

## The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents

ABBREVIATIONS. BP, blood pressure; NHBPEP, National High Blood Pressure Education Program; SBP, systolic blood pressure; DBP, diastolic blood pressure; NHANES, National Health and Nutrition Examination Survey; JNC 7, Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; NHLBI, National Heart, Lung, and Blood Institute; ABPM, ambulatory blood pressure monitoring; CVD, cardiovascular disease; BMI, body mass index; PRA, plasma renin activity; DSA, digital-subtraction angiography; ACE, angiotensin-converting enzyme; MRA, magnetic resonance angiography; CT, computed tomography; LVH, left ventricular hypertrophy.

### INTRODUCTION

Considerable advances have been made in detection, evaluation, and management of high blood pressure (BP), or hypertension, in children and adolescents. Because of the development of a large national database on normative BP levels throughout childhood, the ability to identify children who have abnormally elevated BP has improved. On the basis of developing evidence, it is now apparent that primary hypertension is detectable in the young and occurs commonly. The long-term health risks for hypertensive children and adolescents can be substantial; therefore, it is important that clinical measures be taken to reduce these risks and optimize health outcomes.

The 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 1987 Task Force Report on High Blood Pressure in Children and Adolescents."<sup>1</sup>

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 gender, 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,  $\geq 95$ th 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.<sup>2</sup>
- 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,<sup>2</sup> 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

Received for publication Apr 29, 2004; accepted May 12, 2004.

Reprint requests to Edward J. Roccella, National High Blood Pressure Education Program, National Heart, Lung, and Blood Institute, National Institutes of Health, Bldg 31, Room 4A10, Center Dr, MSC 2480, Bethesda, MD 20892. E-mail: roccele@nhlbi.nih.gov

This supplement is a work of the US government, published in the public domain by the American Academy of Pediatrics.

scientific evidence was classified by the system used in the JNC 7.<sup>2</sup> 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 on-site meeting of the working group was conducted to discuss additional 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 diastolic BP (DBP) that is  $\geq 95$ th percentile for gender, age, and height on  $\geq 3$  occasions.
- Prehypertension in children is defined as average SBP or DBP levels that are  $\geq 90$ th percentile but  $< 95$ th percentile.
- As with adults, adolescents with BP levels  $\geq 120/80$  mm Hg should be considered prehypertensive.
- A patient with BP levels  $> 95$ th 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 are  $< 90$ th percentile for gender, age, and height. Hypertension is defined as average SBP or DBP that is  $\geq 95$ th percentile for gender, age, and height on at least 3 separate occasions. Average SBP or DBP levels that are  $\geq 90$ th percentile but  $< 95$ th 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  $\geq 120/80$  mm Hg and recommends the application of preventive health-related behaviors, or therapeutic lifestyle changes, for individuals having SBP levels that exceed 120 mm Hg.<sup>2</sup> It is now recommended that, as with adults, children and adolescents with BP levels  $\geq 120/80$  mm Hg but  $< 95$ th percentile should be considered prehypertensive.

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

### MEASUREMENT OF BP 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  $> 3$  years old who are seen in medical care settings should have their BP measured at least once during every health care episode. Children  $< 3$  years old should have their BP measured in special circumstances (see Table 1).

The BP tables are based on auscultatory measurements; therefore, the preferred method of measurement is auscultation. 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 (ie,  $\sim 2$  cm above the cubital fossa). The use of the bell of the stethoscope may allow softer Korotkoff sounds to be heard better.<sup>3,4</sup> 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.<sup>5</sup> 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.<sup>6,7</sup> The right arm is preferred in repeated measures of BP for consistency and comparison with standard tables and because of the possibility of coarctation of the aorta, which might lead to false (low) readings in the left arm.<sup>8</sup>

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 2 cuffs may be needed for use in adolescents.

**TABLE 1.** Conditions Under Which Children  $< 3$  Years Old Should Have BP Measured

History of prematurity, very low birth weight, 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

By convention, an appropriate cuff size is a cuff with an inflatable bladder width that is at least 40% of the arm circumference at a point midway between the olecranon and the acromion (see [www.americanheart.org/presenter.jhtml?identifier=576](http://www.americanheart.org/presenter.jhtml?identifier=576)).<sup>9,10</sup> For such a cuff to be optimal for an arm, the cuff bladder length should cover 80% to 100% of the circumference of the arm.<sup>1,11</sup> 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 (eg, infant or 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.<sup>12</sup>

SBP is determined by the onset of the “tapping” Korotkoff sounds (K1). Population data in children<sup>1</sup> and risk-associated epidemiologic data in adults<sup>13</sup> 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 mm Hg. Under these circumstances, the BP measurement should be repeated with less pressure on the head of the stethoscope.<sup>4</sup> 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.<sup>14</sup> Because of its environmental toxicity, mercury has been increasingly removed from health care settings. Aneroid manometers are quite accurate when calibrated on a semi-annual basis<sup>15</sup> 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.<sup>16</sup> 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,<sup>17</sup> and they do not always closely match BP values obtained by auscultation.<sup>18</sup> Oscillometric devices must be validated on a regular basis. Protocols for validation

have been developed,<sup>19,20</sup> 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.<sup>16</sup> 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, in which frequent BP measurement is needed. An elevated BP reading obtained with an oscillometric device should be repeated by 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 (ie, 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.

#### ABPM

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.<sup>21–23</sup> 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, ie, 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.

#### BP TABLES

- BP standards based on gender, age, and height provide a precise classification of BP according to body size.
- The revised BP tables now include the 50th, 90th, 95th, and 99th percentiles (with standard deviations) by gender, age, and height.

In children and adolescents, the normal range of BP is determined by body size and age. BP standards that are based on gender, age, and height provide a more precise classification of BP according to body size. This approach avoids misclassifying children who are very tall or very short.

The BP tables are revised to include the new height

**TABLE 2.** Recommended Dimensions for BP Cuff Bladders

Age Range	Width, cm	Length, cm	Maximum Arm Circumference, cm*
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 the bladder to encircle arm by at least 80%.

**TABLE 3.** BP Levels for Boys by Age and Height Percentile

Age, y	BP Percentile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							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
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

The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean. For research purposes, the SDs in Table B1 allow one to compute BP Z scores and percentiles for boys with height percentiles given in Table 3 (ie, 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; and 95% = 1.645, and then computed according to the methodology in steps 2 through 4 described in Appendix B. For children with height percentiles other than these, follow steps 1 through 4 as described in Appendix B.



**TABLE 4.** BP Levels for Girls by Age and Height Percentile

Age, y	BP Percentile	SBP, mm Hg								DBP, mm Hg					
		Percentile of Height								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
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

\* The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean. For research purposes, the SDs in Table B1 allow one to compute BP Z scores and percentiles for girls with height percentiles given in Table 4 (ie, 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; and 95% = 1.645 and then computed according to the methodology in steps 2 through 4 described in Appendix B. For children with height percentiles other than these, follow steps 1 through 4 as described in Appendix B.

percentile data ([www.cdc.gov/growthcharts](http://www.cdc.gov/growthcharts))<sup>24</sup> 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 gender and age are given for boys and girls in Tables 3 and 4. Although new data have been added, the gender, 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 decision-making in the plan for evaluation. Standards for SBP and DBP for infants <1 year old are available.<sup>25</sup> In children <1 year old, 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](http://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 <90th percentile. If the BP is ≥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 >120/80 mm Hg, the patient should be considered to be prehypertensive even if this value is <90th percentile. This BP level typically occurs for SBP at 12 years old and for DBP at 16 years old.

If the child's BP (systolic or diastolic) is ≥95th percentile, the child may be hypertensive, and the measurement must be repeated on at least 2 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 mm Hg >95th percentile; these children would be managed differently from hypertensive children who have BP levels that are 15 to 20 mm Hg 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 to 10 mm Hg 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 mm Hg above the 99th percentile. Stage 2 hypertension is the designation for BP levels that are

**TABLE 5.** Classification of Hypertension in Children and Adolescents, With Measurement Frequency and Therapy Recommendations

	SBP or DBP Percentile*	Frequency of BP Measurement	Therapeutic Lifestyle Changes	Pharmacologic Therapy
Normal	<90th	Recheck at next scheduled physical examination Recheck in 6 mo	Encourage healthy diet, sleep, and physical activity	—
Prehypertension	90th to <95th or if BP exceeds 120/80 even if <90th percentile up to <95th percentile†		Weight-management counseling if overweight; introduce physical activity and diet management‡	None unless compelling indications such as chronic kidney disease, diabetes mellitus, heart failure, or LVH exist
Stage 1 hypertension	95th–99th percentile plus 5 mm Hg	Recheck in 1–2 wk or sooner if the patient is symptomatic; if persistently elevated on 2 additional occasions, evaluate or refer to source of care within 1 mo	Weight-management counseling if overweight; introduce physical activity and diet management‡	Initiate therapy based on indications in Table 6 or if compelling indications (as shown above) exist
Stage 2 hypertension	>99th percentile plus 5 mm Hg	Evaluate or refer to source of care within 1 wk or immediately if the patient is symptomatic	Weight-management counseling if overweight; introduce physical activity and diet management‡	Initiate therapy§

\* For gender, age, and height measured on at least 3 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 Study eating plan could benefit from consultation with a registered or licensed nutritionist to get them started.

