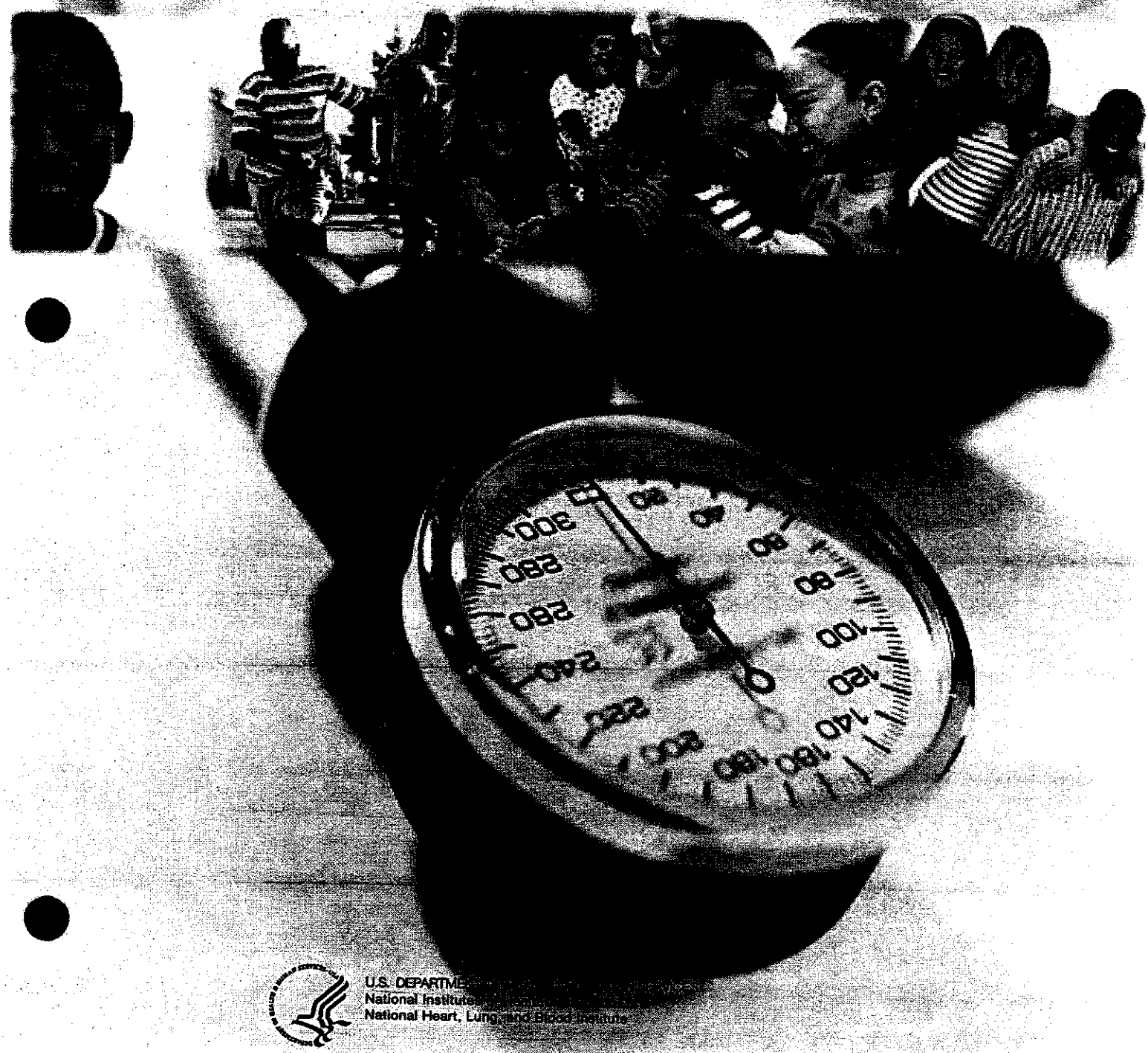
Attachment 6

THE FOURTH REPORT ON THE

Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents



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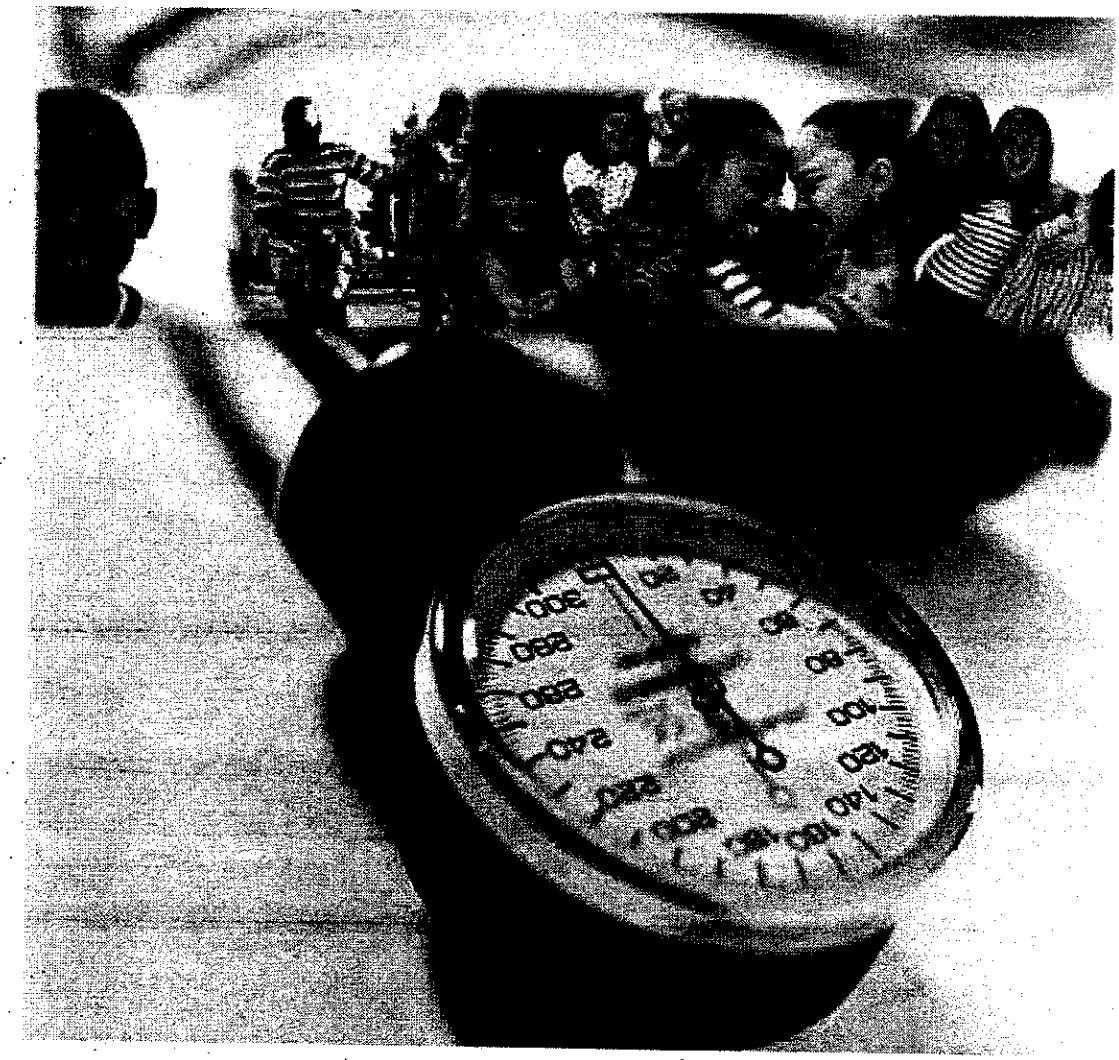

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THE FOURTH REPORT ON THE DIAGNOSIS, EVALUATION, AND TREATMENT OF HIGH BLOOD PRESSURE IN CHILDREN AND ADOLESCENTS

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STAFF

Joanne Karimbakas, M.S., R.D., and Ann Horton, M.S. (American Institutes for Research Health Program, Silver Spring, MD)

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Foreword

This is the fourth report from the National High Blood Pressure Education Program (NHBPEP) Working Group on Children and Adolescents; it updates the previous publication, *Update on the Task Force Report (1987) on High Blood Pressure in Children and Adolescents* (*Pediatrics*. 1996;98:649–58). The purpose of this report is to update clinicians on the latest recommendations concerning the diagnosis, evaluation, and treatment of hypertension in children; recommendations are based on English-language, peer-reviewed, scientific evidence (from 1997 to 2004) and the consensus expert opinion of the NHBPEP Working Group.

This report includes new data from the 1999–2000 National Health and Nutrition Examination Survey (NHANES), as well as revised blood pressure (BP) tables that include the 50th, 90th, 95th, and 99th percentiles by sex, age, and height. Hypertension in children and adolescents continues to be defined as systolic BP (SBP) and/or diastolic BP (DBP) that is, on repeated measurement, at or above the 95th percentile for sex, age, and height. BP between the 90th and 95th percentile in childhood is now termed "prehypertension" and is an indication for lifestyle modifications. New guidelines are provided for the staging of hypertension in children and adolescents, as well as updated recommendations for diagnostic evaluation of hypertensive children. In addition, the report evaluates the evidence of early target-organ damage in children and adolescents with hypertension; provides the rationale for early identification and treatment; and provides revised recommendations, based on recent studies, for the use of antihypertensive drug therapy. Treatment recommendations also include updated evaluation of nonpharmacologic therapies to reduce additional cardiovascular risk factors. The report describes how to identify hypertensive children who need additional evaluation for sleep disorders that may be associated with BP elevation.

Dr. Bonita Falkner has our deep appreciation for leading the members of the NHBPEP Working Group in developing this new report. Dr. Falkner and the Working Group performed diligently and brilliantly to assemble this document in a timely manner. Applying these recommendations to clinical practice will address the important public health issue of improving inadequate BP control.

Barbara Alving, M.D.

