

Assessment and management of hypertension in children and adolescents

Brian W. McCrindle

Abstract | The epidemic of overweight and obesity in youth is increasing the prevalence of prehypertension and hypertension among children and adolescents. The younger the child is at presentation and the more severe the blood pressure abnormality, the more likely a secondary cause of hypertension is to be present. Measurement of blood pressure in children requires adaptation to the age and size of the child. Interpretation must be related to normative values specific for age, sex, and height. Evaluation is primarily aimed at identifying secondary causes of hypertension, associated comorbidities, additional risk factors, and evidence of target-organ damage. Ambulatory blood pressure monitoring is emerging as a useful tool for evaluation of some patients, particularly for those with suspected 'white coat' hypertension. Management of prehypertension and hypertension is directed at the underlying cause, exacerbating factors, and the magnitude of the blood pressure abnormality. Healthy behavioral changes are a primary management tool for treating hypertension and, more particularly, prehypertension and for addressing other cardiovascular risk factors, such as obesity. Pharmacological management is reserved for patients with hypertension who do not respond to behavioral changes, have additional cardiovascular risk factors or diabetes, are symptomatic, or have developed target-organ damage.

McCrindle, B. W. *Nat. Rev. Cardiol.* 7, 155–163 (2010); published online 12 January 2010; doi:10.1038/nrcardio.2009.231

MedscapeCME Continuing Medical Education online

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of MedscapeCME and Nature Publishing Group.

MedscapeCME is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

MedscapeCME designates this educational activity for a maximum of 1.0 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. All other clinicians completing this activity will be issued a certificate of participation. To participate in this journal CME activity: (1) review the learning objectives and author disclosures; (2) study the education content; (3) take the post-test and/or complete the evaluation at <http://www.medscapecme.com/journal/nrcardio>; and (4) view/print certificate.

Learning objectives

Upon completion of this activity, participants should be able to:

- 1 Describe the association between hypertension and left ventricular hypertrophy in children and adolescents.
- 2 Describe the parameters used to define hypertension in children and adolescents.
- 3 Define prehypertension and hypertension in children and adolescents.
- 4 Describe the types of blood pressure abnormalities found in essential and other types of hypertension in children.
- 5 List the most likely causes of secondary hypertension in children.

Competing interests

The author, the Journal Editor B. Mearns and the CME questions author D. Lie declare no competing interests.

Introduction

Hypertension is a well-recognized cardiovascular risk factor in adults, contributing to morbidity and mortality from myocardial infarction, stroke, congestive heart failure, peripheral vascular disease, retinopathy, and end-stage renal disease. No study has been of sufficient duration to determine whether hypertension identified in youth is related to cardiovascular disease in adulthood. In addition, manifest atherosclerotic cardiovascular disease is extremely rare in childhood. Nonetheless, evidence to support an association between elevated blood pressure and atherosclerosis in youth is available from pathology studies and studies of noninvasive markers of atherosclerosis. Blood pressure assessment in youth, either by direct measurement (Bogalusa Heart Study)¹ or by inference (Pathobiological Determinants of Atherosclerosis in Youth Study)^{2,3} is independently correlated with the percentage of intimal surface in the coronary arteries and aorta that are affected by early atherosclerotic lesions, including fatty streaks and fibrous plaques. In addition, clustering of elevated blood pressure and other cardiovascular risk factors, as seen with the epidemic of the metabolic syndrome and obesity, is associated with an exponential increase in atherosclerotic vascular involvement.¹ These correlations are also evident when non-invasive measures of vascular involvement are used in children and young adults. Ultrasonography has shown that increased blood pressure in children and adolescents is associated with endothelial dysfunction in systemic arteries, increased thickness of the arterial intima-media

The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada. brian.mccrindle@sickkids.ca

Key points

- The epidemic of youth obesity is increasing the prevalence of hypertension, primarily related to the metabolic syndrome, which accelerates atherosclerosis and increases the likelihood of target-organ damage
- While primary hypertension is more prevalent in older children and adolescents, secondary hypertension is more prevalent in infants and younger children and those with more severe blood pressure elevation
- Accurate blood pressure measurement in children requires attention to technique, particularly the use of the appropriate cuff size matched to the size of the child's extremity
- For children, blood pressure measurements must be related to population-derived percentile levels based on sex, age, and height, which inform definitions of prehypertension and hypertension
- Ambulatory blood pressure monitoring can be useful in assessing 'white coat' and masked hypertension, blood pressure variability, children at high risk of cardiovascular disease, and effectiveness of antihypertensive agents
- Lifestyle behavioral change is the cornerstone of management, but clinical trials of pharmacological agents in children have expanded the armamentarium for those patients who meet criteria for antihypertensive treatment