§ More than 1 drug may be required.

>5 mm Hg 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 the JNC 7.<sup>2</sup>

#### Using the BP 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 <90th percentile is normal.
  - BP between the 90th and 95th percentile is prehypertension. In adolescents, BP  $\geq$ 120/80 mm Hg is prehypertension, even if this figure is <90th percentile.
  - BP >95th percentile may be hypertension.
6. If the BP is >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 >95th percentile, BP should be staged. If stage 1 (95th percentile to the 99th percentile plus 5 mm Hg), BP measurements should be repeated on 2 more occasions. If hypertension is confirmed, evaluation should proceed as described in Table 7. If BP is stage 2 (>99th percentile plus 5 mm Hg), 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.

#### 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 because of 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.
- Because of 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 ~30% of overweight children (BMI >95th percentile).<sup>26</sup> The strong association of high BP with obesity and the marked increase in the prevalence of childhood obesity<sup>27</sup> 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.<sup>28,29</sup> The clustering of other CVD risk factors that are included in the insulin-resistance syndrome (high triglycerides, low high-density lipoprotein cholesterol, truncal obesity, hyperinsulinemia) is significantly greater among children with high BP than in children with normal BP.<sup>30</sup> Recent reports from studies that examined childhood data estimate that the insulin-resistance syndrome is present in 30% of overweight children with BMI >95th percentile.<sup>31</sup> 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.<sup>31,32</sup> 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 high-density lipoprotein cholesterol, 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 >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 (eg, 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,

**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

heart failure, and stroke in adults.<sup>33,34</sup> Although limited data are available, they suggest an association of sleep-disordered breathing and higher BP in children.<sup>35,36</sup>

Approximately 15% of children snore, and at least 1% to 3% have sleep-disordered breathing.<sup>35</sup> 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.<sup>37</sup>(table 1.1). BEARS addresses 5 major sleep domains that provide a simple but comprehensive screen for the major sleep disorders affecting children 2 to 18 years old. 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 ~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 plan-

**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 $\geq$ 95th percentile
BUN, creatinine, electrolytes, urinalysis, and urine culture	R/O renal disease and chronic pyelonephritis	All children with persistent BP $\geq$ 95th percentile
CBC	R/O anemia, consistent with chronic renal disease	All children with persistent BP $\geq$ 95th percentile
Renal U/S	R/O renal scar, congenital anomaly, or disparate renal size	All children with persistent BP $\geq$ 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 $\geq$ 95th percentile; family history of hypertension or CVD; 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 $\geq$ 95th percentile
Retinal exam	Identify retinal vascular changes	Patients with comorbid risk factors and BP 90th–94th percentile; all patients with BP $\geq$ 95th percentile
Additional evaluation as indicated		
ABPM	Identify white-coat hypertension, abnormal diurnal BP pattern, BP load	Patients in whom white-coat hypertension is suspected, and when other information on BP pattern is needed
Plasma renin determination	Identify low renin, suggesting mineralocorticoid-related disease	Young children with stage 1 hypertension and any child or adolescent with stage 2 hypertension
Renovascular imaging	Identify renovascular disease	Positive family history of severe hypertension Young children with stage 1 hypertension and any child or adolescent with stage 2 hypertension
Isotopic scintigraphy (renal scan)		
MRA		
Duplex Doppler flow studies		
3-Dimensional CT		
Arteriography: DSA or classic		
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

BUN, blood urea nitrogen; CBC, complete blood count; R/O, rule out; U/S, ultrasound.

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



ning 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 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 with those with stage 1 hypertension.<sup>38</sup> 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 (eg, 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 to 20 mm Hg 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 examination findings in hypertensive children.<sup>39</sup>

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, ~15% of children with arteriographically evident renal artery stenosis have normal PRA values.<sup>40-42</sup> Assays for direct measurement of renin, a different technique than PRA, are commonly used, although extensive normative data in children and adolescents are unavailable.

#### Evaluation for Possible Renovascular Hypertension

Renovascular hypertension is a consequence of an arterial lesion or lesions impeding blood flow to 1 or both kidneys or to  $\geq 1$  intrarenal segments.<sup>43,44</sup> Affected children usually, but not invariably, have markedly elevated BP.<sup>40,44</sup> Evaluation for renovascular disease also should be considered in infants or

**TABLE 8.** Examples of Physical Examination Findings Suggestive of Definable Hypertension

	Finding*	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	Adenotonsillar hypertrophy	Suggests association with sleep-disordered breathing (sleep apnea), snoring
Height/weight	Growth retardation	Chronic renal failure
	Obesity (high BMI)	Primary hypertension
Head and neck	Truncal obesity	Cushing syndrome, insulin resistance syndrome
	Moon facies	Cushing syndrome
	Elfin facies	Williams syndrome
Skin	Webbed neck	Turner syndrome
	Thyromegaly	Hyperthyroidism
	Pallor, flushing, diaphoresis	Pheochromocytoma
	Acne, hirsutism, striae	Cushing syndrome, anabolic steroid abuse
	Café-au-lait spots	Neurofibromatosis
Chest	Adenoma sebaceum	Tuberous sclerosis
	Malar rash	Systemic lupus erythematosus
	Acanthosis nigricans	Type 2 diabetes
	Widely spaced nipples	Turner syndrome
	Heart murmur	Coarctation of the aorta
Abdomen	Friction rub	Systemic lupus erythematosus (pericarditis), collagen-vascular disease, end stage renal disease with uremia
	Apical heave	LVH/chronic hypertension
	Mass	Wilms tumor, neuroblastoma, pheochromocytoma
	Epigastric/flank bruit	Renal artery stenosis
Genitalia	Palpable kidneys	Polycystic kidney disease, hydronephrosis, multicystic-dysplastic kidney, mass (see above)
	Ambiguous/virilization	Adrenal hyperplasia
Extremities	Joint swelling	Systemic lupus erythematosus, collagen vascular disease
	Muscle weakness	Hyperaldosteronism, Liddle syndrome

Adapted from Flynn JT. *Prog Pediatr Cardiol.* 2001;12:177–188.

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

children with other known predisposing factors such as prior umbilical artery catheter placements or neurofibromatosis.<sup>44,45</sup> A number of newer diagnostic techniques are presently available for evaluation of renovascular disease, but experience in their use in pediatric patients is limited. Consequently, the recommended approaches generally use older techniques such as standard intraarterial angiography, digital-subtraction angiography (DSA), and scintigraphy (with or without angiotensin-converting enzyme [ACE] inhibition).<sup>44</sup> As technologies evolve, children should be referred for imaging studies to centers that have expertise in the radiologic evaluation of childhood hypertension.

