known to affect BP, such as neurofibromatosis and tuberous sclerosis.

The definition and diagnosis of pediatric HTN are based on age-, gender-, and height-specific normative BP data. This method is in contrast to absolute values used in the diagnosis of adult HTN. Although the Fourth Report [25] included subjects who were overweight and obese, the 2017 guidelines use only normal-weight children. This change has resulted in a lowering of normal BP cutoffs, because obesity-related high BP skewed previous data toward higher values. When using the new criteria, studies have shown increases in the percentage of children diagnosed with HTN [26]. In a recent analysis of pediatric NHANES participants, comparison of BP classification using both the 2017 guidelines and the 2004 Fourth Report showed an increased prevalence of HTN, 14.2% versus 11.8%, when using the newer criteria [11]. This increase was especially notable among overweight and obese children. Khoury and colleagues [27] showed an increase in prevalence of HTN from 8% to 13% in obese diabetic youth when using the new criteria.

The 2017 guidelines also aimed to align themselves more closely with adult HTN criteria [28]. Children between the ages of 1 and 13 are classified using age-/gender-/height-specific percentile values, whereas children 13 and older, whose pressures are more similar to adults, are classified according to adult criteria. Table 1, adapted from the new guidelines, summarizes the new pediatric BP classification system.

Full tables of new normative data are available at pediatrics.aappublications.org/content/140/3/e20171904.figures-only. If patients have an isolated elevated systolic or diastolic pressure, they are classified according to whichever value is higher. Normative values are based on upper-extremity auscultatory data. Oscillometric measurements are commonly used as an initial screen for BP; however, these devices are known to overestimate BP as compared with auscultation [29].

Because BP is known to vary, the classification of BP status should be made after multiple measurements at different times rather than based on a single value [7]. For asymptomatic patients found to have elevated BP on screening examination, repeat measurements spaced 6 months apart are recommended, with workup only if elevations are persistent on 3 occasions. For those with stage I HTN, a period of 3 months of persistent BP elevation should occur before further workup is initiated, and for those with measurements in the stage II HTN range, more urgent evaluation is advised [24].

When further evaluation of BP is required, ambulatory BP monitoring (ABPM) is recommended for the most accurate detection of true high BP. ABPM represents one of the major advances in pediatric BP management

Table 1
2017 Pediatric blood pressure classification

	Ages 1 to <13 y[a]	Ages ≥13 y
Normal BP	Systolic blood pressure (SBP) and diastolic blood pressure (DBP) <90th% for gender/age/height	SBP <120 and DBP <80 mm Hg
Elevated BP (previously termed pre-HTN)	SBP or DBP ≥90th% to <95th% for gender/age/height	SBP 120–129 mm Hg with DBP <80 mm Hg
Stage I HTN	SBP or DBP ≥95th% to <95th% + 12 mm Hg for gender/age/height	SBP 130–139 or DBP 80–89 mm Hg
Stage II HTN	SBP or DBP ≥95th% + 12 mm Hg for gender/age/height	SBP ≥140 or DBP ≥90 mm Hg

[a]If values exceed the corresponding values for children ≥13 y, the lower value is used.

over the past 20 years. As compared with office measurements, ABPM in children has shown higher tracking stability with future adult BP [30] and is a more sensitive marker of HTN as compared with casual BP measurement [31]. ABPM in children correlates with markers of target organ damage, including increased pulse wave velocity and carotid intima-medial thickness (cIMT) [32] and left ventricular hypertrophy (LVH) [33–36]. The relationship between ABPM and markers of CV damage is stronger than that with in-office BP measurement [37]. Although there are limited pediatric data on the correlation between intermediate markers of damage and hard cardiovascular outcomes, adult data show this relationship [38]. In ABPM, a small portable oscillometric device is worn for a 24-hour period, including during sleep. BP values are obtained and recorded at 20- to 30-minute intervals. Patients provide a diary, which includes hours of sleep and wake during the monitoring period; using those data, a report is generated that provides information of average awake and asleep BP, BP loads (percentage of time spent with high BP), and dipping status (BP change between awake and asleep periods).

ABPM can identify white coat HTN, which is found in up to half of children referred for elevated BP [39]. The diagnosis of white coat HTN can prevent unnecessary testing and associated costs of further HTN workup. However, those with white coat HTN should continue to be monitored because they may be more likely to develop HTN in the future [40].

