New Clinical Practice Guideline for the Management of High Blood Pressure in Children and Adolescents

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A substantial body of clinical data on elevated blood pressure (BP) in children and adolescents have been published during the past decade. In response to the need to update management guidelines on pediatric hypertension, the American Academy of Pediatrics (AAP) supported development and publication of a new clinical practice guideline on high BP in childhood. Before 1977, there was no consistent definition of hypertension in childhood, and BP was not commonly measured in asymptomatic children or adolescents. Consequently, childhood hypertension had been considered rare and, if detected, the assumption was that it would be secondary to an underlying disorder. In the mid-1970s, the National High Blood Pressure Education (NHBPEP) of the National Heart Lung and Blood Institute (NHLBI) convened a task force to examine available BP data on healthy children to determine the normal BP distribution in children and define the upper limits of BP according to age. Although available BP data at that time were limited by current standards, it was clear that BP levels in children were related to age, with a progressive increase from early childhood through adolescence. In the absence of long-term outcome data, it was not possible to link a level of childhood BP to risk of later cardiovascular events. Therefore, the task force defined hypertension as the BP level that exceeded the 95th percentile on age-related BP distribution curves. The recommendations of this task force on detection, evaluation, and management of hypertension in children and adolescents were published in 1977.1 In addition to providing a framework on diagnosis of hypertension, the publication included information on proper BP measurement in children, diagnostic evaluation for children with elevated BP, and management of BP in hypertensive children.

That report of that NHBPEP Task Force1 constituted the first clinical practice guideline (CPG) for childhood hypertension. Major updates were published in 1987, 1996, and 2004.2–4 Minor updating of antihypertensive drug dosing for children, but no new recommendations related to evaluation or management of high childhood BP, was incorporated into the 2011 NHLBI integrated guideline on pediatric cardiovascular health.5 Since the 2004 Working Group report, findings of many new studies related to childhood hypertension have been published, including data on epidemiology, hypertension-related risk factors, BP management, and target organ damage (TOD). The childhood obesity epidemic during this time period also lead to increased recognition of obesity-associated hypertension in childhood. Considering the knowledge gained from the body of publications since 2004, it was recognized that the pediatric hypertension guidelines needed to be updated.

Several prominent investigators in the field of pediatric hypertension began developing the case with the NHLBI to support an update of the pediatric hypertension CPG. However, the 2013 announcement by the NHLBI6 that it would no longer sponsor the development of new CPGs prompted this group of pediatric hypertension investigators to approach the AAP to sponsor development of a new pediatric hypertension CPG. The AAP agreed to undertake this project in 2014.

The resultant 2017 AAP CPG7 was developed using a rigorous evidence-based approach as recommended by the Institute of Medicine.8 Four primary patient-intervention-comparison-outcome-treatment questions were generated. These patient-intervention-comparison-outcome-treatment questions were used to carry out a systematic review of the literature on childhood hypertension published between January 2004 and July 2016. References so identified were reviewed, assessed for quality and relevance, and then used to generate 30 Key Action Statements, all of which were graded, based on the strength of the available evidence. Such methodology represents a departure from the approach used in the prior NHBPEP pediatric hypertension guidelines but is consistent with the more recent recommendations of the NHLBI on development of CPGs for cardiovascular disease.4 There are also ≈2 dozen additional clinical recommendations in the new CPG that are based on expert opinion on issues for which insufficient evidence was available to generate Key Action Statements. The following summarizes the major points in this new CPG that have changed substantially since publication of the 2004 Fourth Report.4 The full AAP CPG7 contains new BP tables, figures, and supporting information designed to assist clinicians in diagnosing, evaluating, and managing elevated BP and hypertension in children and adolescents.