### Invasive Studies

Intraarterial DSA with contrast is used more frequently than standard angiography, but because of intraarterial injection, this method remains invasive. DSA can be accomplished also 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.<sup>46</sup>

Newer imaging techniques may be used in chil-

dren 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.<sup>47–49</sup> Imaging with magnetic resonance requires that the patient be relatively immobile for extended periods, which is 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 reconstructions of computed tomography (CT) images, or spiral CT with contrast, seem promising in evaluating children who may have renovascular disease.<sup>50</sup>

### 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,<sup>2,51</sup> 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.<sup>52,53</sup> Even hypertension that is less severe contributes to target-organ damage when it occurs with other chronic conditions such as chronic kidney disease.<sup>54–56</sup> Two autopsy studies<sup>57,58</sup> 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<sup>59</sup> and large artery compliance<sup>60</sup> in young adults. Even healthy adolescents with clustering of cardiovascular risk factors demonstrate elevated carotid thickness,<sup>61,62</sup> 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<sup>63</sup> 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% to 38% of children and adolescents with mild, untreated BP elevation.<sup>64–66</sup> Daniels et al<sup>67</sup> evaluated 130 children and adolescents with persistent BP elevation. They reported that 55% of patients had a left ventricular mass index >90th percentile, and 14% had left ventricular mass index >51 g/m<sup>2.7</sup>, 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% had concentric hypertrophy, a pattern that is associated with higher risk for cardiovascular outcomes in adults, and 30% had eccentric hypertrophy, which is associated with intermediate risk for cardiovascular outcomes.<sup>67</sup>

In addition, abnormalities of the retinal vasculature have been reported in adults with hypertension.<sup>68</sup> Few studies of retinal abnormalities have been conducted in children with hypertension. Skalina et al<sup>69</sup> evaluated newborns with hypertension and reported the presence of hypertensive retinal abnormalities in ~50% 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, the intraventricular septal thickness, and the thickness of the left ventricular posterior wall and can be calculated as: left ventricle mass (g) = 0.80 [1.04(intraventricular septal thickness + left ventricular end-diastolic dimension + left ventricular posterior wall thickness)<sup>3</sup> – (left ventricular end-diastolic dimension)<sup>3</sup>] + 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<sup>70</sup> when measurements are made according to the criteria of the American Society of Echocardiography.<sup>71</sup>

Heart size is closely associated with body size.<sup>72</sup> 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<sup>2.7</sup>) be used to index left ventricular mass as described by de Simone et al.<sup>73</sup> 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, because 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<sup>2.7</sup>. This cutpoint is >99th percentile for children and adolescents and is associated with increased morbidity in adults with hypertension.<sup>73</sup> Other references exist for normal children,<sup>74</sup> 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 decision-making. 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. Additional 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 those with hypertension.
- Family-based intervention improves success.

Evidence that supports the efficacy of nonpharmacologic interventions for BP reduction in the treatment of hypertension in children and adolescents is limited. 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<sup>2</sup>: weight reduction in overweight or obese individuals<sup>75</sup>; increased intake of fresh vegetables, fruits, and low-fat dairy (the Dietary Approaches to Stop Hypertension Study eating plan)<sup>76</sup>; dietary sodium reduction<sup>76,77</sup>; increased physical activity<sup>78</sup>; and moderation of alcohol consumption.<sup>79</sup> Smoking cessation has significant cardiovascular benefits.<sup>32</sup> As information on chronic sleep problems evolves, interventions to improve sleep quality also may have a beneficial effect on BP.<sup>80</sup>

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<sup>81–83</sup> in association with weight.<sup>84,85</sup> 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.<sup>30,86–90</sup> Weight control not only decreases BP, it also decreases BP sensitivity to salt<sup>88</sup> and decreases other cardiovascular risk factors such as dyslipidemia and insulin resistance.<sup>32</sup> In studies that achieve a reduction in BMI of ~10%, short-term reductions in BP were in the range of 8 to 12 mm Hg. Although difficult, weight loss, if successful, is extremely effective.<sup>32,91–93</sup> Identifying a complication of overweight such as hypertension can be a helpful motivator for patients and families to make changes. Weight control can render pharmacologic 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 additional weight gain. Steps can be implemented in the primary care setting

even with limited staff and time resources.<sup>32,91</sup> The patient should be encouraged to self-monitor time spent in sedentary activities, including watching television and playing video or computer games, and set goals to progressively decrease these activities to <2 hours per day.<sup>94</sup> 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).<sup>94–96</sup> 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.<sup>32,91,93,97,98</sup> 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 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.<sup>91–93</sup>

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,<sup>99,100</sup> thus far the evidence is too limited to support a clinical recommendation.<sup>101</sup> Lower BP has been associated in children and adolescents with an increased intake of potassium,<sup>100–103</sup> magnesium,<sup>100,101</sup> folic acid,<sup>101,104</sup> unsaturated fat,<sup>100,105,106</sup> and fiber<sup>100,101,104</sup> and lower dietary intake of total fat.<sup>100,101</sup> 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 to 3 mm Hg.<sup>100,103,107–110</sup> Data from 1 randomized trial suggest that sodium intake in infancy may affect BP in adolescence.<sup>111</sup> Similarly, some evidence indicates that breastfeeding may be associated with lower BP in childhood.<sup>112,113</sup> The current recommendation for adequate daily sodium intake is only 1.2 g/day for 4- to 8-year-olds and 1.5 g/day for older children.<sup>114</sup> Because this amount of sodium is substantially lower than current dietary intakes, lowering dietary sodium from the current usual intake may have future benefit. Reduced sodium intake, with calorie restriction, may account for some of the BP improvement associated with weight loss.

Regular physical activity has cardiovascular benefits. A recent meta-analysis that combined 12 randomized trials, for a total of 1266 children and adolescents, concluded that physical activity leads to a small but not statistically significant decrease in BP.<sup>115</sup> However, both regular physical activity and decreasing sedentary activities (such as watching television and playing video or electronic games) are important components of pediatric obesity treatment



and prevention.<sup>32,91–93</sup> 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 <2 hours per day are recommended for the prevention of obesity, hypertension, and other cardiovascular risk factors.<sup>94–96</sup> 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.<sup>116</sup>

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 low-fat 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 which case BP should be lowered to <90th percentile.
- Severe, symptomatic hypertension should be treated with intravenous antihypertensive drugs.

In adults, hypertension is typically a life-long 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.<sup>117</sup> 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,<sup>118,119</sup> 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 first task force report on BP control in children.<sup>120</sup> The number of drugs that have been studied systematically in children has increased also, 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.<sup>121–123</sup> 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 Best Pharmaceuticals for Children Act<sup>123–125</sup> 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 support the preferential use of specific antihypertensive drugs in adults.<sup>2,126</sup> 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,<sup>25,120</sup> 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,<sup>127–130</sup> have been studied in children and, based on short-term use,

TABLE 9. Antihypertensive Drugs for Outpatient Management of Hypertension in Children 1–17 Years Old\*

Class	Drug	Dose†	Dosing Interval	Evidence‡	FDA Labeling§	Comments
ACE inhibitor	Benazepril	Initial: 0.2 mg/kg per d up to 10 mg/d Maximum: 0.6 mg/kg per d up to 40 mg/d	qd	RCT	Yes	<ol style="list-style-type: none"> <li>1. All ACE inhibitors are contraindicated in pregnancy; females of childbearing age should use reliable contraception.</li> <li>2. Check serum potassium and creatinine periodically to monitor for hyperkalemia and azotemia.</li> <li>3. Cough and angioedema are reportedly less common with newer members of this class than with captopril.</li> <li>4. Benazepril, enalapril, and lisinopril labels contain information on the preparation of a suspension; captopril may also be compounded into a suspension.</li> <li>5. FDA approval for ACE inhibitors with pediatric labeling is limited to children <math>\geq 6</math> years of age and to children with creatinine clearance <math>\geq 30</math> ml/min per 1.73m<sup>2</sup>.</li> </ol>
	Captopril	Initial: 0.3–0.5 mg/kg/dose Maximum: 6 mg/kg per d	tid	RCT, CS	No	
	Enalapril	Initial: 0.08 mg/kg per d up to 5 mg/d Maximum: 0.6 mg/kg per d up to 40 mg/d	qd-bid	RCT	Yes	
	Fosinopril	Children $>50$ kg: Initial: 5–10 mg/d Maximum: 40 mg/d	qd	RCT	Yes	
	Lisinopril	Initial: 0.07 mg/kg per d up to 5 mg/d Maximum: 0.6 mg/kg per d up to 40 mg/d	qd	RCT	Yes	
Angiotensin-receptor blocker	Quinapril	Initial: 5–10 mg/d Maximum: 80 mg/d	qd	RCT, EO	No	<ol style="list-style-type: none"> <li>1. All ARBs are contraindicated in pregnancy; females of childbearing age should use reliable contraception.</li> <li>2. Check serum potassium, creatinine periodically to monitor for hyperkalemia and azotemia.</li> <li>3. Losartan label contains information on the preparation of a suspension.</li> <li>4. FDA approval for ARBs is limited to children <math>\geq 6</math> years of age and to children with creatinine clearance <math>\geq 30</math> ml/min per 1.73m<sup>2</sup>.</li> </ol>
	Irbesartan	6–12 years: 75–150 mg/d $\geq 13$ years: 150–300 mg/d	qd	CS	Yes	
	Losartan	Initial: 0.7 mg/kg per d up to 50 mg/d Maximum: 1.4 mg/kg per d up to 100 mg/d	qd	RCT	Yes	
$\alpha$ - and $\beta$ -Blocker	Labetalol	Initial: 1–3 mg/kg per d Maximum: 10–12 mg/kg per d up to 1200 mg/d	bid	CS, EO	No	<ol style="list-style-type: none"> <li>1. Asthma and overt heart failure are contraindications.</li> <li>2. Heart rate is dose-limiting.</li> <li>3. May impair athletic performance.</li> <li>4. Should not be used in insulin-dependent diabetics.</li> </ol>
$\beta$ -Blocker	Atenolol	Initial: 0.5–1 mg/kg per d Maximum: 2 mg/kg per d up to 100 mg/d	qd-bid	CS	No	<ol style="list-style-type: none"> <li>1. Noncardioselective agents (propranolol) are contraindicated in asthma and heart failure.</li> <li>2. Heart rate is dose-limiting.</li> <li>3. May impair athletic performance.</li> <li>4. Should not be used in insulin-dependent diabetics.</li> <li>5. A sustained-release formulation of propranolol is available that is dosed once-daily.</li> </ol>
	Bisoprolol/HCTZ	Initial: 2.5/6.25 mg/d Maximum: 10/6.25 mg/d	qd	RCT	No	
	Metoprolol	Initial: 1–2 mg/kg per d Maximum: 6 mg/kg per d up to 200 mg/d	bid	CS	No	
	Propranolol	Initial: 1–2 mg/kg per d Maximum: 4 mg/kg per d up to 640 mg/d	bid-tid	RCT, EO	Yes	
Calcium channel blocker	Amlodipine	Children 6–17 years: 2.5–5 mg once daily	qd	RCT	Yes	<ol style="list-style-type: none"> <li>1. Amlodipine and isradipine can be compounded into stable extemporaneous suspensions.</li> <li>2. Felodipine and extended-release nifedipine tablets must be swallowed whole.</li> <li>3. Isradipine is available in both immediate-release and sustained-release formulations; sustained-release form is dosed qd or bid.</li> <li>4. May cause tachycardia.</li> </ol>
	Felodipine	Initial: 2.5 mg/d Maximum: 10 mg/d	qd	RCT, EO	No	
	Isradipine	Initial: 0.15–0.2 mg/kg per d Maximum: 0.8 mg/kg per d up to 20 mg/d	tid-qid	CS, EO	No	
	Extended-release nifedipine	Initial: 0.25–0.5 mg/kg per d Maximum: 3 mg/kg per d up to 120 mg/d	qd-bid	CS, EO	No	