Barbara M. Alving, M.D.
Acting Director
National Heart, Lung, and Blood Institute
and
Chair
National High Blood Pressure Education Program
Coordinating Committee

Introduction

Considerable advances have been made in detection, evaluation, and management of high blood pressure, or hypertension, in children and adolescents. Because of the development of a large national database on normative blood pressure (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 purpose of this report is to update clinicians on the latest scientific evidence regarding BP in children and to provide recommendations for diagnosis, evaluation, and treatment of hypertension based on available evidence and consensus expert opinion of the Working Group when evidence was lacking. This publication is the fourth report from the National High Blood Pressure Education Program (NHBPEP) Working Group on Children and Adolescents and updates the previous 1996 publication, *Update on the Task Force Report (1987) on High Blood Pressure in Children and Adolescents.*[1]

This report includes the following information:

- New data, from the 1999–2000 National Health and Nutrition Examination Survey (NHANES), have been added to the childhood BP database, and the BP data have been reexamined. The revised BP tables now include the 50th, 90th, 95th, and 99th percentiles by sex, age, and height.
- Hypertension in children and adolescents continues to be defined as systolic BP (SBP) and/or diastolic BP (DBP) that is, on repeated measurement, at or above the 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.[2]
- The evidence of early target-organ damage in children and adolescents with hypertension is evaluated, and the rationale for early identification and treatment is provided.
- Based on recent studies, revised recommendations for use of antihypertensive drug therapy are provided.
- Treatment recommendations include updated evaluation of nonpharmacologic therapies to reduce additional cardiovascular risk factors.
- Information is included on the identification of hypertensive children who need additional evaluation for sleep disorders.

Methods

In response to the request of the NHBPEP Chair and Director of the National Heart, Lung, and Blood Institute (NHLBI) regarding the need to update the JNC 7 report,[2] some NHBPEP Coordinating Committee members suggested that the NHBPEP Working Group Report on Hypertension in Children and Adolescents should be revisited. Thereafter, the NHLBI Director directed the NHLBI staff to examine issues that might warrant a new report on children. Several prominent clinicians and scholars were asked to develop background manuscripts on selected issues related to hypertension in children and adolescents. Their manuscripts synthesized the available scientific evidence. During the spring and summer of 2002, NHLBI staff and the chair of the 1996 NHBPEP Working Group report on hypertension in children and adolescents reviewed the scientific issues addressed in the background manuscripts as well as contemporary policy issues. Subsequently, the staff noted that a critical mass of new information had been identified, thus warranting the appointment of a panel to update the earlier NHBPEP Working Group Report. The NHLBI Director appointed the authors of the background papers and other national experts to serve on the new panel. The chair and NHLBI staff developed a report outline and timeline to complete the work in 5 months.

The background papers served as focal points for review of the scientific evidence at the first meeting. The members of the Working Group were assembled into teams, and each team prepared specific sections of the report. In developing the focus of each section, the Working Group was asked to consider the peer-reviewed scientific literature published in English since 1997. The scientific evidence was classified by the system used in the JNC 7.[2] The chair assembled the sections submitted by each team into the first draft of the report. The draft report was distributed to the Working Group for review and comment. These comments were assembled and used to create the second draft. A subsequent onsite meeting of the Working Group was conducted to discuss further revisions and the development of the third draft document. Amended sections were reviewed, critiqued, and incorporated into the third draft. After editing by the chair for internal consistency, the fourth draft was created. The Working Group reviewed this draft, and conference calls were conducted to resolve any remaining issues that were identified. When the Working Group approved the final document, it was distributed to the Coordinating Committee for review.

Definition of Hypertension

- *Hypertension is defined as average SBP and/or DBP that is greater than or equal to the 95th percentile for sex, age, and height on three or more occasions.*
- *Prehypertension in children is defined as average SBP or DBP levels that are greater than or equal to the 90th percentile, but less than the 95th percentile.*
- *As with adults, adolescents with BP levels greater than or equal to 120/80 mmHg should be considered prehypertensive.*
- *A patient with BP levels above the 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.*

The definition of hypertension in children and adolescents is based on the normative distribution of BP in healthy children. Normal BP is defined as SBP and DBP that is less than the 90th percentile for sex, age, and height. Hypertension is defined as average SBP or DBP that is greater than or equal to the 95th percentile for sex, age, and height on at least three separate occasions. Average SBP or DBP levels that are greater than or equal to the 90th percentile, but less than the 95th percentile, had been designated as "high normal" and were considered to be an indication of heightened risk for developing hypertension. This designation is consistent with the description of "prehypertension" in adults. The JNC 7 Committee now defines prehypertension as a BP level that is equal to or greater than 120/80 mmHg and recommends the application of preventive health-related behaviors, or therapeutic lifestyle changes, for individuals having SBP levels that exceed 120 mmHg.[2] It is now recommended that, as with adults, children and adolescents with BP levels at 120/80 mmHg or above, but less than the 95th percentile, should be considered prehypertensive.

The term white-coat hypertension defines a clinical condition in which the patient has BP levels that are above the 95th percentile when measured in a physician's office or clinic, whereas the patient's average BP is below the 90th percentile outside of a clinical setting.

Measurement of Blood Pressure in Children

- *Children >3 years old who are seen in a medical setting should have their BP measured.*
- *The preferred method of BP measurement is auscultation.*
- *Correct measurement requires a cuff that is appropriate to the size of the child's upper arm.*
- *Elevated BP must be confirmed on repeated visits before characterizing a child as having hypertension.*
- *Measures obtained by oscillometric devices that exceed the 90th percentile should be repeated by auscultation.*

Children over the age of 3 years who are seen in medical care settings should have their BP measured at least once during every health care episode. Children under age 3 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. As discussed below, oscillometric devices are convenient and minimize observer error, but they do not provide measures that are identical to auscultation. To confirm hypertension, the BP in children should be measured with a standard clinical sphygmomanometer, using a stethoscope placed over the brachial artery pulse, proximal and medial to the cubital fossa, and below the bottom edge of the cuff (i.e., about 2 cm above the cubital fossa). The use of the bell of the stethoscope may allow softer Korotkoff sounds to be heard better.[3,4] The use of an appropriately sized cuff may preclude the placement of the stethoscope in this precise location, but there is little evidence that significant inaccuracy is introduced, either if the head of the stethoscope is slightly out of position or if there is contact between the cuff and the stethoscope. Preparation of the child for standard measurement can affect the BP level just as much as technique.[5] Ideally, the child whose BP is to be measured should have avoided stimulant drugs or foods, have been sitting quietly for 5 minutes, and seated with his or her back supported, feet on the floor and right arm supported, cubital fossa at heart level.[6,7] The right arm is preferred in repeated measures of BP for consistency and comparison to standard tables and because of the possibility of

TABLE 1

Conditions Under Which Children <3 Years Old Should Have Blood Pressure Measured

- History of prematurity, very low birthweight, or other neonatal complication requiring intensive care
- Congenital heart disease (repaired or nonrepaired)
- Recurrent urinary tract infections, hematuria, or proteinuria
- Known renal disease or urologic malformations
- Family history of congenital renal disease
- Solid organ transplant
- Malignancy or bone marrow transplant
- Treatment with drugs known to raise BP
- Other systemic illnesses associated with hypertension (neurofibromatosis, tuberous sclerosis, etc.)
- Evidence of elevated intracranial pressure

TABLE 2

Recommended Dimensions for Blood Pressure Cuff Bladders

[illegible]	[illegible]	[illegible]	[illegible]
Newborn	4	8	10
Infant	6	12	15
Child	9	18	22
Small adult	10	24	26
Adult	13	30	34
Large adult	16	38	44
Thigh	20	42	52

* Calculated so that the largest arm would still allow bladder to encircle arm by at least 80 percent.

coarctation of the aorta, which might lead to false (low) readings in the left arm.[8]

Correct measurement of BP in children requires use of a cuff that is appropriate to the size of the child's upper right arm. The equipment necessary to measure BP in children, ages 3 through adolescence, includes child cuffs of different sizes and must also include a standard adult cuff, a large adult cuff, and a thigh cuff. The latter two cuffs may be needed for use in adolescents.

By convention, an appropriate cuff size is a cuff with an inflatable bladder width that is at least 40 percent of the arm circumference at a point midway between the olecranon and the acromion. (See www.americanheart.org/presenter.jhtml?identifier=576.)[9,10] For such a cuff to be optimal for an arm, the cuff bladder length should cover 80–100 percent of the circumference of the arm.[1,11] Such a requirement demands that the bladder width-to-length ratio be at least 1:2. Not all commercially available cuffs are manufactured with this ratio. Additionally, cuffs labeled for certain age populations (e.g., infant cuffs, child cuffs) are constructed with widely disparate dimensions. Accordingly, the Working Group recommends that standard cuff dimensions for children be adopted. (See table 2.) BP measurements are overestimated to a greater degree with a cuff that is too small than they are underestimated by a cuff that is too large. *If a cuff is too small, the next largest cuff should be used, even if it appears large.* If the appropriate cuffs are used, the cuff size effect is obviated.[12]

SBP is determined by the onset of the "tapping" Korotkoff sounds (K1). Population data in children[1] and risk-associated epidemiological data in adults[13] have established the fifth Korotkoff sound (K5), or the disappearance of Korotkoff sounds, as the definition of DBP. In some children, Korotkoff sounds can be heard to 0 mmHg. Under these circumstances, the BP measurement should be repeated with less pressure on the head of the stethoscope.[4] Only if the very low K5 persists should K4 (muffling of the sounds) be recorded as the DBP.

The standard device for BP measurements has been the mercury manometer.[14] Because of its environmental toxicity, mercury has been increasingly removed from health care settings. Aneroid manometers are quite accurate when calibrated on a semiannual basis[15] and are recommended when mercury-column devices cannot be obtained.

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.[16] 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,[17] and they do not always closely match BP values obtained by auscultation.[18] Oscillometric devices must be validated on a regular basis. Protocols for validation have been developed,[19,20] but the validation process is very difficult.

Two advantages of automatic devices are their ease of use and the minimization of observer bias or digit preference.[16] Use of the automated devices is preferred for BP measurement in newborns and young infants, in whom auscultation is difficult, and in the intensive care setting where frequent BP measurement is needed. An elevated BP reading obtained with an oscillometric device should be repeated using auscultation.

