Hypertension in Children and Adolescents: Diagnosis, Evaluation, and Treatment.

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Introduction

Considerable advances have been made in detection, evaluation, and management of high blood pressure (BP), or hypertension, in children and adolescents. Because of the development of a database on normative BP levels throughout childhood, the ability to identify children who have abnormally elevated BP has improved. On the basis of developing evidence, it is now apparent that primary hypertension is detectable in the young and occurs commonly. The long-term health risks for hypertensive children and adolescents can be substantial; therefore, it is important that clinical measures be taken to reduce these risks and optimize health outcomes. The challenge to the individual practitioner still remains to be the measurement of blood pressure in a child who may not be cooperative in addition to the pressure of larger number of outpatients to be evaluated.

Definition of Hypertension

Hypertension in children and adolescents continues to be defined as systolic BP (SBP) and/or diastolic BP (DBP), that is, on repeated measurement, $\geq$95th percentile. BP between the 90th and 95th percentile in childhood had been designated “high normal.” To be consistent with the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), this level of BP will now be termed prehypertensive” and is an indication for lifestyle modifications.(1)

• Hypertension is defined as average SBP and/or diastolic BP (DBP) that is $\geq$95th percentile for gender, age, and height on 3 occasions.

• Prehypertension in children is defined as average SBP or DBP levels that are $\geq$90th percentile but $\leq$95th percentile.

• As with adults, adolescents with BP levels >120/80 mm Hg should be considered prehypertensive.

• A patient with BP levels >95th percentile in a physician's office or clinic, who is normotensive outside a clinical setting, has "white-coat hypertension." Ambulatory BP monitoring (ABPM) is usually required to make this diagnosis. Normal BP is defined as SBP and DBP that are >90th percentile for gender, age, and height.

Average SBP or DBP levels that are >90th percentile but <95th percentile had been designated as "high normal" and were considered to be an indication of heightened risk for developing hypertension. The term white-coat hypertension defines a clinical condition in which the patient has BP levels that are >95th percentile when measured in a physician's office or clinic, whereas the patient's average BP is <90th percentile outside of a clinical setting.

When to measure BP in children

Children >3 years old who are seen in medical care settings should have their BP measured at least once during every health care episode. Children <3 years old should have their BP measured in special circumstances (see Table 1). The BP tables are based on auscultatory measurements; therefore, the preferred method of measurement is auscultation.

How to measure BP in Children

Auscultation remains the recommended method of BP measurement in children under most circumstances. Oscillometric devices measure mean arterial BP and then calculate systolic and diastolic values.

The BP tables are based on auscultatory measurements; therefore, the preferred method of measurement is auscultation. As discussed below, oscillometric devices are convenient and minimize observer error, but they do not provide measures that are identical to auscultation.

Population data in children and risk-associated epidemiologic data in adults have established the fifth Korotkoff sound (K5), or the disappearance of Korotkoff sounds, as the definition of DBP.

Oscillometric devices measure mean arterial BP and then calculate systolic and diastolic values. The algorithms used by companies are proprietary and differ from company to company and device to device. These devices can yield results that vary widely when one is compared with another, and they do not always closely match BP values obtained by auscultation.

What are the normal values (Table 2)

BP standards based on gender, age, and height provide a precise classification of BP according to body size. The revised BP tables now include the 50th, 90th, 95th, and 99th percentiles (with standard deviations) by gender, age, and height. In children and adolescents, the normal range of BP is determined by body size and age. BP standards that are based on gender, age, and height provide a more precise classification of BP according to body size. This approach avoids misclassifying children who are very tall or very short.

Follow Up of Hypertension when first detected

This is well defined in table 3. If the BP is normal i.e. < 90th centile then it has to be reevaluated again which could be at next visit or within a year again. If the patient is prehypertensive then the BP can be rechecked again within 6 months. On the other hand if the patient has stage 1 hypertension, it can be rechecked within a week; if the patient has stage 2 hypertension or symptomatic stage 1 hypertension it would need immediate further evaluation.

History and Physical Findings Suggestive of Definable Hypertension

There has been a definite correlation between the degree of sleep a child has and the incidence of hypertension. It is therefore imperative that history of adequate sleep be recorded in all patients with suspected, recorded hypertension or with prehypertension. In addition risk factors like smoking (in adolescents), diet and exercise apart from a detailed family history of hypertension, coronary artery disease in the adults <45years be recorded. The evaluation should also include the history taking and evaluation of co-morbidities like obesity, hypercholesterolemia and diabetes. History towards past renal disease as an etiology of the child' problems should also be taken.