**TABLE 9.** Antihypertensive Drugs for Outpatient Management of Hypertension in Children 1–17 Years Old\*

Class	Drug	Dose†	Dosing Interval	Evidence‡	FDA Labeling§	Comments
Central $\alpha$ -agonist	Clonidine	Children $\geq 12$ years: Initial: 0.2 mg/d Maximum: 2.4 mg/d	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.
Diuretic	HCTZ	Initial: 1 mg/kg per d Maximum: 3 mg/kg per d up to 50 mg/d	qd	EO	Yes	1. All patients treated with diuretics should have electrolytes monitored shortly after initiating therapy and periodically thereafter.
	Chlorthalidone	Initial: 0.3 mg/kg per d Maximum: 2 mg/kg per d up to 50 mg/d	qd	EO	No	2. Useful as add-on therapy in patients being treated with drugs from other drug classes.
	Furosemide	Initial: 0.5–2.0 mg/kg per dose Maximum: 6 mg/kg per d	qd-bid	EO	No	3. Potassium-sparing diuretics (spironolactone, triamterene, amiloride) may cause severe hyperkalemia, especially if given with ACE inhibitor or ARB. 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.
	Spironolactone	Initial: 1 mg/kg per d Maximum: 3.3 mg/kg per d up to 100 mg/d	qd-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.
	Triamterene	Initial: 1–2 mg/kg per d Maximum: 3–4 mg/kg per d up to 300 mg/d	bid	EO	No	
Peripheral $\alpha$ -antagonist	Amiloride	Initial: 0.4–0.625 mg/kg per d Maximum: 20 mg/d	qd	EO	No	
	Doxazosin	Initial: 1 mg/d Maximum: 4 mg/d	qd	EO	No	May cause hypotension and syncope, especially after first dose.
	Prazosin	Initial: 0.05–0.1 mg/kg per d Maximum: 0.5 mg/kg per d	tid	EO	No	
Vasodilator	Terazosin	Initial: 1 mg/d Maximum: 20 mg/d	qd	EO	No	
	Hydralazine	Initial: 0.75 mg/kg per d Maximum: 7.5 mg/kg per d up to 200 mg/d	qid	EO	Yes	1. Tachycardia and fluid retention are common side effects. 2. Hydralazine can cause a lupus-like syndrome in slow acetylators.
	Minoxidil	Children <12 years: Initial: 0.2 mg/kg per d Maximum: 50 mg/d Children $\geq 12$ years: Initial: 5 mg/d Maximum: 100 mg/d	qd-tid	CS, EO	Yes	3. Prolonged use of minoxidil can cause hypertrichosis. 4. Minoxidil is usually reserved for patients with hypertension resistant to multiple drugs.

FDA indicates Federal Drug Administration; ARB indicates 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 indicates 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.

**TABLE 10.** Antihypertensive Drugs for Management of Severe Hypertension in Children 1–17 Years Old

Drug	Class	Dose*	Route	Comments
Most useful† Esmolol	$\beta$ -Blocker	100–500 $\mu\text{g}/\text{kg}$ per 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 per dose	IV, IM	Should be given every 4 h when given IV bolus. Recommended dose is lower than FDA label.
Labetalol	$\alpha$ - and $\beta$ -Blocker	Bolus: 0.2–1.0 mg/kg per dose up to 40 mg/dose Infusion: 0.25–3.0 mg/kg per h	IV bolus or infusion	Asthma and overt heart failure are relative contraindications.
Nicardipine	Calcium channel blocker	1–3 $\mu\text{g}/\text{kg}$ per min	IV infusion	May cause reflex tachycardia.
Sodium nitroprusside	Vasodilator	0.53–10 $\mu\text{g}/\text{kg}$ per min	IV infusion	Monitor cyanide levels with prolonged (>72 h) use or in renal failure; or coadminister with sodium thiosulfate.
Occasionally useful‡ Clonidine	Central $\alpha$ -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 per 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 $\mu\text{g}/\text{kg}$ per 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 per dose	po	Stable suspension can be compounded.
Minoxidil	Vasodilator	0.1–0.2 mg/kg per dose	po	Most potent oral vasodilator, long-acting.

FDA indicates Food and Drug Administration; IM, intramuscular; IV, intravenous; po, oral.

\* All dosing recommendations are based on expert opinion or case series data except as otherwise noted.

† Useful for hypertensive emergencies and some hypertensive urgencies.

‡ Useful for hypertensive urgencies and some hypertensive emergencies.

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.<sup>2</sup>

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/hydrochlorothiazide,<sup>131</sup> 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 <95th percentile for gender, age, and height, whereas for children with chronic renal disease, diabetes, or hypertensive target-organ damage, the goal BP should be <90th percentile for gender, age, and height. Again, this approach is similar to the recommended treatment of hypertension in adults with additional cardiovascular risk factors or comorbid conditions.<sup>2</sup>

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 also may 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 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