Normative values for ABPM based on sleep/wake status, gender, and height have been published [41,42]. Table 2 provides a classification scheme for ABPM results. ABPM classification relies on mean BPs during both sleep and wake periods as well as BP loads (percentage of time above the 95th% value). Other parameters, such as BP dipping (percentage difference between mean wake and mean sleep values), are also used in risk-stratification, however are not part of the classification scheme.

Table 2
Ambulatory blood pressure classification

White coat HTN	Clinic BP ≥95th% (SBP or DBP), ABPM mean awake and asleep SBP and DBP <95th%, loads all <25%
Pre-HTN	Mean awake and asleep SBP and DBP <95th%, at least 1 load ≥25%
Ambulatory HTN	Mean awake or asleep SBP or DBP ≥95th%, at least 1 load ≥25%
Severe ambulatory HTN	Mean awake or asleep SBP or DBP ≥95th%, at least 1 load >50%
Masked HTN	Normal clinic BP, ABPM mean awake or asleep SBP or DBP ≥95th%, at least 1 load ≥25%

It is important to note that ABPM classification does not line up fully with casual BP classification. For instance, severe ambulatory HTN is not equivalent to stage II HTN. Whereas casual BP classification is based on absolute BP values, ambulatory BP classification is the BP means as well as the percentage of time spent with high BP. Consultation with an HTN specialist is recommended for ABPM interpretation.

Workup

Whereas historically, pediatric HTN was thought to be largely due to secondary causes, newer studies have found that primary HTN is an equally important cause of high BP and is the predominant diagnosis in children over 6 years of age [43]. A positive family history for HTN was also an independent predictor of primary HTN [43], as is obesity [44].

Based on these data, the 2017 guidelines recommend against extensive secondary evaluation in children ≥6 years old, who have a positive family history for HTN and are overweight, and who do not have symptoms or findings concerning for specific secondary cause [24]. These recommendations are in contrast to the Fourth Report [25], which recommended at least complete blood count, comprehensive metabolic panel, renal ultrasound with Doppler, and echocardiogram in all children diagnosed with HTN. Of course, careful and accurate history and physical examination must be obtained to avoid a missed diagnosis of secondary cause. Furthermore, the 2017 guidelines do not explicitly define their recommendation regarding extent of evaluation.

Among those with secondary HTN, renal and renovascular disorders remain the most common causes. Evaluation of renovascular HTN is based on renin profiling (serum renin and aldosterone measurement) and renovascular imaging. The sensitivity of Doppler ultrasound varies based on age and weight, with best results noted in normal-weight children ≥8 years old [45,46]. Alternative imaging, such as computed tomography or magnetic resonance angiography, may be preferred in children not meeting these criteria. Other common causes include aortic coarctation, endocrine disorders, including hyperthyroidism and mineralocorticoid excess, monogenic HTN,

and certain syndromes. Sleep apnea is another common risk factor for pediatric HTN and should be assessed in patients with signs of disordered sleep. Box 1 lists common causes of secondary HTN. Evaluation for secondary causes should be based on signs, symptoms, and index of suspicion. Management of secondary causes should focus on the underlying disorder and may differ from standard recommendations for primary HTN. Treatment of specific secondary causes is beyond the scope of this article.

Echocardiogram is recommended if there is a consideration of starting pharmacologic therapy for HTN in order to assess for the presence of LVH. Although there are many different echocardiographic methods and measurements used for determining left ventricular mass index and LVH [47,48], the current guidelines use left ventricular mass of greater than 51 $g/m^{2.7}$ in children older than 8 years, or greater than 115 g/body surface area in boys and greater than 95 g/BSA in girls less than that age. It is important to note that BSA-based measurements result in lower prevalence of left ventricular hypertrophy as compared with height-indexed 95th percentile [49,50]. However, less emphasis overall is placed on echocardiographic findings in the current guidelines, because evidence of LVH is not discussed as a clear indication for pharmacologic treatment as it is in the Fourth Report.

Additional markers of cardiovascular damage include increased cIMT as determined by carotid ultrasound, increased arterial stiffness as measured by increased pulse wave velocity, and impaired endothelial function as measured by flow-mediated dilatation. Although research on these methods in both the pediatric and the adult populations is ongoing [27], these tests are currently not commonly available in clinical practice, including among HTN specialists. However, they may continue to grow in importance given their ability to detect early cardiovascular damage in this population [51].