Physical exam could also reveal the etiology though primary hypertension would be the most common cause. Vital signs evaluation could reveal persistent tachycardia which would then indicate hyperthyroidism, pheochromocytoma, neuroblastoma or primary hypertension. Similarly decreased lower limb pulses would indicate the presence of coarctation of aorta or Takayasu's disease. Retinal changes of hypertension would indicate severe hypertension, which would more likely be associated with secondary hypertension. On ear, nose, and throat exam if severe adenotonsillar hypertrophy is noted one should suspect hypertension related to sleep-disordered breathing. Plotting

height and weight would indicate chronic renal failure while in obese patients with high body mass index one would suspect primary hypertension. On the other hand truncal obesity would indicate cushing syndrome or insulin resistance syndrome. Williams syndrome could cause hypertension and would be associated with Elfin facies. Presence of webbed neck in a child with hypertension would indicate Turner's syndrome (associated with hypertension). Other similar leading findings in a child suspected to have hypertension would indicate a definite etiology and have been summarised in table 4.

Sleep And Hypertension

Although limited data are available, they suggest an association of sleep-disordered breathing and higher BP in children. (2,3) Approximately 15% of children snore, and at least 1% to 3% have sleep-disordered breathing.(2) Because of the associations with hypertension and the frequency of occurrence of sleep disorders, particularly among overweight children, a history of sleeping patterns should be obtained in a child with hypertension.

Laboratory Screening in the Hypertensive Child

As per the AAP recommendations initial screening in all children with hypertension would include a CBC, urea, creatinine, urine routine and renal ultrasound (to rule out renal scar or a congenital anomaly). In addition, the tests would also include evaluation of the co-morbidities, target organ damage, renovascular imaging and additional tests as indicated (table 5).

Renin Profiling

Plasma renin level or plasma renin activity (PRA) is a useful screening test for mineralocorticoidrelated diseases. With these disorders, the PRA is very low or unmeasurable by the laboratory and may be associated with relative hypokalemia. PRA levels are higher in patients who have renal artery stenosis. However, 15% of children with arteriographically evident renal artery stenosis have normal PRA values. (4-6) Assays for direct measurement of renin, a different technique than PRA, are commonly used, although extensive normative data in children and adolescents are unavailable.

Evaluation for Possible Renovascular Hypertension

Renovascular hypertension is a consequence of an arterial lesion or lesions impeding blood flow to 1 or both kidneys. (7,8) Affected children usually, but not invariably, have markedly elevated BP. (4,8) Evaluation for renovascular disease also should be considered in infants or children with other known predisposing factors such as prior umbilical artery catheter placements or neurofibromatosis. (8,9) A number of newer diagnostic techniques are presently available for evaluation of renovascular disease, but experience in their use in pediatric patients is limited. Consequently, the recommended approaches generally use older techniques such as standard intraarterial angiography, digital-subtraction angiography (DSA), and cintigraphy (with or without angiotensin-converting enzyme [ACE] inhibition).(8) As technologies evolve, children should be referred for imaging studies to centers that have expertise in the radiologic evaluation of childhood hypertension.

Therapeutic Lifestyle Changes

• Weight reduction is the primary therapy for obesity-related hypertension. Prevention of excess or abnormal weight gain will limit future increases in BP.

• Regular physical activity and restriction of sedentary activity will improve efforts at weight management and may prevent an excess increase in BP over time.

• Dietary modification should be strongly encouraged in children and adolescents who have BP levels in the prehypertensive range as well as those with hypertension.

• Family-based intervention improves success. On the basis of large, randomized, controlled trials, the following lifestyle modifications are recommended in adults2: weight reduction in overweight or obese individuals (9); increased intake of fresh vegetables, fruits, and low-fat dairy (the Dietary Approaches to Stop Hypertension Study eating plan)76; dietary sodium reduction (10,11); increased physical activity (12); and moderation of alcohol consumption. (13) Smoking cessation has significant cardiovascular benefits. (14) As information on chronic sleep problems evolves, interventions to improve sleep quality also may have a beneficial effect on BP.(15) Sodium reduction in children and adolescents has been associated with small reductions in BP in the range of 1 to 3 mm Hg. (16) Data from 1 randomized trial suggest that sodium intake in infancy may affect BP in adolescence.(17) Similarly, some evidence indicates that breastfeeding may be associated with lower BP in childhood. (18,19) The current recommendation for adequate daily sodium intake is only 1.2 g/day for 4- to 8-year-olds and 1.5 g/day for older children. (20) Because this amount of sodium is substantially lower than current dietary intakes, lowering dietary sodium from the current usual intake may have future benefit. Reduced sodium intake, with calorie restriction, may account for some of the BP improvement associated with weight loss.