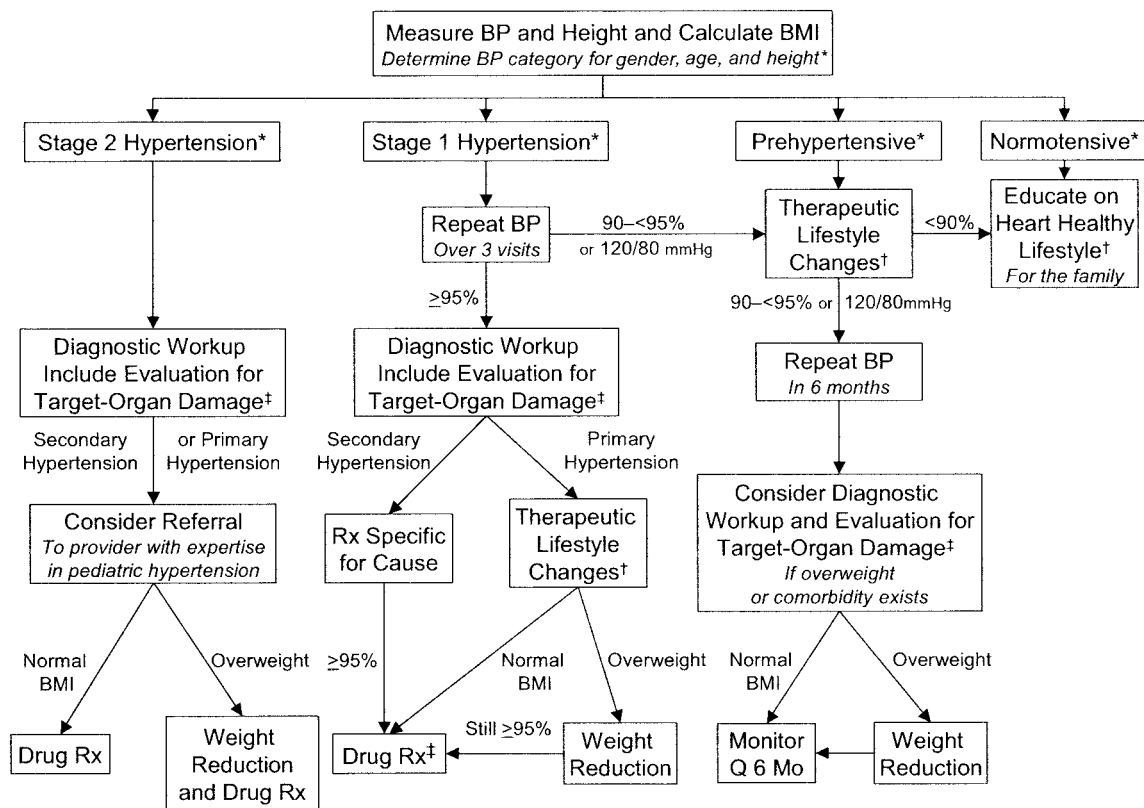


Fig 1. Management algorithm. Rx indicates prescription; Q, every. \*, See Tables 3, 4, and 5; †, diet modification and physical activity; ‡, especially if younger, very high BP, little or no family history, diabetic, or other risk factors.

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  $\leq 25\%$  over the first 8 hours after presentation and then gradually normalizing the BP over 26 to 48 hours.<sup>132,133</sup> 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 decision-making. The algorithm also emphasizes the inclusion of evaluation for target-organ damage in

children with established stage 1 and stage 2 hypertension.

#### APPENDIX A. DEMOGRAPHIC DATA

See page 572.

#### APPENDIX B. COMPUTATION OF BLOOD PRESSURE PERCENTILES FOR ARBITRARY GENDER, AGE, AND HEIGHT

To compute the SBP percentile of a boy who is age  $y$  years and height  $h$  inches with  $SBP = x$  mm Hg:

1. Refer to the most recent Centers for Disease Control and Prevention 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 ( $\mu$ ) for boys of age  $y$  years and height  $h$  inches given by

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

where  $\alpha, \beta_1, \dots, \beta_4$  and  $\gamma_1, \dots, \gamma_4$  are given in the third column of Table B1.

3. Then convert the boy's observed SBP to a  $Z$  score ( $Zbp$ ) given by  $Zbp = (x - \mu) / \sigma$ , where  $\sigma$  is given in the third column of Table B1.
4. To convert the BP  $Z$  score to a percentile ( $P$ ), compute  $P = \Phi(Zbp) \times 100\%$ , where  $\Phi(Z)$  = area under a standard normal distribution to the left of

APPENDIX A. Demographic Data on Height/Blood Pressure Distribution Curves by Study Population

Source	Age, y	Gender		Ethnic Group							Persons Visits SBP Available	Persons Visits DBP.5 Available	Total No. of Persons Visits
		Male	Female	Black	Hispanic	White	Asian	Native American	Other	Missing			
National Institutes of Health Pittsburgh	6–17	1896	1751	600	0	2963	0	0	84	0	3647	3609	3647
	1–5	148	137	108	0	176	0	0	0	1	3647	3609	3647
Dallas	13–17	5916	5649	5266	1570	4729	0	0	0	0	285	0	285
											893	0	893
Bogalusa	1–17	3751	3607	2480	0	4878	0	0	0	0	11 565	11 565	11 565
											21 860	21 852	21 860
Houston	3–17	1457	1377	637	1341	748	23	0	0	85	7358	0	7358
											15 882	0	15 882
South Carolina	4–17	3167	3263	3110	0	3320	0	0	0	0	2834	0	2834
											2834	0	2834
Iowa	5–17	2099	1993	0	0	4092	0	0	0	0	6430	6368	6430
											6430	6368	6430
Providence	1–3	230	231	24	4	431	0	0	2	0	4092	0	4092
											4092	0	4092
Minnesota	9–17	9991	9418	3422	555	11 311	1677	644	1800	0	461	371	461
											898	560	898
NHANES III	5–17	2465	2577	1770	1830	1324	64	10	12	32	19 409	19 207	19 409
											19 409	19 207	19 409
NHANES 1999–2000	8–17	1041	1063	605	988	437	0	0	74	0	5042	4304	5042
											5042	4304	5042
Total (percent of total)	1–17	32 161 (51)	31 066 (49)	18 022 (29)	6288 (10)	34 409 (54)	1764 (3)	654 (1)	1972 (3)	118 (0)	2104	2076	2104
											2104	2076	2104
											63 227	47 500	63 227
											83 091	57 976	83 091

DBP .5, DBP (Korotkoff 5).

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

**TABLE B1.** Regression Coefficients From Blood Pressure Regression Models

Variable Name	Symbol	Systolic BP		Diastolic BP5	
		Male	Female	Male	Female
Intercept	$\alpha$	102.19768	102.01027	61.01217	60.50510
Age					
Age-10	$\beta_1$	1.82416	1.94397	0.68314	1.01301
(Age-10) <sup>2</sup>	$\beta_2$	0.12776	0.00598	-0.09835	0.01157
(Age-10) <sup>3</sup>	$\beta_3$	0.00249	-0.00789	0.01711	0.00424
(Age-10) <sup>4</sup>	$\beta_4$	-0.00135	-0.00059	0.00045	-0.00137
Normalized height					
Zht	$\gamma_1$	2.73157	2.03526	1.46993	1.16641
Zht <sup>2</sup>	$\gamma_2$	-0.19618	0.02534	-0.07849	0.12795
Zht <sup>3</sup>	$\gamma_3$	-0.04659	-0.01884	-0.03144	-0.03869
Zht <sup>4</sup>	$\gamma_4$	0.00947	0.00121	0.00967	-0.00079
Standard deviation	$\sigma$	10.7128	10.4855	11.6032	10.9573
$\rho^*$		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

The coefficients were obtained from mixed-effects linear regression models. Diastolic BP5 indicates diastolic measurement at Korotkoff 5.

\* The value of  $\rho$  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 1 age.

Z. Thus, if  $Zbp = 1.28$ , then  $\Phi(Zbp) = 0.90$  and the BP percentile =  $0.90 \times 100\% = 90\%$ .

- To compute percentiles for SBP for girls, DBP (K5) for boys, and DBP (K5) for girls, use the regression coefficients from the fourth, fifth, and sixth columns of Table B1.

For example, a 12-year-old boy, with height at the 90th percentile for his age-gender group, has a height Z score = 1.28, and his expected SBP ( $\mu$ ) is  $\mu = 102.19768 + 1.82416(2) + 0.12776(2^2) + 0.00249(2^3) - 0.00135(2^4) + 2.73157(1.28) - 0.19618(1.28)^2 - 0.04659(1.28)^3 + 0.00947(1.28)^4 = 109.46$  mm Hg. Suppose his actual SBP is 120 mm Hg ( $x$ ); his SBP Z score then equals  $(x - \mu)/\sigma = (120 - 109.46)/10.7128 = 0.984$ . The corresponding SBP percentile =  $\Phi(0.984) \times 100\% = 83.7$ th percentile.