Normative BP Data and BP Tables

The NHBPEP childhood BP database used to generate the BP levels and percentiles in the 2004 Fourth Report7 included overweight and obese children from the 1999 to 2000 National Health and Nutrition Examination Survey. A reanalysis of the

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NHBPEP database in 2008 demonstrated that exclusion of overweight and obese children resulted in BP values that were on average 2 to 3 mm Hg lower than those in the 2004 Fourth Report. Considering these findings and the known effects of obesity on BP, the AAP commissioned development of a new set of normative BP values for the new CPG that are based only on data from normal weight children in the NHBPEP database. The new tables provide systolic and diastolic BP values at the 50th, 90th, and 95th percentiles, and the 95th percentile+12 mm Hg (to denote stage 2 hypertension) according to sex, age, and height. The BP tables in the 2004 Fourth Report also provided sex, age, and height percentile-adjusted systolic and diastolic BP values at the 50th, 90th, 95th, and 99th percentiles. Although precise, the tables are complex and difficult to use in clinical practice. The detailed tables may have contributed to under-recognition of childhood hypertension. It was also recognized that automated BP devices are commonly used to measure BP in clinic settings while the pediatric BP tables are based on measurements obtained by auscultation. To facilitate detection of elevated BP in pediatric clinical practice, the 2017 AAP CPG includes a simplified table to be used for screening purposes. The table lists systolic and diastolic BP values at the 90th percentile, a BP level that should prompt further measurement, and if confirmed as elevated, the BP reading should be confirmed by auscultation.

**Definition of Hypertension in Children and Adolescents**

An important update in the 2017 AAP CPG is a change in the definition of hypertension in children and adolescents. Because there are still no data that link a BP level in childhood with heightened risk for subsequent adverse cardiovascular outcome, the AAP CPG uses the same statistical method to define hypertension in children that was used in the prior NHBPEP supported guidelines. In children <13 years of age, hypertension is defined as systolic or diastolic BP ≥95th percentile on the new sex, age, and height tables. Also in children, the BP level designating stage 2 hypertension has also been changed to BP ≥95th percentile+12 mm Hg. For adolescents ≥13 years of age, there is a significant change in definition of hypertension. An examination of the new pediatric BP tables indicates that the 90th percentile for adolescents ≥13 years of age is close to a systolic BP of 120 mm Hg and diastolic BP is <80 mm Hg. Also, the 95th percentile in adolescents ≥13 years of age approximates 130 mm Hg. Therefore, the 2017 AAP CPG has used the new adult BP cut-points to define hypertension in adolescents ≥13 years of age. These changes in the definition of hypertension in adolescents were made to align with terminology and BP cut-points in a new CPG for adult hypertension to be issued by the American College of Cardiology and American Heart Association. This change also serves to simplify detection and management of hypertensive adolescents. Also, to be consistent with the new CPG adult hypertension guideline, the term pre-hypertension was replaced with the term elevated BP to designate BP levels considered to be at heightened risk for developing hypertension. The revised BP definitions and staging/classifications in children and adolescents are summarized as follows:

1. Normal BP: BP <90th percentile for age, sex, and height; or <120/<80 mm Hg for adolescents ≥13 years old; Elevated BP: BP reading ≥90th percentile and <95th percentile for age, sex, and height; or 120 to 129/<80 mm Hg for adolescents ≥13 years old;
2. Hypertension: BP ≥95th percentile for age, sex, and height; or ≥130/80 mm Hg for adolescents ≥13 years old. Hypertensive-level BP is further staged as follows:
3. Stage 1 hypertension: BP ≥95th percentile for age, sex, and height to <95th percentile+12 mm Hg; or 130 to 139/80 to 89 mm Hg for adolescents ≥13 years of age; and Stage 2 hypertension: BP ≥95th percentile+12 mm Hg for age, sex, and height; or >140/90 mm Hg for adolescents ≥13 years of age.

**Routine BP Screening, Diagnosis, and Ambulatory BP Monitoring**

Although the prior NHBPEP guidelines recommended routine measurement of BP in children and adolescents for screening purposes at every healthcare encounter, the 2017 AAP CPG recommends that routine BP screening be performed only at annual preventive care visits unless the patient has a predisposing condition associated with hypertension, such as obesity, diabetes mellitus, heart disease, or kidney disease. Such a recommendation acknowledges the controversy on routine screening of BP in childhood to some extent but still supports regular screening as a potential way to uncover cases of secondary hypertension. Diagnosis of hypertension is still based on demonstration of elevated or hypertensive-level BP at 3 separate encounters unless the patient is symptomatic. For diagnosis of hypertension, BP measurement by auscultation remains the preferred measurement method. The CPG also includes detailed recommendations for the correct technique of office BP measurement, along with a link to an AAP-produced video illustrating the procedure.