Pharmacologic Therapy of Childhood Hypertension

Indications for antihypertensive drug therapy in children include secondary hypertension and insufficient response to lifestyle modifications. Other indications are summarised in Table 6. Recent clinical trials have expanded the number of drugs that have pediatric dosing information. Dosing recommendations for many of the newer drugs are provided in Table 7. Pharmacologic therapy, when indicated, should be initiated with a single drug. Acceptable drug classes for use in children include ACE inhibitors, angiotensin-receptor blockers blockers, calcium channel blockers, and diuretics. The goal for antihypertensive treatment in children should be reduction of BP to <95th percentile unless concurrent conditions are present, in which case BP should be lowered to <90th percentile. Severe, symptomatic hypertension should be treated with intravenous antihypertensive drugs.

Table 1

Conditions under Which Children < 3 Years Old Should Have BP Measured

1. History of prematurity, very low birth weight, or other neonatal complications
2. Congenital heart disease (repaired or nonrepaired)
3. Recurrent urinary tract infections, hematuria, or proteinuria
4. Known renal disease or urologic malformations
5. Family history of congenital renal disease
6. Solid-organ transplant
7. Malignancy or bone marrow transplant
8. Treatment with drugs known to raise BP (eg. Steroids, beta agonists for asthma)
9. Other systemic illnesses associated with hypertension (neurofibromatosis, tuberous sclerosis, etc)
10. Evidence of elevated intracranial pressure

Table 2

Normal Values for Blood Pressure for age and height of the patient

(Table attached in PDF)

Table 3

Outpatient re-evaluation of Hypertension

	SBP or DBP Percentile*	Frequency of BP Measurement
Normal	<90th	Recheck at next scheduled physical examination
Prehypertension	90th to <95th or if BP exceeds 120/80 even if <90th percentile up to <95th percentile†	Recheck in 6 mo
Stage 1 hypertension	95th–99th percentile plus 5 mm Hg	Recheck in 1–2 wk or sooner if the patient is symptomatic; if persistently elevated on 2 additional occasions, evaluate or refer to source of care within 1 mo
Stage 2 hypertension	>99th percentile plus 5 mm Hg	Evaluate or refer to source of care within 1 wk or immediately if the patient is symptomatic

Table 4

Indicators on Physical Exam of Etiology of Hypertension in a Child

Thyromegaly	Hyperthyroidism
Acne, hirsutism, striae	Cushing syndrome, anabolic steroid abuse
Cafe´-au-lait spots	Neurofibromatosis
Adenoma sebaceum	Tuberous sclerosis
Malar rash	Systemic lupus erythematosus
Acanthrosis nigricans	Type 2 diabetes
Chest widely spaced nipples	Turner syndrome
Heart murmur	Coarctation of the aorta
Friction rub	Systemic lupus erythematosus (pericarditis), collagenvascular, end stage renal disease with uremia
Abdomen Mass	Wilms tumor, neuroblastoma, pheochromocytoma
Epigastric/flank bruit	Renal artery stenosis
Palpable kidneys	Polycystic kidney disease, hydronephrosis, multicysticdysplastic kidney
Genitalia Ambiguous/virilization	Adrenal hyperplasia
Extremities Joint swelling	Systemic lupus erythematosus, collagen vascular ds
Muscle weakness	Hyperaldosteronism, Liddle syndrome

Table 5

Laboratory Evaluation in Child with Hypertension

Study or Procedure	Purpose	Target Population
Evaluation for identifiable causes		
BUN, creatinine, electrolytes, urinalysis, and urine culture	R/O renal disease and chronic pyelonephritis	All children with persistent BP ≥95th percentile
CBC	R/O anemia, consistent with chronic renal disease	All children with persistent BP ≥95th percentile
Renal U/S	R/O renal scar, congenital anomaly, or disparate renal size	All children with persistent BP ≥95th percentile
Evaluation for comorbidity		
Fasting lipid panel, fasting glucose	Identify hyperlipidemia, identify metabolic abnormalities	Overweight patients with BP at 90th–94th percentile; all patients with BP ≥95th percentile; family history of hypertension or CVD; child with chronic renal disease
Polysomnography	Identify sleep disorder in association with hypertension	History of loud, frequent snoring
Evaluation for target-organ damage		
Echocardiogram	Identify LVH and other indications of cardiac involvement	Patients with comorbid risk factors* and BP 90th–94th percentile; all patients with BP ≥ 95th percentile
Retinal exam	Identify retinal vascular changes	Patients with comorbid risk factors and BP 90th–94th percentile; all patients with BP ≥ 95th percentile
Additional evaluation as indicated		
ABPM	Identify white-coat hypertension, abnormal diurnal BP pattern, BP load	Patients in whom white-coat hypertension is suspected, and when other information on BP pattern is needed
Plasma renin determination	Identify low renin, suggesting mineralocorticoid-related disease	Young children with stage 1 hypertension and any child or adolescent with stage 2 hypertension