Elevated BP must be confirmed on repeated visits before characterizing a child as having hypertension. Confirming an elevated BP measurement is important, because BP at high levels tends to fall on subsequent measurement as the result of (1) an accommodation effect (i.e., reduction of anxiety by the patient from one visit to the next), and (2) regression to the mean. BP level is not static but varies even under standard resting conditions. Therefore, except in the presence of severe hypertension, a more precise characterization of a person's BP level is an average of multiple BP measurements taken over weeks to months.

AMBULATORY BLOOD PRESSURE MONITORING

Ambulatory BP monitoring (ABPM) refers to a procedure in which a portable BP device, worn by the patient, records BP over a specified period, usually 24 hours. ABPM is very useful in the evaluation of hypertension in children.[21–23] By frequent measurement and recording of BP, ABPM enables computation of the mean BP during the day, night, and over 24 hours as well as various measures to determine the degree to which BP exceeds the upper limit of normal over a given time period (i.e., the BP load). ABPM is especially helpful in the evaluation of white-coat hypertension, as well as the risk for hypertensive organ injury, apparent drug resistance, and hypotensive symptoms with antihypertensive drugs. ABPM is also useful for evaluating patients for whom more information on BP patterns is needed, such as those with episodic hypertension, chronic kidney disease, diabetes, and autonomic dysfunction. Conducting ABPM requires specific equipment and trained staff. Therefore, ABPM in children and adolescents should be used by experts in the field of pediatric hypertension who are experienced in its use and interpretation.

Blood Pressure Tables

- *BP standards based on sex, 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 sex, 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 sex, 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.

The BP tables are revised to include the new height percentile data (www.cdc.gov/growthcharts/)[24] as well as the addition of BP data from the NHANES 1999–2000. Demographic information on the source of the BP data is provided in appendix A. The 50th, 90th, 95th, and 99th percentiles of SBP and DBP (using K5) for height by sex and age are given for boys and girls in tables 3 and 4. Although new data have been added, the sex, age, and height BP levels for the 90th and 95th percentiles have changed minimally from the last report. The 50th percentile has been added to the tables to provide the clinician with the BP level at the midpoint of the normal range. Although the 95th percentile provides a BP level that defines hypertension, management decisions about children with hypertension should be determined by the degree or severity of hypertension. Therefore, the 99th percentile has been added to facilitate clinical decisionmaking in the plan for evaluation. Standards for SBP and DBP for infants younger than 1 year are available.[25] In children younger than 1 year, SBP has been used to define hypertension.

To use the tables in a clinical setting, the height percentile is determined by using the newly revised CDC Growth Charts (www.cdc.gov/growthcharts/). The child's measured SBP and DBP are compared with the numbers provided in the table (boys or girls) according to the child's age and height percentile. The child is normotensive if the BP is below the 90th percentile. If the BP is equal to or above the 90th percentile, the BP measurement should be repeated at that visit to verify an elevated BP. BP measurements between the 90th and 95th percentiles indicate prehypertension and warrant reassessment and consideration of other risk factors. (See table 5.) In addition, if an adolescent's BP is greater than 120/80 mmHg, the patient should be considered to be prehypertensive even if this value is less than the 90th percentile. This BP level typically occurs for SBP at age 12 years and for DBP at age 16 years.

If the child's BP (systolic or diastolic) is at or above the 95th percentile, the child may be hypertensive, and the measurement must be repeated on at least two additional occasions to confirm the diagnosis. Staging of BP, according to the extent to which a child's BP exceeds the 95th percentile, is helpful in developing a management plan for evaluation and treatment that is most appropriate for an individual patient. On repeated measurement, hypertensive children may have BP levels that are only a few mmHg above the 95th percentile; these children would be managed differently from hypertensive children who have BP levels that are 15–20 mmHg above the 95th percentile. An important clinical decision is to determine which hypertensive

children require more immediate attention for elevated BP. The difference between the 95th and 99th percentiles is only 7–10 mmHg and is not large enough, particularly in view of the variability in BP measurements, to adequately distinguish mild hypertension—where limited evaluation is most appropriate—from more severe hypertension where more immediate and extensive intervention is indicated. Therefore, Stage 1 hypertension is the designation for BP levels that range from the 95th percentile to 5 mmHg above the 99th percentile. Stage 2 hypertension is the designation for BP levels that are higher than 5 mmHg above the 99th percentile. Once confirmed on repeated measures, Stage 1 hypertension allows time for evaluation before initiating treatment unless the patient is symptomatic. Patients with Stage 2 hypertension may need more prompt evaluation and pharmacologic therapy. Symptomatic patients with Stage 2 hypertension require immediate treatment and consultation with experts in pediatric hypertension. These categories are parallel to the staging of hypertension in adults, as noted in JNC 7.[2]

USING THE BLOOD PRESSURE TABLES

1. Use the standard height charts to determine the height percentile.

2. Measure and record the child's SBP and DBP.

3. Use the correct gender table for SBP and DBP.

4. Find the child's age on the left side of the table. Follow the age row horizontally across the table to the intersection of the line for the height percentile (vertical column).

5. There, find the 50th, 90th, 95th, and 99th percentiles for SBP in the left columns and for DBP in the right columns.

   - BP less than the 90th percentile is normal.

   - BP between the 90th and 95th percentile is prehypertension. In adolescents, BP equal to or exceeding 120/80 mmHg is prehypertension, even if this figure is less than the 90th percentile.

   - BP greater than the 95th percentile may be hypertension.

6. If the BP is greater than the 90th percentile, the BP should be repeated twice at the same office visit, and an average SBP and DBP should be used.

7. If the BP is greater than the 95th percentile, BP should be staged. If Stage 1 (95th percentile to the 99th percentile plus 5 mmHg), BP measurements should be repeated on two more occasions. If hypertension is confirmed, evaluation should proceed as described in table 7. If BP is Stage 2 (>99th percentile plus 5 mmHg), prompt referral should be made for evaluation and therapy. If the patient is symptomatic, immediate referral and treatment are indicated. Those patients with a compelling indication, as noted in table 6, would be treated as the next higher category of hypertension.

TABLE 3

Blood Pressure Levels for Boys by Age and Height Percentile*

Age (Year)	BP Percentile ↓	Systolic BP (mmHg) ← Percentile of Height →							Diastolic BP (mmHg) ← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90

Age (Year)	BP Percentile ↓	Systolic BP (mmHg) ← Percentile of Height →							Diastolic BP (mmHg) ← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

BP, blood pressure

* The 90th percentile is 1.28 SD, 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean. For research purposes, the standard deviations in appendix table B–1 allow one to compute BP Z-scores and percentiles for boys with height percentiles given in table 3 (i.e., the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z-scores given by (5% = -1.645; 10% = -1.28; 25% = -0.68; 50% = 0; 75% = 0.68; 90% = 1.28; 95% = 1.645) and then computed according to the methodology in steps 2–4 described in appendix B. For children with height percentiles other than these, follow steps 1–4 as described in appendix B.

TABLE 4

Blood Pressure Levels for Girls by Age and Height Percentile*

Age (Year)	BP Percentile ↓	Systolic BP (mmHg) ← Percentile of Height →							Diastolic BP (mmHg) ← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88

Age (Year)	BP Percentile ↓	Systolic BP (mmHg) ← Percentile of Height →							Diastolic BP (mmHg) ← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

BP, blood pressure

* The 90th percentile is 1.28 SD, 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean. For research purposes, the standard deviations in appendix table B–1 allow one to compute BP Z-scores and percentiles for girls with height percentiles given in table 4 (i.e., the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z-scores given by (5% = -1.645; 10% = -1.28; 25% = -0.68; 50% = 0; 75% = 0.68; 90% = 1.28; 95% = 1.645) and then computed according to the methodology in steps 2–4 described in appendix B. For children with height percentiles other than these, follow steps 1–4 as described in appendix B.

TABLE 5

Classification of Hypertension in Children and Adolescents, With Measurement Frequency and Therapy Recommendations

[illegible]	[illegible]	[illegible]	Nonpharmacologic Lifestyle Changes	Pharmacologic Therapy
Normal	<90th	Recheck at next scheduled physical examination.	Encourage healthy diet, sleep, and physical activity.	—
Prehypertension	90th to <95th or if BP exceeds 120/80 mmHg even if below 90th percentile up to <95th percentile†	Recheck in 6 months.	Weight-management counseling if overweight, introduce physical activity and diet management.‡	None unless compelling indications such as CKD, diabetes mellitus, heart failure, or LVH exist
Stage 1 hypertension	95th percentile to the 99th percentile plus 5 mmHg	Recheck in 1–2 weeks or sooner if the patient is symptomatic; if persistently elevated on two additional occasions, evaluate or refer to source of care within 1 month.	Weight-management counseling if overweight, introduce physical activity and diet management.‡	Initiate therapy based on indications in Table 6 or if compelling indications as above.
Stage 2 hypertension	>99th percentile plus 5 mmHg	Evaluate or refer to source of care within 1 week or immediately if the patient is symptomatic.	Weight-management counseling if overweight, introduce physical activity and diet management.‡	Initiate therapy.§

BP, blood pressure; CKD, chronic kidney disease; DBP, diastolic blood pressure; LVH, left ventricular hypertrophy; SBP, systolic blood pressure

* For sex, age, and height measured on at least three separate occasions; if systolic and diastolic categories are different, categorize by the higher value.

† This occurs typically at 12 years old for SBP and at 16 years old for DBP.

‡ Parents and children trying to modify the eating plan to the Dietary Approaches to Stop Hypertension (DASH) eating plan could benefit from consultation with a registered or licensed nutritionist to get them started.

§ More than one drug may be required.