Ambulatory BP monitoring (ABPM) is recommended in several places within the 2017 AAP CPG, including the following:

1. Confirmation of the diagnosis of hypertension in children and adolescents with repeatedly elevated office BP readings; Confirmation of suspected white-coat hypertension;
2. Evaluation for masked hypertension in children and adolescents with a history of repaired coarctation of the aorta;
3. Evaluation of BP pattern and risk for hypertensive TOD in children and adolescents with high-risk conditions, such as chronic kidney disease (CKD);
4. Evaluation for possible hypertension in children and adolescents with obstructive sleep apnea syndrome;
5. Evaluation of BP in pediatric heart and kidney transplant recipients;
6. Assessment of treatment effectiveness in children and adolescents receiving antihypertensive medications; and
7. Monitoring of treatment efficacy and possible masked hypertension in children and adolescents with CKD.

A standardized approach to the performance of ABPM is recommended that is essentially the same approach that is outlined in the 2014 American Heart Association Scientific Statement on pediatric ABPM. Finally, routine performance...
of ABPM to confirm hypertension is also recommended from a cost-effectiveness standpoint, given the high prevalence of white-coat hypertension in children. That endorsement is predicated on the assumption that patients found to have white-coat hypertension would not undergo further diagnostic workup, such as extensive laboratory testing and imaging.

The focus on ABPM is consistent with other recent consensus recommendations for its use in adults, including the NICE (National Institute for Health and Care Excellence) guideline,14 and the most recent recommendations from the United States Preventative Services Task Force.15 However, although both of these adult guidelines state that home BP monitoring could be used as an alternative to ABPM if ABPM were unavailable, the AAP subcommittee found insufficient evidence to support the use of home BP monitoring for the diagnosis of hypertension in children and adolescents. The recommendation not to use home BP monitoring for diagnosis may lead to problems with full implementation of the ABPM recommendations in the 2017 AAP CPG as many primary care providers may not have ready access to pediatric ABPM. Until ABPM becomes more widely available, reliance on office BP measurements and subspecialty referral may need to be substituted when ABPM is not immediately available.

**Hypertensive TOD: Left Ventricular Hypertrophy**

Based on several cross-sectional studies, it has been recognized that evidence of TOD can be detected in hypertensive children and adolescents. Left ventricular hypertrophy (LVH) has been the most commonly studied form of TOD in children and adolescents because it is readily assessed by echocardiography. The 2004 Fourth Report recommended routine performance of echocardiography to assess for possible LVH as part of the hypertension evaluation and adopted an indexed left ventricular (LV) mass of 51.7 g/m^2.7^ as the cut-point for diagnosing LVH. Since publication of the Fourth Report in 2004, several new approaches to diagnosing and defining LVH in children and adolescents have been published, leading to uncertainty on the correct definition of pediatric LVH.16

Given that uncertainty, the AAP subcommittee convened a special panel of pediatric cardiologists to perform a detailed examination of the literature on pediatric LVH, with an emphasis on establishing a consensus indexed LV mass cut-point for diagnosis of LVH, as well as examination of when echocardiography should be performed. The resulting recommendations have important differences from the recommendations that appeared in the 2004 Fourth Report:

1. **Definition of LVH:** Similar to the 2004 Fourth Report, the panel recommended that a LV mass >51 g/m^2.7^ should be used to define LVH for children and adolescents greater than age 8 years of age but that LVH could also be defined as LV mass >115 g/body surface area for boys and LV mass >95 g/body surface area for girls. The panel recognized that additional study is needed to better understand the clinical significance of LV mass between the 95th percentile based on published normative data17 and the 51 g/m^2.7 LMH cut-point. Other forms of cardiac TOD: Both concentric LVH and decreased LV ejection fraction are defined and discussed in the new CPG; these cardiac parameters were not explicitly defined in the 2004 Fourth Report.

2. **Timing of echocardiography:**

3. Whereas the 2004 Fourth Report recommended that echocardiograms be obtained in all hypertensive children and adolescents at the time of diagnosis of hypertension, it is now recommended that echocardiograms be obtained to assess for cardiac TOD at the time initiation of pharmacological treatment is considered. Additional time points for consideration of echocardiography include monitoring of known TOD and when concentric LVH or reduced LV ejection fraction is present on the initial echocardiogram.

