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Pediatric hypertension: Often missed and mismanaged

Delayed recognition of hypertension in children can have lasting consequences. The resources detailed here—including Web-based calculators and at-a-glance tables—can facilitate diagnosis and treatment.

Robert Gauer, MD; Megan Belprez, MD; Caitlyn Rerucha, MD
Womack Army Medical Center, Family Medicine Residency Program, Fort Bragg, NC

robert.l.gauer2.civ@mail.mil

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PRACTICE RECOMMENDATIONS

› *Screen for hypertension in all children over the age of 3 at every visit.* C

› *Order laboratory evaluation, echocardiography, and renovascular imaging for all children given a diagnosis of hypertension.* C

› *Advise parents that children with prehypertension and stage 1 hypertension without target-organ damage are eligible to participate in competitive athletics, but those with stage 2 hypertension, target-organ damage, or symptomatic hypertension should not engage in high-static sports (eg, gymnastics, weightlifting, wrestling) until BP is well controlled.* C

Strength of recommendation (SOR)

A Good-quality patient-oriented evidence

B Inconsistent or limited-quality patient-oriented evidence

C Consensus, usual practice, opinion, disease-oriented evidence, case series

Childhood hypertension is on the rise: Recent data from the National Health and Nutrition Survey suggest 10% of children and adolescents have prehypertension and 4% have hypertension.[1-4] Unfortunately, the condition often is missed. In a study of 14,187 children and adolescents who had at least 3 well-child visits at an outpatient academic medical center, 507 patients met the criteria for hypertension, yet only 131 (26%) had this diagnosis documented in their electronic health record.[5]

In a survey of 89 pediatricians, >50% of respondents said they were not familiar with the most current published recommendations for diagnosing and treating pediatric hypertension.[6] Respondents also indicated that the most common reason for not initiating pharmacotherapy for children with hypertension was a lack of familiarity with appropriate antihypertensive agents (54%), followed by concern for adverse medication effects. Delayed diagnosis, evaluation, and treatment of hypertension in young patients can increase the likelihood of serious consequences, including target-organ damage such as left ventricular hypertrophy (LVH). In this review, we'll describe the factors that put children and adolescents at risk for hypertension, and offer an evidence-based approach to diagnosis and treatment.

Obesity is a key risk factor

An estimated 17% of children aged 2 to 19 are obese.[7] Obesity increases a child's risk for hypertension by approximately 3- to 5-fold, and body mass index (BMI) is greater in children with primary hypertension compared with those with secondary hypertension.[8] Hypertension is more common among Hispanic and non-Hispanic black male children and adolescents compared with their white counterparts; these ethnic dispari-

ties are not found in females.[9,10] Poor diets and physical inactivity further contribute to obesity and hypertension risk. Children who were born preterm or had a very low birth weight also are at increased risk.[11]

Unchecked hypertension can lead to cardiac, vascular damage

Some children and adolescents with undiagnosed and untreated hypertension have evidence of target-organ damage, including cardiac dysfunction and pathologic vascular abnormalities. LVH is present in 20% to 41% of children and adolescents with hypertension.[12,13] Carotid intima-media thickness, an established surrogate marker for atherosclerosis, is abnormally increased in children with hypertension, even after adjusting for BMI.[14] Other target organ effects include impaired cognitive function, reduced glomerular filtration rate, microalbuminuria, and retinal arteriolar narrowing.[15-17]

Pediatric hypertension may persist into adulthood. A meta-analysis of more than 50 studies found that elevated blood pressure (BP) in childhood increases the risk for hypertension as an adult.[18]

NHLBI recommendations call for a BP check at every visit

The National Heart, Lung, and Blood Institute (NHLBI) Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents ("the 4th Report") recommends measuring BP in all children over age 3 during every health care visit.[12] Children under age 3 should have their BP checked in certain circumstances, including preterm delivery, congenital heart disease, recurrent urinary tract infections, renal/urologic disease, organ transplantation, malignancy, and systemic illnesses associated with hypertension.[12] The 4th Report is endorsed by the American Academy of Pediatrics (AAP); however, the American Academy of Family Physicians and the US Preventive Services Task Force have concluded that the evidence is insufficient to recommend for or against routine screening for hypertension in children and adolescents to reduce the risk of cardiovascular disease (CVD).[19,20]

Normal BP standards for children and adolescents are based on gender, age, and height percentile.