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

Clinical Evaluation of Confirmed Hypertension

Study or Procedure	Purpose	Target Population
Evaluation for identifiable causes		
History, including sleep history, family history, risk factors, diet, and habits such as smoking and drinking alcohol; physical examination	History and physical examination help focus subsequent evaluation	All children with persistent BP ≥95th percentile
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 cardiovascular disease. Child with chronic renal disease
Drug screen	Identify substances that might cause hypertension	History suggestive of possible contribution by substances or drugs
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
Further evaluation as indicated		
Ambulatory BP monitoring	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 Positive family history of severe hypertension
Renovascular imaging • Isotopic scintigraphy (renal scan) • Magnetic resonance angiography • Duplex Doppler flow studies • 3-Dimensional CT • Arteriography: DSA or classic	Identify renovascular disease	Young children with Stage 1 hypertension and any child or adolescent with Stage 2 hypertension
Plasma and urine steroid levels	Identify steroid-mediated hypertension	Young children with Stage 1 hypertension and any child or adolescent with Stage 2 hypertension
Plasma and urine catecholamines	Identify catecholamine-mediated hypertension	Young children with Stage 1 hypertension and any child or adolescent with Stage 2 hypertension

BP, blood pressure; BUN, blood urea nitrogen; CBC, complete blood count; CT, computerized tomography; DSA, digital subtraction angiography; LVH, left ventricular hypertrophy; R/O, rule out; U/S, ultrasound

* Comorbid risk factors also include diabetes mellitus and kidney disease.

Primary Hypertension and Evaluation for Comorbidities

- *Primary hypertension is identifiable in children and adolescents.*
- *Both hypertension and prehypertension have become a significant health issue in the young due to the strong association of high BP with overweight and the marked increase in the prevalence of overweight children.*
- *The evaluation of hypertensive children should include assessment for additional risk factors.*
- *Due to an association of sleep apnea with overweight and high BP, a sleep history should be obtained.*

High BP in childhood had been considered a risk factor for hypertension in early adulthood. However, primary (essential) hypertension is now identifiable in children and adolescents. Primary hypertension in childhood is usually characterized by mild or Stage 1 hypertension and is often associated with a positive family history of hypertension or cardiovascular disease (CVD). Children and adolescents with primary hypertension are frequently overweight. Data on healthy adolescents obtained in school health-screening programs demonstrate that the prevalence of hypertension increases progressively with increasing body mass index (BMI), and hypertension is detectable in approximately 30 percent of overweight children (BMI >95th percentile).[26] The strong association of high BP with obesity and the marked increase in the prevalence of childhood obesity[27] indicate that both hypertension and prehypertension are becoming a significant health issue in the young. Overweight children frequently have some degree of insulin resistance—a prediabetic condition. Overweight and high BP are also components of the insulin-resistance syndrome or metabolic syndrome, a condition of multiple metabolic risk factors for CVD as well as for type 2 diabetes.[28,29] The clustering of other CVD risk factors that are included in the insulin-resistance syndrome (high triglycerides, low high-density lipoprotein cholesterol [HDL-C], truncal obesity, hyperinsulinemia) is significantly greater among children with high BP than in children with normal BP.[30] Recent reports from studies that examined childhood data estimate that the insulin-resistance syndrome is present in 30 percent of overweight children with BMI greater than the 95th percentile.[31] Historically, hypertension in childhood was considered a simple independent risk factor for CVD, but its link to the other risk factors in the insulin-resistance syndrome indicates that a broader approach is more appropriate in affected children.

Primary hypertension often clusters with other risk factors.[31,32] Therefore, the medical history, physical examination, and laboratory evaluation of hypertensive children and adolescents should include a comprehensive assessment for additional cardiovascular risk. These risk factors, in addition to high BP and overweight, include low plasma HDL-C, elevated plasma triglyceride, and abnormal glucose tolerance. Fasting plasma insulin concentration is generally elevated, but an elevated insulin concentration may be reflective only of obesity and is not diagnostic of the insulin-resistance syndrome. To identify other cardiovascular risk factors, a fasting lipid panel and fasting glucose level should be obtained in children who are overweight and

have BP between the 90th and 94th percentile and in all children with BP greater than the 95th percentile. If there is a strong family history of type 2 diabetes, a hemoglobin A1c or glucose tolerance test may also be considered. These metabolic risk factors should be repeated periodically to detect changes in the level of cardiovascular risk over time. Fewer data are available on the utility of other tests in children (e.g., plasma uric acid, or homocysteine and lp(a) levels), and the use of these measures should depend on family history.

Sleep disorders, including sleep apnea, are associated with hypertension, coronary artery disease, heart failure, and stroke in adults.[33,34] Although limited data are available, they suggest an association of sleep-disordered breathing and higher BP in children.[35,36]

Approximately 15 percent of children snore, and at least 1–3 percent have sleep-disordered breathing.[35] 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. One practical strategy for identifying children with a sleep problem or sleep disorder is to obtain a brief sleep history, using an instrument called BEARS.[37(table 1.1)] BEARS addresses five major sleep domains that provide a simple but comprehensive screen for the major sleep disorders affecting children ages 2–18. The components of BEARS include: Bedtime problems, Excessive daytime sleepiness, Awakenings during the night, Regularity and duration of sleep, and Sleep-disordered breathing (snoring). Each of these domains has an age-appropriate trigger question and includes responses of both parent and child, as appropriate. This brief screening for sleep history can be completed in about 5 minutes.

In a child with primary hypertension, the presence of any comorbidity that is associated with hypertension carries the potential to increase the risk for CVD and can have an adverse effect on health outcome. Consideration of these associated risk factors and appropriate evaluation in those children in whom the hypertension is verified are important in planning and implementing therapies that reduce the comorbidity risk as well as control BP.

Evaluation for Secondary Hypertension

- *Secondary hypertension is more common in children than in adults.*
- *Because overweight is strongly linked to hypertension, BMI should be calculated as part of the physical examination.*
- *Once hypertension is confirmed, BP should be measured in both arms and in a leg.*
- *Very young children, children with Stage 2 hypertension, and children or adolescents with clinical signs that suggest systemic conditions associated with hypertension should be evaluated more completely than in those with Stage 1 hypertension.*

Secondary hypertension is more common in children than in adults. The possibility that some underlying disorder may be the cause of the hypertension should be considered in every child or adolescent who has elevated BP. However, the extent of an evaluation for detection of a possible underlying cause should be individualized for each child. Very young children, children with Stage 2 hypertension, and children or adolescents with clinical signs that suggest the presence of systemic conditions associated with hypertension should be evaluated more extensively as compared to those with Stage 1 hypertension.[38] Present technologies may facilitate less invasive evaluation than in the past, although experience in using newer modalities with children is still limited.

A thorough history and physical examination are the first steps in the evaluation of any child with persistently elevated BP. Elicited information should aim to identify not only signs and symptoms due to high BP but also clinical findings that might uncover an underlying systemic disorder. Thus, it is important to seek signs and symptoms suggesting renal disease (gross hematuria, edema, fatigue), heart disease (chest pain, exertional dyspnea, palpitations), and diseases of other organ systems (e.g., endocrinologic, rheumatologic). Past medical history should elicit information to focus the subsequent evaluation and to uncover definable causes of hypertension. Questions should be asked about prior hospitalizations, trauma, urinary tract infections, snoring and other sleep problems. Questions should address family history of hypertension, diabetes, obesity, sleep apnea, renal disease, other CVD (hyperlipidemia, stroke), and familial endocrinopathies. Many drugs can increase BP, so it is important to inquire directly about use of over-the-counter, prescription, and illicit drugs. Equally important are specific questions aimed at identifying the use of nutritional supplements, especially preparations aimed at enhancing athletic performance.

PHYSICAL EXAMINATION

The child's height, weight, and percentiles for age should be determined at the start of the physical examination. Because obesity is strongly linked to hypertension, BMI should be calculated from the height and weight, and the BMI percentile should be calculated. Poor growth may indicate an underlying chronic illness. When hypertension is confirmed, BP should be measured in both arms and in a leg. Normally, BP is 10–20 mmHg higher in the legs than the arms. If the leg BP is lower than the arm BP, or if femoral pulses are weak or absent, coarctation of the aorta may be present. Obesity alone is an insufficient explanation for diminished femoral pulses in the

presence of high BP. The remainder of the physical examination should pursue clues found on history and should focus on findings that may indicate the cause and severity of hypertension. Table 8 lists important physical exam findings in hypertensive children.[39]

The physical examination in hypertensive children is frequently normal except for the BP elevation. The extent of the laboratory evaluation is based on the child's age, history, physical examination findings, and level of BP elevation. The majority of children with secondary hypertension will have renal or renovascular causes for the BP elevation. Therefore, screening tests are designed to have a high likelihood of detecting children and adolescents who are so affected. These tests are easily obtained in most primary care offices and community hospitals. Additional evaluation must be tailored to the specific child and situation. The risk factors, or comorbid conditions, associated with primary hypertension should be included in the evaluation of hypertension in all children, as well as efforts to determine any evidence of target-organ damage.

ADDITIONAL DIAGNOSTIC STUDIES FOR HYPERTENSION

Additional diagnostic studies may be appropriate in the evaluation of hypertension in a child or adolescent, particularly if there is a high degree of suspicion that an underlying disorder is present. Such procedures are listed in table 7. ABPM, discussed previously, has application in evaluating both primary and secondary hypertension. ABPM is also used to detect white-coat hypertension.

RENIN PROFILING

Plasma renin level or plasma renin activity (PRA) is a useful screening test for mineralocorticoid-related 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, approximately 15 percent of children with arteriographically evident renal artery stenosis have normal PRA values.[40–42] 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 one or both kidneys or to one or more intrarenal segments.[43,44] Affected children usually, but not invariably, have markedly elevated BP.[40,44] 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.[44,45] 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 intra-arterial angiography, digital-subtraction angiography (DSA), and scintigraphy (with or without angiotensin-converting enzyme [ACE] inhibition).[44] As technologies evolve, children should be referred for imaging studies to centers that have expertise in the radiological evaluation of childhood hypertension.