## REFERENCES

### Classification of Evidence

The scheme used for classification of the evidence is as follows: M indicates 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 follow-up studies); X, cross-sectional survey (also known as prevalence studies); PR, previous review or position statements; and C, clinical interventions (nonrandomized). These symbols are appended to the citations in the reference list in parentheses. 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](http://www.nhlbi.nih.gov/about/nhbpep/index.htm)).<sup>2,134-138</sup>

- National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents: a working group report from the National High Blood Pressure Education Program. *Pediatrics*. 1996;98:649-658(PR)
- Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA*. 2003;289:2560-2572(PR)

- Prineas RJ, Jacobs D. Quality of Korotkoff sounds: bell vs diaphragm, cubital fossa vs brachial artery. *Prev Med*. 1983;12:715-719
- Londe S, Klitzner TS. Auscultatory blood pressure measurement—effect of pressure on the head of the stethoscope. *West J Med*. 1984;141:193-195
- Prineas RJ. Blood pressure in children and adolescents. In: Bulpitt CJ, ed. *Epidemiology of Hypertension*. New York, NY: Elsevier; 2000:86-105. Birkenhager WH and Reid JL, eds. *Handbook of Hypertension*, Vol. 20.
- Mourad A, Carney S, Gillies A, Jones B, Nanra R, Trevillian P. Arm position and blood pressure: a risk factor for hypertension? *J Hum Hypertens*. 2003;17:389-395
- Netea RT, Lenders JW, Smits P, Thien T. Both body and arm position significantly influence blood pressure measurement. *J Hum Hypertens*. 2003;17:459-462
- Rocchini AP. Coarctation of the aorta and interrupted aortic arch. In: Moller JH, Hoffmann U, eds. *Pediatric Cardiovascular Medicine*. New York, NY: Churchill Livingstone; 2000:570
- Gomez-Marin O, Prineas RJ, Rastam L. Cuff bladder width and blood pressure measurement in children and adolescents. *J Hypertens*. 1992;10:1235-1241
- American Heart Association. Home monitoring of high blood pressure. Available at: [www.americanheart.org/presenter.jhtml?identifier=576](http://www.americanheart.org/presenter.jhtml?identifier=576). Accessed March 18, 2004
- Prineas RJ. Measurement of blood pressure in the obese. *Ann Epidemiol*. 1991;1:321-336(PR)
- Ostchega Y, Prineas RJ, Paulose-Ram R, Grim CM, Willard G, Collins D. National Health and Nutrition Examination Survey 1999-2000: effect of observer training and protocol standardization on reducing blood pressure measurement error. *J Clin Epidemiol*. 2003;56:768-774
- Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360:1903-1913(M)
- Jones DW, Appel LJ, Sheps SG, Roccella EJ, Lenfant C. Measuring blood pressure accurately: new and persistent challenges. *JAMA*. 2003;289:1027-1030(PR)
- Canzanello VJ, Jensen PL, Schwartz GL. Are aneroid sphygmomanometers accurate in hospital and clinic settings? *Arch Intern Med*. 2001;161:729-731(PR)
- Butani L, Morgenstern BZ. Are pitfalls of oscillometric blood pressure measurements preventable in children? *Pediatr Nephrol*. 2003;18:313-318(PR)
- Kaufmann MA, Pargger H, Drop LJ. Oscillometric blood pressure measurements by different devices are not interchangeable. *Anesth Analg*. 1996;82:377-381
- Park MK, Menard SW, Yuan C. Comparison of auscultatory and oscillometric blood pressures. *Arch Pediatr Adolesc Med*. 2001;155:50-53(RA)
- O'Brien E, Pickering T, Asmar R, et al. Working Group on Blood Pressure Monitoring of the European Society of Hypertension Inter-

- national Protocol for validation of blood pressure measuring devices in adults. *Blood Press Monit*. 2002;7:3-17(PR)
20. O'Brien E, Coats A, Owens P, et al. Use and interpretation of ambulatory blood pressure monitoring: recommendations of the British hypertension society. *BMJ*. 2000;320:1128-1134(PR)
  21. Sorof JM, Portman RJ. Ambulatory blood pressure measurements. *Curr Opin Pediatr*. 2001;13:133-137
  22. Simckes AM, Srivastava T, Alon US. Ambulatory blood pressure monitoring in children and adolescents. *Clin Pediatr (Phila)*. 2002;41:549-564(PR)
  23. Lurbe E, Sorof JM, Daniels SR. Clinical and research aspects of ambulatory blood pressure monitoring in children. *J Pediatr*. 2004;144:7-16(PR)
  24. Centers for Disease Control and Prevention, National Center for Health Statistics. 2000 CDC growth charts: United States. Available at: www.cdc.gov/growthcharts. Accessed March 18, 2004
  25. Task Force on Blood Pressure Control in Children. Report of the Second Task Force on Blood Pressure Control in Children—1987. National Heart, Lung, and Blood Institute, Bethesda, Maryland. *Pediatrics*. 1987;79:1-25(PR)
  26. Sorof J, Daniels S. Obesity hypertension in children: a problem of epidemic proportions. *Hypertension*. 2002;40:441-447(PR)
  27. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999-2000. *JAMA*. 2002;288:1728-1732(X)
  28. Reaven GM. Insulin resistance/compensatory hyperinsulinemia, essential hypertension, and cardiovascular disease. *J Clin Endocrinol Metab*. 2003;88:2399-2403
  29. National Cholesterol Education Program. Third report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. NIH Publication 02-5215. Bethesda, MD: National Heart, Lung, and Blood Institute, National Cholesterol Education Program; 2002 (PR)
  30. Sinaiko AR, Steinberger J, Moran A, Prineas RJ, Jacobs DR Jr. Relation of insulin resistance to blood pressure in childhood. *J Hypertens*. 2002;20:509-517(RA)
  31. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the Third National Health and Nutrition Examination Survey, 1988-1994. *Arch Pediatr Adolesc Med*. 2003;157:1-827(X)
  32. Williams CL, Hayman LL, Daniels SR, et al. Cardiovascular health in childhood: a statement for health professionals from the Committee on Atherosclerosis, Hypertension, and Obesity in the Young (AHOY) of the Council on Cardiovascular Disease in the Young, American Heart Association. *Circulation*. 2002;106:143-160(PR)
  33. Quan SF, Gersh BJ. Cardiovascular consequences of sleep-disordered breathing: past, present and future: report of a workshop from the National Center on Sleep Disorders Research and the National Heart, Lung, and Blood Institute. *Circulation*. 2004;109:951-957
  34. Strohl KP. Invited commentary: to sleep, perchance to discover. *Am J Epidemiol*. 2002;155:394-395
  35. Marcus CL, Greene MG, Carroll JL. Blood pressure in children with obstructive sleep apnea. *Am J Respir Crit Care Med*. 1998;157:1098-1103(X)
  36. Enright PL, Goodwin JL, Sherrill DL, Quan JR, Quan SF. Blood pressure elevation associated with sleep-related breathing disorder in a community sample of white and Hispanic children: the Tucson Children's Assessment of Sleep Apnea study. *Arch Pediatr Adolesc Med*. 2003;157:901-904(F)
  37. Mindell JA, Owens JA. *A Clinical Guide to Pediatric Sleep: Diagnosis and Management of Sleep Problems*. Philadelphia, PA: Lippincott, Williams & Wilkins; 2003:10
  38. Sinaiko AR. Hypertension in children. *N Engl J Med*. 1996;335:1968-1973(PR)
  39. Flynn JT. Evaluation and management of hypertension in childhood. *Prog Pediatr Cardiol*. 2001;12:177-188(PR)
  40. Hiner LB, Falkner B. Renovascular hypertension in children. *Pediatr Clin North Am*. 1993;40:123-140(PR)
  41. Dillon MJ, Ryness JM. Plasma renin activity and aldosterone concentration in children. *Br Med J*. 1975;4(5992):316-319 (X)
  42. Guzzetta PC, Potter BM, Ruley EJ, Majd M, Bock GH. Renovascular hypertension in children: current concepts in evaluation and treatment. *J Pediatr Surg*. 1989;24:1236-1240(C)
  43. Watson AR, Balfe JW, Hardy BE. Renovascular hypertension in childhood: a changing perspective in management. *J Pediatr*. 1985;106:366-372
  44. Dillon MJ. The diagnosis of renovascular disease. *Pediatr Nephrol*. 1997;11:366-372(PR)
  45. Mena E, Bookstein JJ, Holt JF, Fry WJ. Neurofibromatosis and renovascular hypertension in children. *Am J Roentgenol Radium Ther Nucl Med*. 1973;118:39-45(RE)
  46. Shahdaddpuri J, Frank R, Gauthier BG, Siegel DN, Trachtman H. Yield of renal arteriography in the evaluation of pediatric hypertension. *Pediatr Nephrol*. 2000;14:816-819(RE)
  47. Binkert CA, Debatin JF, Schneider E, et al. Can MR measurement of renal artery flow and renal volume predict the outcome of percutaneous transluminal renal angioplasty? *Cardiovasc Intervent Radiol*. 2001;24:233-239(F)
  48. Marcos HB, Choyke PL. Magnetic resonance angiography of the kidney. *Semin Nephrol*. 2000;20:450-455(PR)
  49. Debatin JF, Spritzer CE, Grist TM, et al. Imaging of the renal arteries: value of MR angiography. *AJR Am J Roentgenol*. 1991;157:981-990(F)
  50. Vade A, Agrawal R, Lim-Dunham J, Hartoin D. Utility of computed tomographic renal angiogram in the management of childhood hypertension. *Pediatr Nephrol*. 2002;17:741-747(RE)
  51. MacMahon S, Peto R, Cutler J, et al. Blood pressure, stroke, and coronary heart disease. Part 1, prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. *Lancet*. 1990;335:765-774(F)
  52. Still JL, Cottom D. Severe hypertension in childhood. *Arch Dis Child*. 1967;42:34-39(PR)
  53. Gill DG, Mendes dC, Cameron JS, Joseph MC, Ogg CS, Chantler C. Analysis of 100 children with severe and persistent hypertension. *Arch Dis Child*. 1976;51:951-956(F)
  54. Johnstone LM, Jones CL, Grigg LE, Wilkinson JL, Walker RG, Powell HR. Left ventricular abnormalities in children, adolescents and young adults with renal disease. *Kidney Int*. 1996;50:998-1006(X)
  55. Mitsnefes MM, Daniels SR, Schwartz SM, Khoury P, Strife CF. Changes in left ventricular mass in children and adolescents during chronic dialysis. *Pediatr Nephrol*. 2001;16:318-323(F)
  56. Mitsnefes MM, Kimball TR, Witt SA, Glascock BJ, Khoury PR, Daniels SR. Left ventricular mass and systolic performance in pediatric patients with chronic renal failure. *Circulation*. 2003;107:864-868(X)
  57. Berenson GS, Srinivasan SR, Bao W, Newman WP III, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. *N Engl J Med*. 1998;338:1650-1656(F)
  58. McGill HC Jr, McMahan CA, Zieske AW, Malcom GT, Tracy RE, Strong JP. Effects of nonlipid risk factors on atherosclerosis in youth with a favorable lipoprotein profile. *Circulation*. 2001;103:1546-1550
  59. Davis PH, Dawson JD, Riley WA, Lauer RM. Carotid intimal-medial thickness is related to cardiovascular risk factors measured from childhood through middle age: the Muscatine Study. *Circulation*. 2001;104:2815-2819(F)
  60. Arnett DK, Glasser SP, McVeigh G, et al. Blood pressure and arterial compliance in young adults: the Minnesota Children's Blood Pressure Study. *Am J Hypertens*. 2001;14:200-205(F)
  61. Knoflach M, Kiechl S, Kind M, et al. Cardiovascular risk factors and atherosclerosis in young males: ARMY study (Atherosclerosis Risk-Factors in Male Youngsters). *Circulation*. 2003;108:1064-1069(X)
  62. Sanchez A, Barth JD, Zhang L. The carotid artery wall thickness in teenagers is related to their diet and the typical risk factors of heart disease among adults. *Atherosclerosis*. 2000;152:265-266
  63. Barnes VA, Treiber FA, Davis H. Impact of transcendental meditation on cardiovascular function at rest and during acute stress in adolescents with high normal blood pressure. *J Psychosom Res*. 2001;51:597-605(RA)
  64. Belsha CW, Wells TG, McNiece KL, Seib PM, Plummer JK, Berry PL. Influence of diurnal blood pressure variations on target organ abnormalities in adolescents with mild essential hypertension. *Am J Hypertens*. 1998;11:410-417(F)
  65. Sorof JM, Alexandrov AV, Cardwell G, Portman RJ. Carotid artery intimal-medial thickness and left ventricular hypertrophy in children with elevated blood pressure. *Pediatrics*. 2003;111:61-66
  66. Hanevold C, Waller J, Daniels S, Portman R, Sorof J. The effects of obesity, gender, and ethnic group on left ventricular hypertrophy and geometry in hypertensive children: a collaborative study of the International Pediatric Hypertension Association. *Pediatrics*. 2004;113:328-333(X)
  67. Daniels SR, Loggie JM, Khoury P, Kimball TR. Left ventricular geometry and severe left ventricular hypertrophy in children and adolescents with essential hypertension. *Circulation*. 1998;97:1907-1911(X)
  68. Svardsudd K, Wedel H, Aurell E, Tibblin G. Hypertensive eye ground changes. Prevalence, relation to blood pressure and prognostic importance. The study of men born in 1913. *Acta Med Scand*. 1978;204:159-167(F)