Does the child have hypertension? That depends on several factors

Determining whether a child has hypertension requires that you consult national BP standards to determine if he or she is within the normal range. Normal BP standards for children and adolescents are based on gender, age, and height percentile, and provide a precise classification based on body size.[12] These tables are available from the NHLBI Web site at http://www.nhlbi.nih.gov/guidelines/hypertension/child_tbl.htm. Height percentiles in these tables correspond with the Centers for Disease Control and Prevention (CDC) growth charts published in 2000.[21] The Baylor College of Medicine Children's Nutrition Research Center has a web-based calculator to help physicians determine BP percentiles in children and adolescents; it is available at http://www.bcm.edu/bodycomplab/Flashapps/BPVAgeChartpage.html. The International Pediatric Hypertension Association also offers BP charts and calculators at http://www.iphapediatrichypertension.org.

The diagnostic parameters for pediatric hypertension are listed in **TABLE 1**.[12] The higher systolic or diastolic BP percentile value is used to determine a child's overall BP category. A child is considered normotensive if the BP is <90th percentile. Hypertension is an average systolic or diastolic BP that is ≥95th percentile on at least 3 separate occasions. Stage 1 hypertension is BP levels ranging from the 95th percentile to 5 mm Hg above the 99th percentile, and stage 2 hypertension is BP levels greater than 5 mm Hg above the 99th percentile.

For example, assume you are evaluating a 12-year-old boy who is 61 inches tall and has a BP of 129/87 mm Hg. According to the CDC growth charts, his height puts him in the 75th percentile for his age. Using the NHLBI chart, you determine that he falls in the 95th-99th percentile for BP, and thus, using the categories in **TABLE 1**, is given a diagnosis of Stage 1 hypertension.

Accurate BP measurement requires using an appropriate cuff size that covers

TABLE 1

Making the diagnosis[12]

Once you've taken your patient's blood pressure (BP) and determined what height percentile he or she is in, you can determine BP percentile based on charts from the National Heart, Lung, and Blood Institute at http://www.nhlbi.nih.gov/guidelines/hypertension/child_tbl.htm. This percentile is then used to determine whether your young patient has hypertension.

Blood pressure parameters	Diagnosis
SBP and DBP <90th percentile	Normal
SBP or DBP 90-95th percentile or >120/80 mm Hg (even if <90th percentile)	Prehypertension
SBP or DBP 95th to 5 mm Hg above 99th percentile	Stage 1 hypertension
SBP or DBP >99th percentile + 5 mm Hg	Stage 2 hypertension

DBP, diastolic blood pressure; SBP, systolic blood pressure.

80% of the child's upper arm. When the child is between cuff sizes, use the larger cuff because small cuffs overestimate BP readings. BP readings should be taken on the right arm with the arm supported at heart level after the child has been sitting quietly for at least 5 minutes.[12] One study showed that the initial BP readings taken in the triage area were significantly higher—often by >10 mm Hg—compared with follow-up measurements in the examination room.[22]

The preferred method of BP measurement is auscultation; however, oscillometric devices also are acceptable. These devices are easier to use, help eliminate digit bias, and minimize observer variation, but they typically read approximately 6 to 9 mm Hg higher than auscultation.[23] For any BP measurement obtained by oscillometry that is >90th percentile, repeat the measurement by auscultation at least twice during the same office visit, and use an average of the repeated measurements.[12] Obtain measurements of a lower extremity when you suspect congenital heart disease (eg, aortic coarctation). For any patient in whom you confirm a BP measurement >95th percentile, repeat the measurement within 2 weeks; for BPs >99th percentile, reevaluation should occur within one week.

Ambulatory BP monitoring (ABPM). Because BP measurements have a circadian pattern (higher during the day and reduced by 10% during sleep[24]) an ABPM device that provides 50 to 60 readings over 24 hours can be useful when evaluating children and adolescents for white-coat hypertension (elevated clinic BP with normal ambulatory BP), masked hypertension (normal clinic BP with elevated ambulatory BP), prehypertension and secondary hypertension (BP generally does not follow circadian patterns).[25] ABPM is more accurate than BP self-measurement, but usually is limited to children older than age 5.