INVASIVE STUDIES

Intra-arterial DSA with contrast is used more frequently than standard angiography, but, because of intra-arterial injection, this method remains invasive. DSA also can be accomplished by using a rapid injection of contrast into a peripheral vein, but quality of views and the size of pediatric veins make this technique useful only for older children. DSA and formal arteriography are still considered the "gold standard," but these studies should be undertaken only when surgical or invasive interventional radiologic techniques are being contemplated for anatomic correction.[46]

TABLE 8

Examples of Physical Examination Findings Suggestive of Definable Hypertension*

	Findings†	Possible Etiology
Vital signs	Tachycardia	Hyperthyroidism, pheochromocytoma, neuroblastoma, primary hypertension
	Decreased lower extremity pulses; drop in BP from upper to lower extremities	Coarctation of the aorta
Eyes	Retinal changes	Severe hypertension, more likely to be associated with secondary hypertension
Ear, nose, and throat (ENT)	Adenotonsillar hypertrophy	Suggests association with sleep-disordered breathing (sleep apnea), snoring
Height/weight	Growth retardation	Chronic renal failure
	Obesity (high BMI)	Primary hypertension
	Truncal obesity	Cushing syndrome, insulin resistance syndrome
Head and neck	Moon facies	Cushing syndrome
	Elfin facies	Williams syndrome
	Webbed neck	Turner syndrome
	Thyromegaly	Hyperthyroidism
Skin	Pallor, flushing, diaphoresis	Pheochromocytoma
	Acne, hirsutism, striae	Cushing syndrome, anabolic steroid abuse
	Café-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), collagen-vascular disease, end stage renal disease with uremia
	Apical heave	Left ventricular hypertrophy/chronic hypertension
Abdomen	Mass	Wilms tumor, neuroblastoma, pheochromocytoma
	Epigastric/flank bruit	Renal artery stenosis
	Palpable kidneys	Polycystic kidney disease, hydronephrosis, multicystic-dysplastic kidney, mass (see above)
Genitalia	Ambiguous/virilization	Adrenal hyperplasia
Extremities	Joint swelling	Systemic lupus erythematosus, collagen vascular disease
	Muscle weakness	Hyperaldosteronism, Liddle syndrome

BMI, body mass index, BP, blood pressure

* Adapted from Flynn, JT. Evaluation and management of hypertension in childhood. *Prog Pediatr Cardiol* 2001;12:177–88.

† Findings listed are examples of physical findings and do not represent all possible physical findings.

Newer imaging techniques may be used in children with vascular lesions. Magnetic resonance angiography (MRA) is increasingly feasible for the evaluation of pediatric renovascular disease, but it is still best for detecting abnormalities in the main renal artery and its primary branches.[47–49] Imaging with magnetic resonance requires that the patient be relatively immobile for extended periods—a significant difficulty for small children. At present, studies are needed to assess the effectiveness of MRA in the diagnosis of children with renovascular disease. Newer methods, including 3-dimensional (3-D) reconstructions of computerized tomography (CT) images, or spiral CT with contrast, appear promising in evaluating children who may have renovascular disease.[50]

Target-Organ Abnormalities in Childhood Hypertension

- *Target-organ abnormalities are commonly associated with hypertension in children and adolescents.*
- *Left ventricular hypertrophy (LVH) is the most prominent evidence of target-organ damage.*
- *Pediatric patients with established hypertension should have echocardiographic assessment of left ventricular mass at diagnosis and periodically thereafter.*
- *The presence of LVH is an indication to initiate or intensify antihypertensive therapy.*

Hypertension is associated with increased risk of myocardial infarction, stroke, and cardiovascular mortality in adults,[2,51] and treatment of elevated BP results in a reduction in the risk for cardiovascular events.

Children and adolescents with severe elevation of BP are also at increased risk of adverse outcomes, including hypertensive encephalopathy, seizures, and even cerebrovascular accidents and congestive heart failure.[52,53] Even hypertension that is less severe contributes to target-organ damage when it occurs with other chronic conditions, such as chronic kidney disease.[54–56] Two autopsy studies,[57,58] that evaluated tissue from adolescents and young adults who had sudden deaths due to trauma, demonstrated significant relationships between the level of BP, or hypertension, and the presence of atherosclerotic lesions in the aorta and coronary arteries. The exact level and duration of BP elevation that causes target-organ damage in the young has not been established.

One difficulty in the assessment of these relationships is that, until recently, few noninvasive methods could evaluate the effect of hypertension on the cardiovascular system. Noninvasive techniques that use ultrasound can demonstrate structural and functional changes in the vasculature related to BP. Recent clinical studies using these techniques demonstrate that childhood levels of BP are associated with carotid intimal-medial thickness[59] and large artery compliance[60] in young adults. Even healthy adolescents with clustering of cardiovascular risk factors demonstrate elevated carotid thickness,[61,62] and those with BP levels at the higher end of the normal distribution show decreased brachial artery flow-mediated vasodilatation. Overall, evidence is increasing that even mild BP elevation can have an adverse effect on vascular structure and function[63] in asymptomatic young persons.

LVH is the most prominent clinical evidence of target-organ damage caused by hypertension in children and adolescents. With the use of echocardiography to measure left ventricular mass, LVH has been reported in 34–38 percent of children and adolescents with mild, untreated BP elevation.[64–66] Daniels et al. evaluated 130 children and adolescents with persistent BP elevation.[67] They reported that 55 percent of patients had a left ventricular mass index greater than the 90th percentile, and 14 percent had left ventricular mass index above 51 $g/m^{2.7}$, a value in adults with hypertension that has been associated with a fourfold greater risk of adverse cardiovascular outcomes. When left ventricular geometry was examined in hypertensive children,

17 percent had concentric hypertrophy, a pattern that is associated with higher risk for cardiovascular outcomes in adults, and 30 percent had eccentric hypertrophy, which is associated with intermediate risk for cardiovascular outcomes.[67]

In addition, abnormalities of the retinal vasculature have been reported in adults with hypertension.[68] Few studies of retinal abnormalities have been conducted in children with hypertension. Skalina et al. evaluated newborns with hypertension[69] and reported the presence of hypertensive retinal abnormalities in approximately 50 percent of their patients. On repeat examination, after the resolution of hypertension, these abnormalities had disappeared.

CLINICAL RECOMMENDATION

Echocardiography is recommended as a primary tool for evaluating patients for target-organ abnormalities by assessing the presence or absence of LVH. Left ventricular mass is determined from standard echocardiographic measurements of the left ventricular end-diastolic dimension (LVED), the intraventricular septal thickness (IVS), and the thickness of the left ventricular posterior wall (LVPW) and can be calculated as: LV Mass (g) = 0.80 [1.04 $(IVS + LVED + LVPW)^3 - (LVED)^3$] + 0.6 (with echocardiographic measurements in centimeters). From these measures, the left ventricular mass can be calculated by using the equation of Devereux et al.[70] when measurements are made according to the criteria of the American Society of Echocardiography.[71]

Heart size is closely associated with body size.[72] Left ventricular mass index is calculated to standardize measurements of left ventricular mass. Several methods for indexing left ventricular mass have been reported, but it is recommended that height ($m^{2.7}$) be used to index left ventricular mass, as described by de Simone et al.[73] This method accounts for close to the equivalent of the effect of lean body mass and excludes the effect of obesity and BP elevation on left ventricular mass. Some echo laboratories use height as the indexing variable. This calculation is also acceptable and is somewhat easier to use, as fewer calculations are needed.

Children and adolescents with established hypertension should have an echocardiogram to determine if LVH is present. A conservative cutpoint that determines the presence of LVH is 51 $g/m^{2.7}$. This cutpoint is above the 99th percentile for children and adolescents and is associated with increased morbidity in adults with hypertension.[73] Other references exist for normal children,[74] but, unlike adults, outcome-based standards for left ventricular mass index are not available for children. In interpreting the left ventricular mass index, it should be remembered that some factors, such as obesity and hypertension, have pathologic effects on the heart, whereas others—such as physical activity, particularly in highly conditioned athletes—may be adaptive.

Ascertainment of left ventricular mass index is very helpful in clinical decisionmaking. The presence of LVH can be an indication for initiating or intensifying pharmacologic therapy to lower BP. For patients who have LVH, the echocardiographic determination of left ventricular mass index should be repeated periodically.

At the present time, additional testing for other target-organ abnormalities (such as determination of carotid intimal-medial thickness and evaluation of urine for microalbuminuria) is not recommended for routine clinical use. Further research will be needed to evaluate the clinical utility of these tests.

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 in those with hypertension.*
- *Family-based intervention improves success.*

Evidence is limited that supports the efficacy of nonpharmacological interventions for BP reduction in the treatment of hypertension in children and adolescents. Data that demonstrate a relationship of lifestyle with BP can be used as the basis for recommendations. On the basis of large randomized controlled trials, the following lifestyle modifications are recommended in adults:[2] weight reduction in overweight or obese individuals;[75] increased intake of fresh vegetables, fruits, and lowfat dairy (the Dietary Approaches to Stop Hypertension Study [DASH] eating plan);[76] dietary sodium reduction;[76,77] increased physical activity;[78] and moderation of alcohol consumption.[79] Smoking cessation has significant cardiovascular benefits.[32] As information on chronic sleep problems evolves, interventions to improve sleep quality may also have a beneficial effect on BP.[80]

The potential for control of BP in children through weight reduction is supported by BP tracking and weight-reduction studies. BP levels track from childhood through adolescence and into adulthood[81–83] in association with weight.[84,85] Because of the strong correlation between weight and BP, excessive weight gain is likely to be associated with elevated BP over time. Therefore, maintenance of normal weight gain in childhood should lead to less hypertension in adulthood.

Weight loss in overweight adolescents is associated with a decrease in BP.[30,86–90] Weight control not only decreases BP, it also decreases BP sensitivity to salt[88] and decreases other cardiovascular risk factors, such as dyslipidemia and insulin resistance.[32] In studies that achieve a reduction in BMI of about 10 percent, short-term reductions in BP were in the range of 8–12 mmHg. Although difficult, weight loss, if successful, is extremely effective.[32,91–93] Identifying a complication of overweight, such as hypertension, can be a helpful motivator for patients and families to make changes. Weight control can render pharmacological treatment unnecessary but should not delay drug use when indicated.