69. Skalina ME, Annable WL, Kliegman RM, Fanaroff AA. Hypertensive retinopathy in the newborn infant. *J Pediatr*. 1983;103:781-786(X)
70. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol*. 1986;57:450-458(RE)
71. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation*. 1978;58:1072-1083
72. Daniels SR, Kimball TR, Morrison JA, Khoury P, Witt S, Meyer RA. Effect of lean body mass, fat mass, blood pressure, and sexual maturation on left ventricular mass in children and adolescents. Statistical, biological, and clinical significance. *Circulation*. 1995;92:3249-3254(X)
73. de Simone G, Daniels SR, Devereux RB, et al. Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. *J Am Coll Cardiol*. 1992;20:1251-1260(F)
74. Daniels SR, Kimball TR, Morrison JA, Khoury P, Meyer RA. Indexing left ventricular mass to account for differences in body size in children and adolescents without cardiovascular disease. *Am J Cardiol*. 1995;76:699-701(X)
75. He J, Whelton PK, Appel LJ, Charleston J, Klag MJ. Long-term effects of weight loss and dietary sodium reduction on incidence of hypertension. *Hypertension*. 2000;35:544-549(F)
76. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *N Engl J Med*. 2001;344:3-10(RA)
77. Vollmer WM, Sacks FM, Ard J, et al. Effects of diet and sodium intake on blood pressure: subgroup analysis of the DASH-sodium trial. *Ann Intern Med*. 2001;135:1019-1028(RA)
78. Whelton SP, Chin A, Xin X, He J. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. *Ann Intern Med*. 2002;136:493-503(M)
79. Xin X, He J, Frontini MG, Ogden LG, Motsamai OI, Whelton PK. Effects of alcohol reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension*. 2001;38:1112-1117(M)
80. Ayas NT, White DP, Manson JE, et al. A prospective study of sleep duration and coronary heart disease in women. *Arch Intern Med*. 2003;163:205-209(X)
81. Cook NR, Gillman MW, Rosner BA, Taylor JO, Hennekens CH. Combining annual blood pressure measurements in childhood to improve prediction of young adult blood pressure. *Stat Med*. 2000;19:2625-2640(F)
82. Lauer RM, Mahoney LT, Clarke WR. Tracking of blood pressure during childhood: the Muscatine Study. *Clin Exp Hypertens A*. 1986;8:515-537(F)
83. Lauer RM, Clarke WR. Childhood risk factors for high adult blood pressure: the Muscatine Study. *Pediatrics*. 1989;84:633-641(F)
84. Clarke WR, Woolson RF, Lauer RM. Changes in ponderosity and blood pressure in childhood: the Muscatine Study. *Am J Epidemiol*. 1986;124:195-206(F)
85. Burke V, Beilin LJ, Dunbar D. Tracking of blood pressure in Australian children. *J Hypertens*. 2001;19:1185-1192(F)
86. Figueroa-Colon R, Franklin FA, Lee JY, von Almen TK, Suskind RM. Feasibility of a clinic-based hypocaloric dietary intervention implemented in a school setting for obese children. *Obes Res*. 1996;4:419-429(RA)
87. Wabitsch M, Hauner H, Heinze E, et al. Body-fat distribution and changes in the atherogenic risk-factor profile in obese adolescent girls during weight reduction. *Am J Clin Nutr*. 1994;60:54-60(C)
88. Rocchini AP, Key J, Bondie D, et al. The effect of weight loss on the sensitivity of blood pressure to sodium in obese adolescents. *N Engl J Med*. 1989;321:580-585(C)
89. Rocchini AP, Katch V, Anderson J, et al. Blood pressure in obese adolescents: effect of weight loss. *Pediatrics*. 1988;82:16-23(RA)
90. Sinaiko AR, Gomez-Marín O, Prineas RJ. Relation of fasting insulin to blood pressure and lipids in adolescents and parents. *Hypertension*. 1997;30:1554-1559(X)
91. Robinson TN. Behavioural treatment of childhood and adolescent obesity. *Int J Obes Relat Metab Disord*. 1999;23(suppl 2):S52-S57 (PR)
92. Epstein LH, Myers MD, Raynor HA, Saelens BE. Treatment of pediatric obesity. *Pediatrics*. 1998;101:554-570(PR)
93. Barlow SE, Dietz WH. Obesity evaluation and treatment: expert committee recommendations. The Maternal and Child Health Bureau, Health Resources and Services Administration and the Department of Health and Human Services. *Pediatrics*. 1998;102(3). Available at: [www.pediatrics.org/cgi/content/full/102/3/e29](http://www.pediatrics.org/cgi/content/full/102/3/e29) (PR)
94. Krebs NF, Jacobson MS. Prevention of pediatric overweight and obesity. *Pediatrics*. 2003;112:424-430(PR)
95. U.S. Department of Health and Human Services. *The Surgeon General's Call to Action to Prevent and Decrease Overweight and Obesity*. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, Office of the Surgeon General; 2001 (PR)
96. Gutin B, Owens S. Role of exercise intervention in improving body fat distribution and risk profile in children. *Am J Human Biol*. 1999;11:237-247(RA)
97. Siega-Riz AM, Popkin BM, Carson T. Trends in breakfast consumption for children in the United States from 1965-1991. *Am J Clin Nutr*. 1998;67:748S-756S
98. Warren JM, Henry CJ, Simonite V. Low glycemic index breakfasts and reduced food intake in preadolescent children. *Pediatrics*. 2003;112(5). Available at: [www.pediatrics.org/cgi/content/full/112/5/e414](http://www.pediatrics.org/cgi/content/full/112/5/e414) (RA)
99. Gillman MW, Hood MY, Moore LL, Nguyen US, Singer MR, Andon MB. Effect of calcium supplementation on blood pressure in children. *J Pediatr*. 1995;127:186-192(RA)
100. Simons-Morton DG, Hunsberger SA, Van Horn L, et al. Nutrient intake and blood pressure in the Dietary Intervention Study in Children. *Hypertension*. 1997;29:930-936(RA)
101. Simons-Morton DG, Obarzanek E. Diet and blood pressure in children and adolescents. *Pediatr Nephrol*. 1997;11:244-249(PR)
102. Miller JZ, Weinberger MH, Christian JC. Blood pressure response to potassium supplementation in normotensive adults and children. *Hypertension*. 1987;10:437-442(C)
103. Sinaiko AR, Gomez-Marín O, Prineas RJ. Effect of low sodium diet or potassium supplementation on adolescent blood pressure. *Hypertension*. 1993;21:989-994(RA)
104. Falkner B, Sherif K, Michel S, Kushner H. Dietary nutrients and blood pressure in urban minority adolescents at risk for hypertension. *Arch Pediatr Adolesc Med*. 2000;154:918-922(X)
105. Stern B, Heyden S, Miller D, Latham G, Klimas A, Pilkington K. Intervention study in high school students with elevated blood pressures. Dietary experiment with polyunsaturated fatty acids. *Nutr Metab*. 1980;24:137-147(C)
106. Goldberg RJ, Ellison RC, Hosmer DW Jr, et al. Effects of alterations in fatty acid intake on the blood pressure of adolescents: the Exeter-Andover Project. *Am J Clin Nutr*. 1992;56:71-76(F)
107. Cooper R, Van Horn L, Liu K, et al. A randomized trial on the effect of decreased dietary sodium intake on blood pressure in adolescents. *J Hypertens*. 1984;2:361-366(RA)
108. Falkner B, Michel S. Blood pressure response to sodium in children and adolescents. *Am J Clin Nutr*. 1997;65:618S-621S(PR)
109. Gillum RF, Elmer PJ, Prineas RJ. Changing sodium intake in children. The Minneapolis Children's Blood Pressure Study. *Hypertension*. 1981;3:698-703(RA)
110. Howe PR, Cobiac L, Smith RM. Lack of effect of short-term changes in sodium intake on blood pressure in adolescent schoolchildren. *J Hypertens*. 1991;9:181-186(RA)
111. Geleijnse JM, Hofman A, Witteman JC, Hazebroek AA, Valkenburg HA, Grobbee DE. Long-term effects of neonatal sodium restriction on blood pressure. *Hypertension*. 1997;29:913-917(RA)
112. Martin RM, Ness AR, Gunnell D, Emmett P, Smith GD. Does breastfeeding in infancy lower blood pressure in childhood? The Avon Longitudinal Study of Parents and Children (ALSPAC). *Circulation*. 2004;109:1259-1266(F)
113. Wilson AC, Forsyth JS, Greene SA, Irvine L, Hau C, Howie PW. Relation of infant diet to childhood health: seven year follow up of cohort of children in Dundee infant feeding study. *BMJ*. 1998;316:21-25(F)
114. Panel of Dietary Intakes for Electrolytes and Water, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate*. Washington, DC: National Academies Press; 2004. Available at: [www.nap.edu/books/0309091691/html](http://www.nap.edu/books/0309091691/html). Accessed March 18, 2004 (PR)
115. Kelley GA, Kelley KS, Tran ZV. The effects of exercise on resting blood pressure in children and adolescents: a meta-analysis of randomized controlled trials. *Prev Cardiol*. 2003;6:8-16(M)
116. American Academy of Pediatrics, Committee on Sports Medicine and Fitness. Athletic participation by children and adolescents who have systemic hypertension. *Pediatrics*. 1997;99:637-638(PR)
117. Klag MJ, Whelton PK, Randall BL, et al. Blood pressure and end-stage renal disease in men. *N Engl J Med*. 1996;334:13-18(F)
118. Yusuf HR, Giles WH, Croft JB, Anda RF, Casper ML. Impact of multiple risk factor profiles on determining cardiovascular disease risk. *Prev Med*. 1998;27:1-9(X)