4. Finally, the CPG suggests that repeat echocardiography could be considered when patients do not have TOD at time of initial echocardiographic assessment, in patients with stage 2 hypertension, secondary hypertension, or incompletely treated stage 1 hypertension. In these patients, the purpose of repeat echocardiography would be to assess for development or worsening of TOD.

The 2017 AAP CPG also addresses testing for other forms of hypertensive TOD that are used in adult cardiovascular medicine, including assessment of carotid intimal–medial thickness and assessment of pulse wave velocity and microalbuminuria. Although it is recognized that such studies are informative from a research standpoint in hypertensive children and adolescents, their routine clinical use is not endorsed at this time.

**Antihypertensive Drug Therapy and Treatment Goals**

For adult patients with hypertension, there is substantial evidence that supports benefit of pharmacological treatment for primary prevention of future cardiovascular events. Because of lack of similar evidence in children and adolescents, indications for antihypertensive medications in children and adolescents have been more opinion based. Although there is now efficacy and safety information on many antihypertensive medications, less information is available on long-term safety of these drugs in children. Recommendations for drug treatment in the 2004 Fourth Report were, therefore, mostly limited to patients with secondary forms of hypertension, those with hypertensive TOD, and those with confirmed stage 2 hypertension, with 1 additional recommendation that drug treatment be considered for patients with persistent hypertension despite lifestyle changes.4

A similarly limited set of indications for antihypertensive medications is found in the 2017 AAP CPG. These indications are:

1. Persistent hypertension despite lifestyle modification, especially with an abnormal echocardiogram; Symptomatic hypertension;
2. Stage 2 hypertension without a modifiable risk factor; or
3. Any stage of hypertension in patients with diabetes mellitus or CKD.

The major difference in 2017 compared with 2004 is that nearly all of the newer antihypertensive medications have been studied in children as a result of legislative initiatives in the United States and Europe, resulting in a wider variety of agents with pediatric efficacy and safety data that are available for treatment when drug therapy is indicated. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers,
long-acting calcium channel blockers, or thiazide diuretics are the recommended initial agents for pediatric patients with primary hypertension, and a strong recommendation is made for use of an angiotensin-converting enzyme inhibitors or angiotensin receptor blockers as the initial agent in hypertensive patients with CKD, diabetes mellitus, or proteinuria. As in the 2004 Fourth Report, an updated list of recommended drug doses is provided.

BP treatment targets in the 2017 AAP CPG are straightforward: goal BP is <90th percentile for age, or <130/80 mm Hg, whichever is lower (based on office/casual BP readings). These targets are based on new data published since the 2004 Fourth Report that have shown that hypertensive TOD can appear at BP levels between the 90th and 95th percentiles and that BP reduction below the 90th percentile can reverse LVH. Recommendations for hypertensive children and adolescents with CKD, however, are different: BP should be monitored by ABPM, and the recommended goal BP is a 24-hour mean arterial pressure <50th percentile. This recommendation is based on compelling data from the ESCAPE trial (Effect of Strict Blood Pressure Control and ACE Inhibition on the Progression of CRF in Pediatric Patients) that demonstrated a slower rate of progression of CKD in patients treated to 24-hour mean arterial pressure <50th percentile compared with those treated to a 24-hour mean arterial pressure of <90th percentile.18

Conclusions
The 2017 AAP CPG is a comprehensive document that addresses numerous aspects of the evaluation and management of high BP in children and adolescents. It is the first pediatric hypertension guideline to be developed from a strict evidence-based approach as recommended by the NHLBI and the first to be aligned as much as possible with a new hypertension guideline for adults. Although many of its recommendations are similar to those found in the 2004 Fourth Report, the many studies on childhood BP and hypertension published since 2004 provided informative data that have led to notable modifications of the 2004 recommendations, as well as generation of entirely new recommendations. It is expected that as additional studies are conducted in the forthcoming years, further updates will reflect new evidence and will provide additional guidance to clinicians who identify and evaluate children and adolescents with high BP.

Disclosures
None.

References
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