Emphasis on the management of complications rather than on overweight shifts the aim of weight management from an aesthetic to a health goal. In motivated families, education or simple behavior modification can be successful in achieving moderate weight loss or preventing further weight gain. Steps can be implemented in the primary care setting even with limited staff and time resources.[32,91] The patient should be encouraged to self-monitor time spent in sedentary activity, including watching television and playing video or computer games, and to set goals to progressively decrease these activities to less than 2 hours per day.[94] The family and patient should identify physical activities that the child enjoys,

engage in them regularly, and self-monitor time spent in physical activities (30–60 minutes per day should be achieved).[94–96] Dietary changes can involve portion-size control, decrease in consumption of sugar-containing beverages and energy-dense snacks, increase in consumption of fresh fruits and vegetables, and regular meals including a healthy breakfast.[32,91,93,97,98] Consultation with a nutritionist can be useful and provide customized recommendations. During regular office visits, the primary care provider can supervise the child's progress in self-monitoring and accomplishing goals and can provide support and positive feedback to the family. Some patients will benefit from a more intense and comprehensive approach to weight management from a multidisciplinary and specialized team if available.[91–93]

Despite the lack of firm evidence about dietary intervention in children, it is generally accepted that hypertensive individuals can benefit from a dietary increase in fresh vegetables, fresh fruits, fiber, and nonfat dairy, as well as a reduction of sodium. Despite some suggestion that calcium supplements may decrease BP in children,[99,100] so far the evidence is too limited to support a clinical recommendation.[101] Lower BP has been associated in children and adolescents with an *increased* intake of potassium,[100–103] magnesium,[100,101] folic acid,[101,104] unsaturated fat,[100,105,106] and fiber,[100,101,104] and lower dietary intake of total fat.[100,101] However, these associations are small and insufficient to support dietary recommendations for specific, individual nutrients.

Sodium reduction in children and adolescents has been associated with small reductions in BP, in the range of 1–3 mmHg.[101,103,107–110] Data from one randomized trial suggest that sodium intake in infancy may affect BP in adolescence.[111] Similarly, some evidence indicates that breastfeeding may be associated with lower BP in childhood.[112,113] The current recommendation for adequate daily sodium intake is only 1.2 g/day for 4- to 8-year-old children and 1.5 g/day for older children.[114] Since 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.

Regular physical activity has cardiovascular benefits. A recent meta-analysis that combined 12 randomized trials, for a total of 1,266 children and adolescents, concluded that physical activity leads to a small, but not statistically significant, decrease in BP.[115] However, both regular physical activity and decreasing sedentary activity—such as watching television and playing video or electronic games—are important components of pediatric obesity treatment and prevention.[32,91–93] Weight-reduction trials consistently report better results when physical activity and/or prevention of sedentary activity are included in the treatment protocol. Therefore, regular aerobic physical activity (30–60 minutes of moderate physical activity on most days) and limitation of sedentary activities to less than 2 hours per day are recommended for the prevention of obesity, hypertension, and other cardiovascular risk factors.[94–96] With the exception of power lifting, resistance training is also helpful. Competitive sports participation should be limited only in the presence of uncontrolled Stage 2 hypertension.[116]

The scope of hypertension as a public health problem in adults is substantial. Poor health-related behaviors such as physical inactivity, unfavorable dietary patterns, and excessive weight gain raise the risk for future hypertension. The therapeutic lifestyle changes discussed above may have benefit for all children in prevention of future disease, including primary hypertension. Accordingly, appropriate health recommendations for all children and adolescents are regular physical activity; a diet with limited sodium but rich in fresh fruits, fresh vegetables, fiber, and lowfat dairy; and avoiding excess weight gain.

Pharmacologic Therapy of Childhood Hypertension

- *Indications for antihypertensive drug therapy in children include secondary hypertension and insufficient response to lifestyle modifications.*
- *Recent clinical trials have expanded the number of drugs that have pediatric dosing information. Dosing recommendations for many of the newer drugs are provided.*
- *Pharmacologic therapy, when indicated, should be initiated with a single drug. Acceptable drug classes for use in children include ACE inhibitors, angiotensin-receptor blockers, beta-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 that case, BP should be lowered to <90th percentile.*
- *Severe, symptomatic hypertension should be treated with intravenous antihypertensive drugs.*

In adults, hypertension is typically a lifelong condition. Most hypertensive patients will need to remain on medications for the rest of their lives. Usually, adults readily accept this fact, given the known long-term adverse consequences of untreated or undertreated hypertension.[117] In children, however, the long-term consequences of untreated hypertension are unknown. Additionally, no data are available on the long-term effects of antihypertensive drugs on growth and development. Therefore, a definite indication for initiating pharmacologic therapy should be ascertained before a drug is prescribed.

Table 6 summarizes the indications for use of antihypertensive drugs in children. These indications include symptomatic hypertension, secondary hypertension, established hypertensive target-organ damage, and failure of nonpharmacologic measures. Other indications for use of antihypertensive drugs can be considered, depending on the clinical situation. For example, because the presence of multiple cardiovascular risk factors (elevated BP, dyslipidemia, tobacco use, etc.) increases cardiovascular risk in an exponential rather than additive fashion,[118,119] antihypertensive therapy could be considered if the child or adolescent is known to have dyslipidemia.

The number of antihypertensive drugs has increased since the publication of the *Report of the Task Force on Blood Pressure Control in Children*.[120] The number of drugs that have been studied systematically in children has also increased, largely because of incentives provided to the pharmaceutical industry under the auspices of the 1997 Food and Drug Administration Modernization Act (FDAMA) and the 2002 Best Pharmaceuticals for Children Act (BPCA).[121–123] These developments have had both negative and positive consequences. Chief among the negative consequences is the lack of reliable pediatric data for older, commonly used compounds with expired patent protection. Currently, no incentives exist for industry-sponsored trials of such drugs, and alternative methods of stimulating pediatric studies, such as those contained in the BPCA,[123–125] have yet to come to fruition. On the other hand, publication of the results of industry-sponsored clinical trials and single-center case series will

provide additional data that can be combined with prior recommendations based on expert opinion and collective clinical experience to guide the use of antihypertensive drugs in children and adolescents who require pharmacologic treatment.

Table 9 contains dosing recommendations for antihypertensive drugs in children 1–17 years old. It should be noted that many other drugs are available in addition to those listed in table 9. Those drugs are not included in the table, however, because few or no pediatric data were available at the time this report was prepared.

Long-term, clinical endpoint data from randomized trials, such as the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), support the preferential use of specific antihypertensive drugs in adults.[2,126] However, pediatric clinical trials of antihypertensive drugs have focused only on their ability to lower BP and have not compared the effects of these drugs on clinical endpoints. Therefore, because all classes of antihypertensive drugs have been shown to lower BP in children, the choice of drug for initial antihypertensive therapy resides in the preference of the responsible physician. Some diuretics and beta-adrenergic blockers, which were recommended as initial therapy in the first and second Task Force Reports,[25,120] have a long history of safety and efficacy based on clinical experience in hypertensive children, and these drugs remain appropriate for pediatric use. Similarly, some members of the newer classes of antihypertensive drugs, including ACE inhibitors, calcium channel blockers, and angiotensin-receptor blockers,[127–130] have been studied in children and, based on short-term use, shown to be safe and well-tolerated with satisfactory BP reductions in hypertensive children.

Specific classes of antihypertensive drugs should be used preferentially in certain hypertensive children with specific underlying or concurrent medical conditions. Examples include the use of ACE inhibitors or angiotensin-receptor blockers in children with diabetes and microalbuminuria or proteinuric renal diseases, and the use of beta-adrenergic blockers or calcium channel blockers in hypertensive children with migraine headaches. This approach is similar to that outlined in the recent JNC 7 report, which recommends specific classes of antihypertensive drugs for use in adults in certain high-risk categories.[2]

All antihypertensive drugs should be prescribed in a similar fashion: The child is initially started on the lowest recommended dose listed in table 9. The dose can be increased until the desired BP goal is achieved. Once the highest recommended dose is reached, or if the child experiences side effects from the drug, a second drug from a different class should be added. Consideration should be given to combining drugs with complementary mechanisms of action, such as an ACE inhibitor with a diuretic, or a vasodilator with a diuretic or beta-adrenergic blocker. Because little pediatric experience is available in using fixed-dose combination products, except for bisoprolol/HCTZ,[131] routine use of these products in children cannot be recommended at this time.

For children with uncomplicated primary hypertension and no hypertensive target-organ damage, the goal BP should be less than the 95th percentile for sex, age, and height, whereas for children with chronic renal disease, diabetes, or hypertensive target-organ damage, the goal BP should be less than the 90th percentile for sex, age, and height. Again, this approach is similar to the recommended treatment of hypertension in adults with additional cardiovascular risk factors or comorbid conditions.[2]

Important adjunctive aspects to the drug therapy of childhood hypertension include ongoing monitoring of target-organ damage as well as BP monitoring, surveillance for drug side effects, periodic monitoring of electrolytes in children treated with ACE inhibitors or diuretics, counseling regarding other cardiovascular risk factors, and continued emphasis on nonpharmacologic measures. It may also be appropriate to consider "step-down" therapy in selected patients. This approach attempts a gradual reduction in the drug after an extended course of good BP control, with

TABLE 9

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

Class	Drug	Dose†
Angiotensin-converting enzyme (ACE) inhibitor	Benazepril	Initial: 0.2 mg/kg/day up to 10 mg/day Maximum: 0.6 mg/kg/day up to 40 mg/day
	Captopril	Initial: 0.3–0.5 mg/kg/dose Maximum: 6 mg/kg/day
	Enalapril	Initial: 0.08 mg/kg/day up to 5 mg/day Maximum: 0.6 mg/kg/day up to 40 mg/day
	Fosinopril	Children >50 kg: Initial: 5–10 mg/day Maximum: 40 mg/day
	Lisinopril	Initial: 0.07 mg/kg/day up to 5 mg/day Maximum: 0.6 mg/kg/day up to 40 mg/day
	Quinapril	Initial: 5–10 mg/day Maximum: 80 mg/day
Angiotensin-receptor blocker	Irbesartan	6–12 years: 75–150 mg/day ≥13 years: 150–300 mg/day
	Losartan	Initial: 0.7 mg/kg/day up to 50 mg/day Maximum: 1.4 mg/kg/day up to 100 mg/day
α- and β-blocker	Labetalol	Initial: 1–3 mg/kg/day Maximum: 10–12 mg/kg/day up to 1,200 mg/day
β-blocker	Atenolol	Initial: 0.5–1 mg/kg/day Maximum: 2 mg/kg/day up to 100 mg/day
	Bisoprolol/HCTZ	Initial: 2.5/6.25 mg/day Maximum: 10/6.25 mg/day
	Metoprolol	Initial: 1–2 mg/kg/day Maximum: 6 mg/kg/day up to 200 mg/day
	Propranolol	Initial: 1–2 mg/kg/day Maximum: 4 mg/kg/day up to 640 mg/day
Calcium channel blocker	Amlodipine	Children 6–17 years: 2.5–5 mg once daily
	Felodipine	Initial: 2.5 mg/day Maximum: 10 mg/day
	Isradipine	Initial: 0.15–0.2 mg/kg/day Maximum: 0.8 mg/kg/day up to 20 mg/day
	Extended-release nifedipine	Initial: 0.25–0.5 mg/kg/day Maximum: 3 mg/kg/day up to 120 mg/day