119. Kavey RE, Daniels SR, Lauer RM, Atkins DL, Hayman LL, Taubert K. American Heart Association guidelines for primary prevention of atherosclerotic cardiovascular disease beginning in childhood. *Circulation*. 2003;107:1562–1566(PR)
120. Blumenthal S, Epps RP, Heavenrich R, et al. Report of the task force on blood pressure control in children. *Pediatrics*. 1977;59:797–820(PR)
121. The Food and Drug Administration Modernization Act of 1997. Pub L 105–115
122. Wells TG. Trials of antihypertensive therapies in children. *Blood Press Monit*. 1999;4:189–192(PR)
123. Flynn JT. Successes and shortcomings of the Food and Drug Modernization Act. *Am J Hypertens*. 2003;16:889–891(PR)
124. Best Pharmaceuticals for Children Act of 2002. Pub L 107–109
125. U.S. Department of Health and Human Services, National Institutes of Health. List of drugs for which pediatric studies are needed. *Fed Regist*. 2003;68:2789–2790
126. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA*. 2002;288:2981–2997(RA)
127. Wells T, Frame V, Soffer B, et al. A double-blind, placebo-controlled, dose-response study of the effectiveness and safety of enalapril for children with hypertension. *J Clin Pharmacol*. 2002;42:870–880(F)
128. Soffer B, Zhang Z, Miller K, Vogt BA, Shahinfar S. A double-blind, placebo-controlled, dose-response study of the effectiveness and safety of lisinopril for children with hypertension. *Am J Hypertens*. 2003;16:795–800(RA)
129. Sakarcan A, Tenney F, Wilson JT, et al. The pharmacokinetics of irbesartan in hypertensive children and adolescents. *J Clin Pharmacol*. 2001;41:742–749
130. Trachtman H, Frank R, Mahan JD, et al. Clinical trial of extended-release felodipine in pediatric essential hypertension. *Pediatr Nephrol*. 2003;18:548–553(RA)
131. Sorof JM, Cargo P, Graepel J, et al. Beta-blocker/thiazide combination for treatment of hypertensive children: a randomized double-blind, placebo-controlled trial. *Pediatr Nephrol*. 2002;17:345–350(RA)
132. Adelman RD, Coppo R, Dillon MJ. The emergency management of severe hypertension. *Pediatr Nephrol*. 2000;14:422–427(PR)
133. Vaughan CJ, Delanty N. Hypertensive emergencies. *Lancet*. 2000;356:411–417(PR)
134. Sheps SG, Roccella EJ. Reflections on the sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Curr Hypertens Rep*. 1999;1:342–345(PR)
135. Ingelfinger JR. Renovascular disease in children. *Kidney Int*. 1993;43:493–505(PR)
136. World Health Organization. World health report 2002: reducing risks, promoting healthy life. Geneva, Switzerland: 2002. Available at: [www.who.int/whr/2002](http://www.who.int/whr/2002). Accessed March 11, 2004
137. U.S. Department of Health and Human Services, National Heart, Lung, and Blood Institute. National High Blood Pressure Education Program. Available at: [www.nhlbi.nih.gov/about/nhbpep/index.htm](http://www.nhlbi.nih.gov/about/nhbpep/index.htm). Accessed March 18, 2004
138. JNC 6. National High Blood Pressure Education Program. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med*. 1997;157:2413–2446(PR)

Copyright of Pediatrics is the property of American Academy of Pediatrics and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.