Treatment

Lifestyle modification is recommended for all patients with elevated BP as well as those with asymptomatic stage I HTN. Patients with stage II HTN, with symptomatic HTN, or with underlying chronic kidney disease (CKD) or diabetes mellitus (DM) may require pharmacologic treatment from the outset of diagnosis [24]. A combination of diet and exercise modifications is recommended, because this is more effective than either alone in lowering BP [52].

Dietary focus should be on fresh fruits and vegetables, lean proteins, and low-fat dairy products, key components of the DASH diet [53]. Although much of traditional literature focuses on sodium restriction in the management of HTN, recent adult studies have provided more conflicting evidence. The 2015 to 2020 Dietary Guidelines for Americans [54] recommend a sodium intake of less than 2300 mg/d, and in some cases less than 1500 mg/d. However, studies of the association between sodium intake and cardiovascular outcomes have shown varying effects, with many showing increased mortality at both the highest and the lowest intakes of sodium despite decreases in BP [55,56].

Box 1: Common causes of secondary hypertension

Renal

- Congenital anomalies of the kidney and urinary tract and obstructive uropathy
- Reflux nephropathy
- Cystic kidney disease
- Glomerulonephritis
- Renovascular disease (renal artery stenosis, fibromuscular dysplasia, arteritis)

Cardiovascular

- Aortic coarctation and midaortic syndrome

Endocrine

- Hyperthyroidism
- Hyperaldosteronism
- Congenital adrenal hyperplasia
- Apparent mineralocorticoid excess
- Hypercalcemia
- Pheochromocytoma

Monogenic

- Liddle syndrome
- Gordon syndrome

Oncologic

- Wilms tumor
- Neuroblastoma

Syndromic

- Neurofibromatosis I
- Tuberous sclerosis
- Turner syndrome
- Williams syndrome

Drugs

- Steroids
- Stimulants
- Caffeine
- Illicit drugs

Miscellaneous

- Prematurity
- Obstructive sleep apnea

In addition to dietary measures, increases in physical activity and decreased sedentary time are important measures to improve BP and overall cardiovascular health. Sedentary activities should be limited to fewer than 2 hours per day, and 30 to 60 minutes daily of cardiovascular activity is recommended. Although certain high-static and competitive sports participation may temporarily need to be restricted until BP is controlled, there are no restrictions on noncompetitive cardiovascular activity due to HTN [24,57]. Children and adolescents should not be prohibited from participating in these activities pending further evaluation.

Medication

For those who fail therapeutic lifestyle modifications, pharmacologic treatment may be needed. The 2017 guidelines go farther than previous reports in suggesting first-line agents for HTN. An angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker is recommended as first line for anyone with CKD, DM, or proteinuria unless there is an absolute contraindication. In other cases of primary HTN, ACEi may also be used as a first-line agent, with consideration of a calcium-channel blocker or thiazide as first line in African American children because of decreased response to ACE inhibitors [58]. Beta-blockers are not recommended for first-line treatment because of their increased side-effect profile. Regardless of the medication initiated, dose maximization of a single agent should be used before adding additional medication. Although the Fourth Report recommended a BP goal of less than 95th% for gender/age/height except for those with underlying comorbid conditions, such as CKD and diabetes, the 2017 guidelines propose stricter goals of less than 90th% (or <130/80 mm Hg) for all patients with HTN. Even lower targets may be beneficial, as evidenced by the ESCAPE trial [59], which showed improved outcomes in those with lower BP goals.

SUMMARY

Early diagnosis of pediatric HTN is important to prevent both short- and long-term target organ damage and adverse outcomes. The recently published 2017 clinical practice guidelines serve as an update to the 2004 Fourth Report and provide recommendations on the diagnosis, workup, and management of pediatric high BP. The new guidelines provide updated normative BP data using normal-weight children, in order to more appropriately characterize ideal pediatric BP. Guidelines for evaluation of high BP have been modified to reduce unnecessary testing, and treatment focuses on lifestyle modifications before moving to pharmacologic therapy. The new guidelines propose stricter BP control goals because these may be associated with better long-term outcomes.

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