Dosing Interval	Evidence‡	FDA Labelings§	Comments††
qd	RCT	Yes	1. All ACE inhibitors are contraindicated in pregnancy—females of childbearing age should use reliable contraception.
tid	RCT, CS	No	2. Check serum potassium and creatinine periodically to monitor for hyperkalemia and azotemia.
qd–bid	RCT	Yes	3. Cough and angioedema are reportedly less common with newer members of this class than with captopril.
qd	RCT	Yes	4. Benazepril, enalapril, and lisinopril labels contain information on the preparation of a suspension; captopril may also be compounded into a suspension.
qd	RCT	Yes	5. FDA approval for ACE inhibitors with pediatric labeling is limited to children ≥6 years of age and to children with creatinine clearance ≥30 ml/min/1.73m².
qd	RCT, EO	No	
qd	CS	Yes	1. All ARBs are contraindicated in pregnancy—females of childbearing age should use reliable contraception.
qd	RCT	Yes	2. Check serum potassium, creatinine periodically to monitor for hyperkalemia and azotemia.
			3. Losartan label contains information on the preparation of a suspension.
			4. FDA approval for ARBs is limited to children ≥6 years of age and to children with creatinine clearance ≥30 ml/min/1.73m².
bid	CS, EO	No	1. Asthma and overt heart failure are contraindications.
			2. Heart rate is dose-limiting.
			3. May impair athletic performance.
			4. Should not be used in insulin-dependent diabetics.
qd–bid	CS	No	1. Noncardioselective agents (propranolol) are contraindicated in asthma and heart failure.
qd	RCT	No	2. Heart rate is dose-limiting.
bid	CS	No	3. May impair athletic performance.
			4. Should not be used in insulin-dependent diabetics.
bid–tid	RCT, EO	Yes	5. A sustained-release formulation of propranolol is available that is dosed once-daily.
qd	RCT	Yes	1. Amlodipine and isradipine can be compounded into stable extemporaneous suspensions.
qd	RCT, EO	No	2. Felodipine and extended-release nifedipine tablets must be swallowed whole.
tid–qid	CS, EO	No	3. Isradipine is available in both immediate-release and sustained-release formulations; sustained release form is dosed qd or bid.
qd–bid	CS, EO	No	4. May cause tachycardia.

TABLE 9

Antihypertensive Drugs for Outpatient Management of Hypertension in Children 1–17 Years Old* (continued)

Class	Drug	Dose†
Central α-agonist	Clonidine	Children ≥12 years: Initial: 0.2 mg/day Maximum: 2.4 mg/day
Diuretic	HCTZ	Initial: 1 mg/kg/day Maximum: 3 mg/kg/day up to 50 mg/day
	Chlorthalidone	Initial: 0.3 mg/kg/day Maximum: 2 mg/kg/day up to 50 mg/day
	Furosemide	Initial: 0.5–2.0 mg/kg/dose Maximum: 6 mg/kg/day
	Spironolactone	Initial: 1 mg/kg/day Maximum: 3.3 mg/kg/day up to 100 mg/day
	Triamterene	Initial: 1–2 mg/kg/day Maximum: 3–4 mg/kg/day up to 300 mg/day
	Amiloride	Initial: 0.4–0.625 mg/kg/day Maximum: 20 mg/day
Peripheral α-antagonist	Doxazosin	Initial: 1 mg/day Maximum: 4 mg/day
	Prazosin	Initial: 0.05–0.1 mg/kg/day Maximum: 0.5 mg/kg/day
	Terazosin	Initial: 1 mg/day Maximum: 20 mg/day
Vasodilator	Hydralazine	Initial: 0.75 mg/kg/day Maximum: 7.5 mg/kg/day up to 200 mg/day
	Minoxidil	Children <12 years: Initial: 0.2 mg/kg/day Maximum: 50 mg/day Children ≥12 years: Initial: 5 mg/day Maximum: 100 mg/day

Dosing Interval	Evidence‡	FDA Labelings§	Comments††
bid	EO	Yes	1. May cause dry mouth and/or sedation. 2. Transdermal preparation also available. 3. Sudden cessation of therapy can lead to severe rebound hypertension.
qd	EO	Yes	1. All patients treated with diuretics should have electrolytes monitored shortly after initiating therapy and periodically thereafter.
qd	EO	No	2. Useful as add-on therapy in patients being treated with drugs from other drug classes.
qd–bid	EO	No	3. Potassium-sparing diuretics (spironolactone, triamterene, amiloride) may cause severe hyperkalemia, especially if given with ACE inhibitor or ARB.
qd–bid	EO	No	4. Furosemide is labeled only for treatment of edema but may be useful as add-on therapy in children with resistant hypertension, particularly in children with renal disease.
bid	EO	No	5. Chlorthalidone may precipitate azotemia in patients with renal diseases and should be used with caution in those with severe renal impairment.
qd	EO	No	
qd	EO	No	1. May cause hypotension and syncope, especially after first dose.
tid	EO	No	
qd	EO	No	
qid	EO	Yes	1. Tachycardia and fluid retention are common side effects.
qd–tid	CS, EO	Yes	2. Hydralazine can cause a lupus-like syndrome in slow acetylators. 3. Prolonged use of minoxidil can cause hypertrichosis. 4. Minoxidil is usually reserved for patients with hypertension resistant to multiple drugs.

ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; bid, twice-daily; HCTZ, hydrochlorothiazide; qd, once-daily; qid, four times daily; tid, three times daily

* Includes drugs with prior pediatric experience or recently completed clinical trials.

† The maximum recommended adult dose should not be exceeded in routine clinical practice.

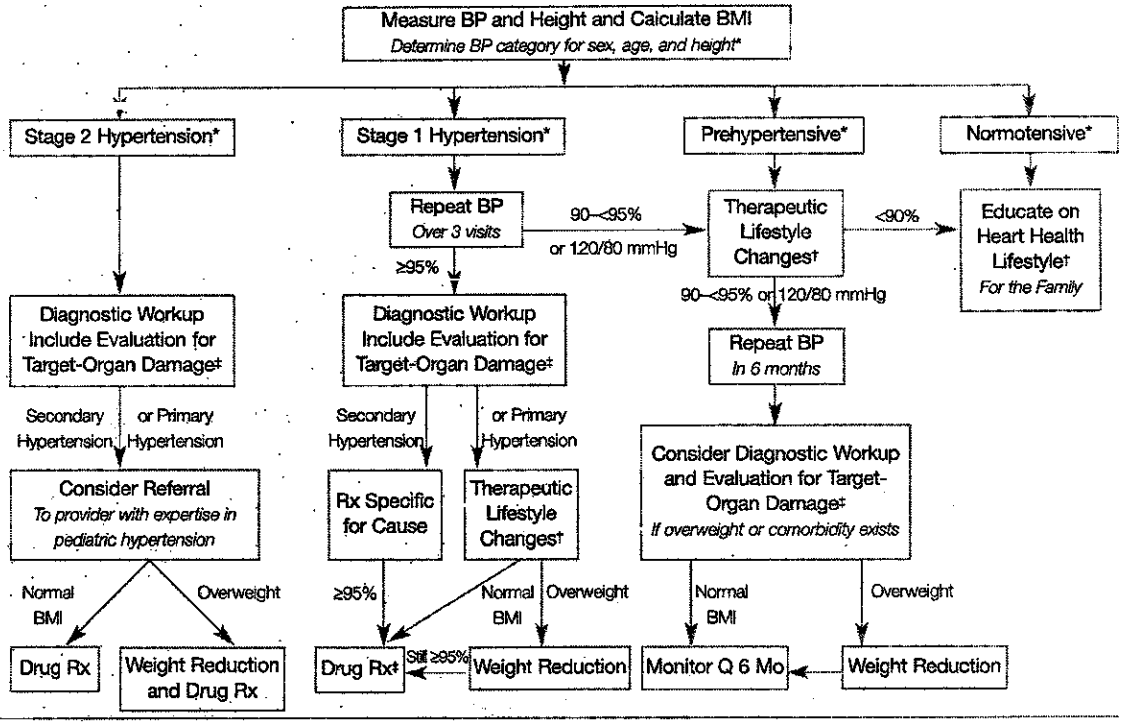
‡ Level of evidence upon which dosing recommendations are based (CS, case series; EO, expert opinion; RCT, randomized controlled trial)

§ FDA-approved pediatric labeling information is available. Recommended doses for agents with FDA-approved pediatric labels are the doses contained in the approved labels. Even when pediatric labeling information is not available, the FDA-approved label should be consulted for additional safety information.

†† Comments apply to all members of each drug class except where otherwise stated.

FIGURE 1

Management Algorithm



BMI, body mass index; BP, blood pressure; Rx, prescription; Q, every.

*See tables 3, 4, and 5.

†Diet modification and physical activity.

‡Especially if younger, very high BP, little or no family history, diabetic, or other risk factors.

the eventual goal of completely discontinuing drug therapy. Children with uncomplicated primary hypertension, especially overweight children who successfully lose weight, are the best candidates for the step-down approach. Such patients require ongoing BP monitoring after the cessation of drug therapy, as well as continued nonpharmacologic treatment, because hypertension may recur.

Severe, symptomatic hypertension with BP well above the 99th percentile occurs in some children, usually those with underlying renal disease, and requires prompt treatment. *Hypertensive emergencies* in children are usually accompanied by signs of hypertensive encephalopathy, typically causing seizures. Hypertensive emergencies should be treated by an intravenous antihypertensive that can produce a controlled reduction in BP, aiming to decrease the pressure by 25 percent or less over the first 8 hours after presentation and then gradually normalizing the BP over 26–48 hours.[132,133] *Hypertensive urgencies* are accompanied by less serious symptoms, such as severe headache or vomiting. Hypertensive urgencies can be treated by either intravenous or oral antihypertensives, depending on the child's symptomatology. Table 10 provides dosing recommendations for treatment of severe hypertension in children when prompt reduction in BP is indicated.