Table 1 | Classification of hypertension in youth*

Category	Systolic or diastolic blood pressure percentile
Normal	<90 th
Prehypertension	90–95 th , or if blood pressure exceeds 120/80mmHg even if <90 th up to <95 th
Stage 1 hypertension	95–99 th plus 5 mmHg
Stage 2 hypertension	>99 th plus 5 mmHg

*Percentiles are based on normative values related to sex, age, and height percentile. If systolic and diastolic categories are different, classify by the higher category.

complex, impaired arterial compliance and distensibility, and increased levels of inflammatory markers.^{4–6} Research using ultrafast CT has shown a positive correlation between blood pressure and coronary artery calcification in adolescents and young adults.⁷ These studies provide consistent and compelling evidence that the atherosclerotic process begins in youth, and is accelerated by increased blood pressure.

In addition to accelerated atherosclerosis, there is also evidence of target-organ damage—primarily left ventricular hypertrophy (LVH). LVH has been reported in about one third of children and adolescents with mild, untreated hypertension and in a greater proportion of those with persistent hypertension.^{4,8,9} LVH can be concentric or eccentric, with concentric being associated with a higher risk of cardiovascular outcomes.⁸ The risk of LVH increases with the severity of hypertension in adolescents, but the odds of LVH are also increased in those with masked and milder hypertension (but not with 'white coat' hypertension), compared with normotensive adolescents.¹⁰ Lande *et al.* showed that, after matching for BMI, children with 'white coat' hypertension had greater left ventricular mass index than normotensive controls, but less than patients with persistent hypertension (26% with LVH).¹¹ Studies have also shown that the presence of concomitant obesity further increases the prevalence

of LVH in youths with hypertension.⁹ In addition, LVH has been shown to be correlated with increased carotid intima–media thickness—an early marker for atherosclerosis—and increasing adiposity in children and adolescents with hypertension.⁴ The working group of the National High Blood Pressure Education Program on Children and Adolescents recommended that the presence of LVH be used to influence therapeutic decisions in patients with hypertension.¹² In this Review, I provide a general overview of hypertension, highlighting evaluation and management aspects of this condition that are specific to infants, children, and adolescents.

Definition of hypertension in youth

The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents¹² provides systolic and diastolic blood pressure levels corresponding to the 50th, 90th, 95th, and 99th percentiles based on the child's sex, age, and height percentile. The height percentile is plotted from normal growth charts.¹³ The blood pressure tables and instructions for using them are available in the report¹² and online.¹⁴

Blood pressure status can be classified on the basis of systolic and diastolic blood pressure percentiles (Table 1). Measurements below the 90th percentile are considered normal. Prehypertension or hypertension are present when measurements of either systolic or diastolic pressure, or both, are at or above the 90th percentile. Blood pressure should be measured at least twice during the same assessment, and confirmed over at least three separate occasions.¹⁵ Prehypertension is present when the measurement is at or above the 90th percentile, but less than the 95th percentile, as well as when blood pressure reaches or exceeds 120/80 mmHg in an adolescent. Hypertension is present when repeated measurements are at or above the 95th percentile. Hypertension is further classified as either stage 1, in which blood pressure ranges from the 95th to the 99th percentile plus 5 mmHg, or stage 2, where blood pressure is above the 99th percentile plus 5 mmHg. 'White coat' hypertension occurs when the patient's blood pressure remains above the 95th percentile when measured in a clinical setting, but is normal when measured in a familiar setting. If hypertension is confirmed, blood pressure should be measured in both arms and a leg. The classification of blood pressure influences decisions on evaluation and management.

Prevalence of hypertension in youth

Population-based studies of blood pressure in children are important in determining the burden of risk, but cohort studies provide important information regarding tracking (the persistence into adulthood of blood pressure abnormalities noted in childhood), which is an evidence component supporting the need for early intervention to reduce blood pressure. Examination of serial cross-sectional data from the National Health and Nutrition Examination Survey in children aged 8–17 years, showed a trend towards an increase in the prevalence of both prehypertension and hypertension in the US (Figure 1).¹⁶ Each

survey showed a higher prevalence of prehypertension in boys than in girls, whereas the prevalence of hypertension was similar for both sexes. Overweight and, particularly, obesity increased the likelihood of both prehypertension and hypertension. Ethnic differences were also noted; particularly the prevalence of prehypertension was higher in non-Hispanic black girls compared with other ethnic groups.¹⁶ However, given the impact of sex, ethnicity or race, anthropometry, and the influence of both genetic and environmental factors on blood pressure, together with variations in measurement technique and definitions, comparisons of the prevalence of hypertension in different populations can be problematic.