Steps to take for clinical evaluation

Start by conducting a thorough history and physical examination, looking for information that can help you select the most appropriate tests for the next phase of evaluation.[8,12] Calculate the patient's BMI to screen for obesity, ask about a family history of hypertension or CVD, and determine if the patient is taking any medications that might cause hypertension, such as amphetamines, corticosteroids, or cyclosporine.[8] Assess for signs and symptoms that suggest an underlying disease, such as renal disease (hematuria, edema, fatigue) or heart disease (chest pain, exertional dyspnea, palpitations).[12]

All children diagnosed with hypertension should be screened for secondary

When the child is between cuff sizes, use the larger cuff because small cuffs overestimate BP readings.

causes **(TABLE 2)**. The recommended evaluation is to obtain a renal function panel, electrolytes, urinalysis, urine culture, complete blood count, renovascular imaging, and echocardiogram.[12] The most common etiologies for secondary hypertension are renal parenchymal disease (68%), renovascular abnormalities (10%), and endocrinopathies (10%).[26] Other causes, such as aortic coarctation, obstructive sleep apnea, iatrogenic factors (eg, toxins, medications, drugs of abuse), and genitourinary abnormalities, account for only a small percentage of cases and should be investigated as clinically indicated.[26]

Renovascular assessment depends on facility expertise. Imaging options include renal ultrasound (with or without Doppler), computed tomography angiography, renal flow scan, and magnetic resonance angiography. These studies have similar sensitivities and specificities.[27] For patients in whom you strongly suspect renovascular disease, renal arteriography (digital subtraction angiography) provides the best images, although it is the most invasive study.[27]

Refer children and adolescents who are found to have significant abnormalities during the initial evaluation to the appropriate specialist. BP measurements often improve when secondary causes are treated.

The most common etiology for secondary hypertension in children and adolescents is renal parenchymal disease.

Which drugs for which patients?

Pharmacologic management is indicated for pediatric patients with stage 1 or stage 2 hypertension, secondary hypertension, and those with evidence of target-organ damage.[12] The goal of therapy is to reduce BP to <95th percentile. In patients with target-organ damage, renal disease, or diabetes mellitus, the goal is <90th percentile.[12,15,28] Intensive management of BP (≤50th percentile) in children with chronic kidney disease has been shown to delay progression to renal failure,[29] but it is uncertain if lower BP goals can slow or prevent additional subclinical target-organ damage.

Pharmacotherapy for hypertensive children or adolescents can be challenging because recommendations of which medication to use are based upon expert opinion and extrapolation from randomized trials of adults. The length of therapy (often lifelong), potential adverse effects, and unproven direct mortality benefit complicate this decision. Medication choice usually is based on physician preference or experience.[12] The most common antihypertensive drugs prescribed are angiotensin-converting enzyme (ACE) inhibitors (26%), followed by diuretics (20%), and beta-blockers (17%).[30,31] The starting doses and other details of medications commonly used to treat pediatric hypertension are listed in **TABLE 3**.[28,32-34]

One approach to choosing an antihypertensive drug for children is to measure the patient's ambulatory plasma renin activity (PRA) level before initiating therapy. Those with high PRA levels (>0.65 ng/mL/h), presumably due to peripheral vasoconstriction, may benefit more from ACE inhibitors, angiotensin receptor blockers (ARBs), or beta-adrenergic antagonists.[35] Individuals with low PRA levels (<0.65 ng/mL/h) maintain higher volume/sodium excess and may benefit more from diuretics or calcium channel blockers.[35]

Ethnicity also may guide medication selection. African American adults do not respond well to ACE inhibitor monotherapy due to decreased PRA and increased salt hypersensitivity.[36] One meta-analysis found that African American children and adolescents had inadequate BP response to 6 individual ACE inhibitors, even at higher doses compared with white children and those of other ethnicities, who showed significant improvement in BP.[37] ARBs may be a more effective alternative for this population.

Most experts recommend initiating a single agent at a low dose.[12] A systematic review found that except for African American children, pediatric patients experienced comparable reductions in BP with ACE inhibitors (10.7/8.1 mm Hg), ARBs (10.5/6.9 mm Hg), and calcium channel blockers (9.3/7.2 mm Hg).[38] In addition, ACE inhibitors and ARBs significantly reduced proteinuria by 49% and 59%, respectively.[38]

Schedule follow-up visits for 2 to 4 weeks (or sooner for patients with stage 2 hypertension) after initiating pharmacotherapy. If BP response is suboptimal, consider increasing the dose before adding a

TABLE 2

Suspect secondary causes of pediatric hypertension? Here's how to proceed

Etiology	Recommended evaluation
Chronic kidney disease	Renal ultrasound, DMSA static scanning, urinalysis for proteinuria and urinary casts
Renovascular hypertension	Plasma renin activity, renal ultrasound, Doppler ultrasound, renal scintigraphy, MRI angiography, angiography
Pheochromocytoma	24-hour urine and plasma catecholamines or metanephrines, MRI, I123 metaiodobenzylguanidine
Primary aldosteronism	Plasma renin activity, plasma aldosterone
Cushing's syndrome	Plasma cortisol, ACTH, 24-hour urinary free cortisol
Aortic coarctation	CXR, echocardiography, MRI angiography, aortography
Genetic	DNA testing
Drug-induced	Ask about consumption or use of oral contraceptives, glucocorticoids, NSAIDs, sympathomimetics, erythropoietin, cyclosporine, tacrolimus, cocaine, amphetamines, metabolic steroids, licorice
Hyperthyroidism	TSH, FT3, FT4
Congenital adrenal hyperplasia	Plasma deoxycorticosterone and corticosterone, 18-hydroxycorticosterone, 18-hydroxydeoxycorticosterone, 11-deoxycortisol
Obstructive sleep apnea	Polysomnography