Table 6

Indications for Antihypertensive Drug Therapy in Children

Symptomatic hypertension

Secondary hypertension

Hypertensive target-organ damage

Diabetes (types 1 and 2)

Persistent hypertension despite nonpharmacologic measures

TABLE 7
Antihypertensive Drugs for Outpatient Management of Hypertension in Children 1–17 Years Old*

Class	Drug	Dose†	Dosing Interval	FDA Labeling§
ACE inhibitor	Benazepril	Initial: 0.2 mg/kg per d up to 10 mg/d Max: 0.6 mg/kg per d up to 40 mg/d	qd	Yes
	Captopril	Initial: 0.3–0.5 mg/kg/dose Max: 6 mg/kg per d	tid	No
	Enalapril	Initial: 0.08 mg/kg per d up to 5 mg/d Max: 0.6 mg/kg per d up to 40 mg/d	qd-bid	Yes
	Fosinopril	Children >50 kg: Initial: 5–10 mg/d Max: 40 mg/d	qd	Yes
	Lisinopril	Initial: 0.07 mg/kg per d up to 5 mg/d Max: 0.6 mg/kg per d up to 40 mg/d	qd	Yes
Angiotensin-receptor blocker	Irbesartan	6–12 years: 75–150 mg/d ≥13 years: 150–300 mg/d	qd	Yes
	Losartan	Initial: 0.7 mg/kg per d up to 50 mg/d Max: 1.4 mg/kg per d up to 100 mg/d	qd	Yes
α- and ß-Blocker	Labetalol	Initial: 1–3 mg/kg per d Max: 10–12 mg/kg per d up to 1200 mg/d	bid	No
ß-Blocker	Atenolol	Initial: 0.5–1 mg/kg per d Max: 2 mg/kg per d up to 100 mg/d	qd-bid	No
	Bisoprolol/HCTZ	Initial: 2.5/6.25 mg/d Max: 10/6.25 mg/d	qd	No
	Metoprolol	Initial: 1–2 mg/kg per d Max: 6 mg/kg per d up to 200 mg/d	bid	No
	Propranolol	Initial: 1–2 mg/kg per d Max: 4 mg/kg per d up to 640 mg/d	bid-tid	Yes
Calcium channel blocker	Amlodipine	Children 6–17 years: 2.5–5 mg once daily	qd	Yes
	Felodipine	Initial: 2.5 mg/d Max: 10 mg/d	qd	No
	Isradipine	Initial: 0.15–0.2 mg/kg per d Max: 0.8 mg/kg per d up to 20 mg/d	tid-qid	No
	Extended-release	Initial: 0.25–0.5 mg/kg per d	qd-bid	No

	nifedipine	Max: 3 mg/kg per d up to 120 mg/d		
Diuretic	HCTZ	Initial: 1 mg/kg per d Max: 3 mg/kg per d up to 50 mg/d	qd	Yes
	Chlorthalidone	Initial: 0.3 mg/kg per d Max: 2 mg/kg per d up to 50 mg/d	qd	No
	Furosemide	Initial: 0.5–2.0 mg/kg per dose Max: 6 mg/kg per d	qd-bid	No
	Spironolactone	Initial: 1 mg/kg per d Max: 3.3 mg/kg per d up to 100 mg/d	qd-bid	No
	Triamterene	Initial: 1–2 mg/kg per d Max: 3–4 mg/kg per d up to 300 mg/d	bid	No
Vasodilator	Hydralazine	Initial: 0.75 mg/kg per d Max: 7.5 mg/kg per d up to 200 mg/d	qid	Yes
	Minoxidil	Children <12 years: Initial: 0.2 mg/kg per d Max: 50 mg/d Children ≥12 years: Initial: 5 mg/d Max: 100 mg/d	qd-tid	Yes

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