Figure 1 is a management algorithm that presents guidelines for evaluation and treatment of Stage 1 and Stage 2 hypertension in children and adolescents. The algorithm summarizes monitoring and intervention recommendations for children and adolescents with prehypertension and hypertension. Included in the algorithm are points at which the presence of overweight is considered in clinical decisionmaking. The algorithm also emphasizes the inclusion of evaluation for target-organ damage in children with established Stage 1 and Stage 2 hypertension.

TABLE 10

Antihypertensive Drugs for Management of Severe Hypertension in Children 1–17 Years Old

Drug	Class	Dose†	Route	Comments
Esmolol	ß-blocker	100–500 mcg/kg/min	iv infusion	Very short-acting—constant infusion preferred. May cause profound bradycardia. Produced modest reductions in BP in a pediatric clinical trial.
Hydralazine	Vasodilator	0.2–0.6 mg/kg/dose	iv, im	Should be given every 4 hours when given iv bolus. Recommended dose is lower than FDA label.
Labetalol	α- and ß-blocker	bolus: 0.2–1.0 mg/kg/dose up to 40 mg/dose infusion: 0.25–3.0 mg/kg/hr	iv bolus or infusion	Asthma and overt heart failure are relative contra-indications.
Nicardipine	Calcium channel blocker	1–3 mcg/kg/min	iv infusion	May cause reflex tachycardia.
Sodium nitroprusside	Vasodilator	0.53–10 mcg/kg/min	iv infusion	Monitor cyanide levels with prolonged (>72 hr) use or in renal failure; or coadminister with sodium thiosulfate.

Drug	Class	Dose*	Route	Comments
Clonidine	Central α-agonist	0.05–0.1 mg/dose may be repeated up to 0.8 mg total dose	po	Side effects include dry mouth and sedation.
Enalaprilat	ACE inhibitor	0.05–0.1 mg/kg/dose up to 1.25 mg/dose	iv bolus	May cause prolonged hypotension and acute renal failure, especially in neonates.
Fenoldopam	Dopamine receptor agonist	0.2–0.8 mcg/kg/min	iv infusion	Produced modest reductions in BP in a pediatric clinical trial in patients up to 12 years.
Isradipine	Calcium channel blocker	0.05–0.1 mg/kg/dose	po	Stable suspension can be compounded.
Minoxidil	Vasodilator	0.1–0.2 mg/kg/dose	po	Most potent oral vasodilator; long-acting.

ACE, angiotensin-converting enzyme; im, intramuscular; iv, intravenous; po, oral.

* Useful for hypertensive emergencies and some hypertensive urgencies.

† All dosing recommendations are based upon expert opinion or case series data except as otherwise noted.

‡ Useful for hypertensive urgencies and some hypertensive emergencies.

APPENDIX A.

Demographic Data

TABLE A-1

Demographic Data on Height/Blood Pressure Distribution Curves by Study Population*

Age Source	(Years)	Gender		Ethnic Group							Person's Visits SBP Available	Person's Visits DBP.5 Available	Total No. of Person's Visits
		Boys	Girls	Black	Hispanic	White	Asian	Native American	Other	Missing			
NIH	6–17	1,896	1,751	600	0	2,963	0	0	84	0	3,647	3,609	3,647
											3,647	3,609	3,647
Pittsburgh	1–5	148	137	108	0	176	0	0	0	1	285	0	285
											893	0	893
Dallas	13–17	5,916	5,649	5,266	1,570	4,729	0	0	0	0	11,565	11,565	11,565
											21,860	21,852	21,860
Bogalusa	1–17	3,751	3,607	2,480	0	4,878	0	0	0	0	7,358	0	7,358
											15,882	0	15,882
Houston	3–17	1,457	1,377	637	1,341	748	23	0	0	85	2,834	0	2,834
											2,834	0	2,834
South Carolina	4–17	3,167	3,263	3,110	0	3,320	0	0	0	0	6,430	6,368	6,430
											6,430	6,368	6,430
Iowa	5–17	2,099	1,993	0	0	4,092	0	0	0	0	4,092	0	4,092
											4,092	0	4,092
Providence	1–3	230	231	24	4	431	0	0	2	0	461	371	461
											898	560	898
Minnesota	9–17	9,991	9,418	3,422	555	11,311	1,677	644	1,800	0	19,409	19,207	19,409
											19,409	19,207	19,409
NHANES III	5–17	2,465	2,577	1,770	1,830	1,324	64	10	12	32	5,042	4,304	5,042
											5,042	4,304	5,042
NHANES 99–00	8–17	1,041	1,063	605	988	437	0	0	74	0	2,104	2,076	2,104
											2,104	2,076	2,104
Total (Percent of Total)	**1–17**	**32,161 (51)**	**31,066 (49)**	**18,022 (29)**	**6,288 (10)**	**34,409 (54)**	**1,764 (3)**	**654 (1)**	**1,972 (3)**	**118 (0)**	**63,227 83,091**	**47,500 57,976**	**63,227 83,091**

DBP.5, diastolic blood pressure (Korotkoff 5); NHANES, National Health and Nutrition Examination Survey; NIH, National Institutes of Health; SBP, systolic blood pressure.

* Table differs from 1997 report updated height percentile used; subjects whose height Z-score was less than –6 or greater than +6 were excluded.

APPENDIX B.

Computation of Blood Pressure Percentiles for Arbitrary Sex, Age, and Height

Computation of Blood Pressure Percentiles for Arbitrary Sex, Age, and Height

- *To compute the systolic blood pressure (SBP) percentile of a boy who is age y years and height h inches with SBP = x mmHg:*

1. Refer to the most recent CDC growth charts, which are available online, and convert the height of h inches to a height Z-score relative to boys of the same age; this is denoted by Zht.

2. Compute the expected SBP (μ) for boys of age y years and height h inches given by

$$\mu = \alpha + \sum_{j=1}^{4} \beta_j (y\text{-}10)^j + \sum_{k=1}^{4} \gamma_k (Zht)^k$$

   where α, $\beta_1 \ldots, \beta_4$ and $\gamma_1 \ldots, \gamma_4$ are given in the 3rd column of appendix table B–1.

3. Then convert the boy's observed SBP to a Z-score (Zbp) given by

$$Zbp = (x - \mu)/\sigma$$

   where σ is given in the 3rd column of appendix table B–1.

4. To convert the bp Z-score to a percentile (P), compute P = Φ (Zbp) x 100% where Φ (Z) = area under a standard normal distribution to the left of Z.

   Thus, if Zbp = 1.28, then Φ (Zbp) = .90 and the bp percentile = .90 x 100% = 90%.

5. To compute percentiles for SBP for girls, diastolic blood pressure (DBP) (K5) for boys, and DBP (K5) for girls, use the regression coefficients from the 4th, 5th, and 6th columns of appendix table B–1.

   For example, a 12-year-old boy, with height at the 90th percentile for his age-sex group, has a height Z-score = 1.28, and his expected SBP (μ) is

$$\mu = 102.19768 + 1.82416\,(2) + 0.12776\,(2^2) + 0.00249\,(2^3) - 0.00135\,(2^4) + 2.73157\,(1.28) - 0.19618\,(1.28)^2 - 0.04659\,(1.28)^3 + 0.00947\,(1.28)^4 = 109.46 \text{ mmHg.}$$

   Suppose his actual SBP is 120 mmHg (x); his SBP Z-score is then:

$$\text{SBP Z-score} = (x - \mu)/\sigma = (120 - 109.46)/10.7128 = 0.984$$

   The corresponding SBP percentile = Φ (0.984) x 100% = 83.7th percentile.

TABLE B-1

Regression Coefficients From Blood Pressure Regression Models*

Variable Name	Symbol	Systolic BP		Diastolic BP5	
		Male	Female	Male	Female
Intercept	α	102.19768	102.01027	61.01217	60.50510
Age					
Age–10	β_1	1.82416	1.94397	0.68314	1.01301
$(Age–10)^2$	β_2	0.12776	0.00598	-0.09835	0.01157
$(Age–10)^3$	β_3	0.00249	-0.00789	0.01711	0.00424
$(Age–10)^4$	β_4	-0.00135	-0.00059	0.00045	-0.00137
Normalized height					
Zht	γ^1	2.73157	2.03526	1.46993	1.16641
Zht^2	γ^2	-0.19618	0.02534	-0.07849	0.12795
Zht^3	γ^3	-0.04659	-0.01884	-0.03144	-0.03869
Zht^4	γ^4	0.00947	0.00121	0.00967	-0.00079
Standard deviation	σ	10.7128	10.4855	11.6032	10.9573
ρ†		0.4100	0.3824	0.2436	0.2598
n (persons)		32,161	31,066	24,057	23,443
n (*visits*)		*42,074*	*41,017*	*29,182*	*28,794*

BP, blood pressure; Diastolic BP5, diastolic measurement at Korotkoff 5.

* The coefficients were obtained from mixed-effects linear regression models.

† The value of ρ represents the correlation between BP measurements at different ages for the same child after correcting for age and Zht. This computation was necessary because some studies contributing to the childhood BP database provided BP at more than one age.

Scheme Used for Classification of the Evidence

M Meta-analysis; use of statistical methods to combine the results from clinical trials

RA Randomized controlled trials; also known as experimental studies

RE Retrospective analyses; also known as case-control studies

F Prospective study; also known as cohort studies, including historical or prospective followup studies

X Cross-sectional survey; also known as prevalence studies

PR Previous review or position statements

C Clinical interventions (nonrandomized)

These symbols are appended to the citations in the reference list. The studies that provided evidence supporting the recommendations of this report were classified and reviewed by the staff and the executive committee. The classification scheme is from the JNC 7 report and other NHBPEP Working Group Reports (www.nhlbi.nih.gov/about/nhbpep/index.htm).[2,134–138]

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NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Phone: 301-592-8573
TTY: 240-629-3255
Fax: 301-592-8563
Web site: http://www.nhlbi.nih.gov

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