ACTH, adrenocorticotropin hormone; CXR, chest x-ray; DMSA, dimercaptosuccinic acid; DNA, deoxyribonucleic acid; FT3, free thyroxine 3; FT4, free thyroxine 4; MRI, magnetic resonance imaging; NSAID, nonsteroidal anti-inflammatory drug; TSH, thyroid-stimulating hormone.

Adapted from: Lurbe E, Cifkova R, Cruickshank JK, et al; European Society of Hypertension. Management of high blood pressure in children and adolescents: recommendation of the European Society of Hypertension. *J Hypertens*. 2009;27:1719-1742.

In patients with target-organ damage, renal disease, or diabetes, the goal of therapy is to reduce BP to <90th percentile.

second agent. If the patient experiences significant adverse effects or has an inadequate BP response, changing to a drug from a different class is recommended.[39] Patients who do not adequately respond to these approaches may require combination therapy; in such cases, strongly consider consultation with pediatric nephrologist or cardiologist.[39] Medication compliance should be verified (eg, by pill counting, parental supervision) in patients who do not respond to therapy. Once BP control has been achieved, visits every 3 to 4 months are appropriate, with periodic laboratory monitoring, especially for children taking diuretics, ACE inhibitors, or ARBs or who have underlying renal disease.

Recommend exercise, but carefully monitor athletes' BP

Encourage obese and overweight children and adolescents to lose weight to maintain a BMI <95th percentile. Current guidelines based on expert opinion recommend that children and adolescents should engage in 60 minutes of daily physical activity.[12] A meta-analysis found physical activity led to a 1% and 3% reduction in systolic and diastolic BP, respectively, although these results were not statistically significant.[40]

Be aware, however, that children and adolescents with hypertension who engage in certain competitive sports can significantly increase their BP and may be at risk for complications.[41] According to the AAP guidelines, patients with stage 2 hypertension should not engage in high-static sports (eg, gymnastics, weightlifting, wrestling, boxing, cycling, decathlon, triathlon) until BP is well controlled.[41] Patients with target-organ damage, uncontrolled hypertension, or symptomatic hypertension should not participate until BP is well controlled. Patients with prehypertension and stage 1 hypertension without tar-

TABLE 3

Pharmacologic options for pediatric hypertension[28,32-34]

Class	Drug	Starting dose (interval)	Comments
ACE inhibitors	Benazepril*†	0.2 mg/kg/d up to 10 mg (qd)	Use in high plasma renin activity, renovascular disease, renal parenchymal disease, proteinuria, CHF, diabetes mellitus, hyperlipidemia, and reactive airway disease. Contraindicated in pregnancy, hyperkalemia, and bilateral renal artery stenosis
	Captopril*	Infant: 0.02-0.5 mg/kg/d (bid-tid) Child: 0.15-1.5 mg/kg/d (bid-tid) Adolescent: 25-100 mg/d up to 450 mg/d	
	Enalapril*†	0.08 mg/kg/d up to 5 mg (qd-bid)	
	Fosinopril†	0.1 mg/kg/d up to 10 mg (qd)	
	Lisinopril*†‡	0.07 mg/kg/d up to 5 mg (qd)	
	Quinapril	5-10 mg/d (qd)	
	Ramipril	2.5 mg/d (qd)	
ARBs	Candesartan†	Ages 1-6 y: 0.2 mg/kg/d (qd) Age >6 y: 4-8 mg/d (qd) Weight >50 kg: 8-16 mg/d (qd)	Same comments as for ACE inhibitors. Concomitant therapy may further reduce proteinuria. Used less commonly than ACE inhibitors
	Irbesartan†	75-150 mg/d (qd)	
	Losartan*†‡	0.7 mg/kg/d up to 50 mg (qd)	
	Olmesartan†	10 mg (<35 kg) (qd) 20 mg (≥35 kg) (qd)	
	Valsartan*†	1.3 mg/kg up to 40 mg/d (qd)	
α – β adrenergic antagonists	Labetalol*	1-3 mg/kg/d up to 1200 mg/d (bid)	Used in the management of CHF
	Carvedilol	0.2 mg/kg/d up to 12.5 mg (bid)	
β adrenergic antagonists	Atenolol*	0.5-1 mg/kg/d (qd-bid)	Use in high plasma renin activity, hyperthyroidism, migraine headache, and neuroadrenergic tumors. Drug of choice in coarctation of the aorta. Avoid in athletes and patients with diabetes
	Bisoprolol/ hydrochlorothiazide	0.04 mg/kg/d up to 2.5/6.25 mg/d (qd)	
	Metoprolol†‡	1-2 mg/kg/d up to 200 mg/d (bid)	
	Propranolol*†	1 mg/kg/d (bid-tid)	

See footnotes on facing page.

ARBs may be a more effective option than ACE inhibitors for African American children and adolescents.

get-organ damage are eligible to participate in competitive athletics. Reassess BP every 6 months in patients who are prehypertensive and every one to 2 weeks for those with stage 1 hypertension. When the patient's BP remains <90th percentile, routine surveillance every 3 to 6 months is recommended.

What about sodium? Encourage parents of pediatric patients with hypertension to limit their child's salt intake to 1.2 g/d for those age 4 to 8 and 1.5 g/d for older children.[42] A meta-analysis found salt reduction decreased systolic BP by 1.2 mm Hg and diastolic BP by 1.3 mm Hg.[43] Though these benefits are small, reducing sodium intake can be one of several lifestyle modifications, such as increased activity and quitting smoking, that can reduce young patients' risk of hypertension and related cardiovascular sequelae. JFP

CORRESPONDENCE
Robert Gauer, MD, Womack Army Medical Center, 2817 Reilly Road, Fort Bragg NC 28310; robert.l.gauer2.civ@mail.mil

TABLE 3

Pharmacologic options for pediatric hypertension[28,32-34] (cont'd)

Class	Drug	Starting dose (interval)	Comments
CCBs	Amlodipine*†‡	0.06 mg/kg/d up to 5 mg (qd)	Consider use in hyperlipidemia, asthma, renal disease, diabetes mellitus, and post-transplantation. Adverse effects are flushing, nausea/vomiting, headache, and edema. Diltiazem reduces proteinuria
	Felodipine	2.5 mg/d up to 10 mg/d (qd)	
	Isradipine*	0.15-0.45 mg/kg/d up to 20 mg/d (tid-qid)	
	Nifedipine XR	0.2-0.50 mg/kg/d (qd-bid)	
	Diltiazem	1.5-2 mg/kg/d (tid)	
Central α agonists	Clonidine*†	5-10 mcg/kg/d (bid-tid)	Avoid abrupt cessation
	Methyldopa*†	5 mg/kg/d (bid-qid)	
Diuretics	Amiloride	5-10 mg/d (qd)	Use in volume dependent-low plasma renin activity and CHF. African American patients respond better to diuretics than they do to other medications. Avoid in athletes
	Chlorothiazide†	10 mg/kg/d (bid)	
	Chlorthalidone	0.3 mg/kg/d up to 50 mg/d (qd)	
	Furosemide*	0.5-2.0 mg/kg/d up to 100 mg/d (qd-bid)	
	Hydrochlorothiazide*†‡	1-3 mg/kg/d (qd)	
	Spironolactone*	1 mg/kg/d (qd-bid)	
	Triamterene	1-2 mg/kg/d (bid)	
Peripheral α antagonists	Doxazosin	1 mg/d up to 4 mg/d (qd)	Higher risk of hypotension and syncope
	Prazosin	0.05-0.1 mg/kg/d up to 20 mg/d (tid)	
	Terazosin	1 mg/d (qd)	
Vasodilators	Hydralazine†	0.75-1 mg/kg/d up to 200 mg/d (bid-qid)	Hydralazine causes systemic lupus erythematosus-like syndrome. Use minoxidil in resistant hypertension, may cause hypertrichosis, contraindicated in CHF
	Minoxidil†	0.1-0.2 mg/kg/d (qd-bid)	

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; bid, twice a day; CCB, calcium channel blocker; CHF, congestive heart failure; qd, once a day; qid, four times a day; tid, three times a day.

* Oral suspension is available for these agents.

† Medication is FDA-approved for treating hypertension in children (check full prescribing information for age/weight restrictions).

‡ Recommended by expert opinion based on available data.

Patients with prehypertension and stage 1 hypertension without target-organ damage generally can participate in competitive sports.

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Though the benefits of reducing sodium intake are small, doing so can be one of several lifestyle modifications to reduce BP in young patients.

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