Longitudinal cohort studies aim to determine the degree to which blood pressure tracks over time, particularly from childhood to adulthood, thus supporting the early identification of high-risk individuals. A meta-analysis of 50 cohort studies showed inconsistencies across studies but correlation coefficients for tracking,¹⁷ which were higher for systolic than diastolic blood pressure (0.38 and 0.28, respectively). The strength of the tracking correlations increased with older baseline age and decreased with longer periods of follow-up. Although subtle variations were found, tracking correlations were not significantly influenced by race and ethnicity or geographic population. Tracking of diastolic blood pressure was weaker for females and stronger when automated measurement devices were used.

Etiology of hypertension in youth

Primary or essential hypertension

Primary or essential hypertension is an epidemic public health problem in adults, but has its origins in childhood. The prevalence of hypertension in adults is age dependent. Overall, hypertension affects about 20% of adults in North America, with a low prevalence of optimal treatment and control, which is of particular concern for patients with diabetes.¹⁸ For young adults aged 18–39 years, isolated systolic hypertension is more prevalent, and has been shown to be associated with male sex, current smoking, obesity, and lower educational level.¹⁹ However, obesity in adults is more likely to be associated with isolated diastolic or combined systolic and diastolic hypertension.²⁰ Primary or essential hypertension, as well as predisposing factors, can be identified in children and adolescents. The increasing prevalence of increased body weight and obesity in youth has been associated with a greater prevalence of prehypertension and hypertension. Insulin resistance has been shown to be independently associated with hypertension, in addition to the degree distribution of adiposity.²¹ Sleep abnormalities are prevalent among obese children and adolescents, and contribute to hypertension in this setting.^{22,23} Childhood obesity might accelerate the manifestation and exacerbate primary hypertension in those individuals with a familial predisposition towards developing elevated blood pressure.²⁴ The genetic basis is likely to be polygenic in nature and reflect multiple pathophysiological mechanisms related to blood pressure homeostasis, although single gene defects associated

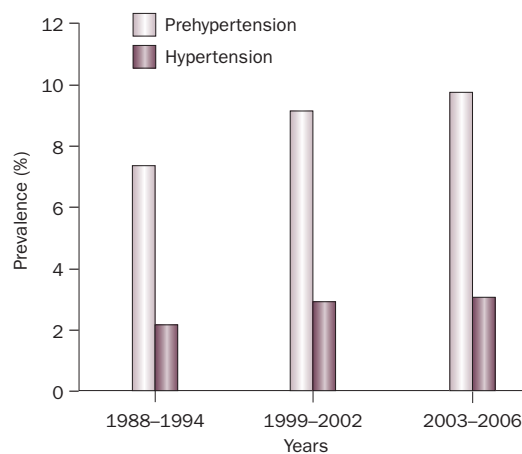


Figure 1 | Prevalence of prehypertension and hypertension in the US between 1988 and 2006 among children aged 8–17 years. Data from Ostchega, Y. *et al.* Trends of elevated blood pressure among children and adolescents: data from the National Health and Nutrition Examination Survey 1988–2006. *Am. J. Hypertens.* **22**, 59–67 (2009).

with hypertension in children are being increasingly defined.²⁵ A study of dietary and lifestyle factors in children showed that elevated systolic blood pressure was related to increased BMI, carbohydrate intake, and time spent in sedentary pursuits.²⁶ Primary or essential hypertension is likely to become increasingly prevalent at younger ages, concomitant with the worsening epidemic of obesity in youth.^{24,27}

Secondary hypertension

By contrast to adult hypertension, high blood pressure in children is likely to have an underlying secondary cause. The younger the child and the greater the degree of blood pressure elevation, the greater the likelihood of a secondary cause. The evaluation of children and adolescents is, therefore, primarily aimed at identifying secondary causes, associated comorbidities, additional risk factors, and evidence of target-organ abnormalities. The prevalence of specific secondary etiologies varies with the age of the patient (Table 2). Exact etiology-specific prevalence estimates are difficult to obtain, given that etiology is not examined in population-based cohort studies, and referral-based clinical studies might be biased towards a particular etiology. Nonetheless, renal parenchymal abnormalities (polycystic renal disease, multicystic dysplastic renal disease, hydronephrosis, chronic pyelonephritis, glomerulonephritides, and chronic renal failure) are estimated to account for about 75% of secondary hypertension in children, followed by renovascular abnormalities (renal artery stenosis or thrombosis, and renal vein thrombosis).²⁸ Both therapeutic and illicit drugs, such as corticosteroids and decongestants, as well as some nutritional substances, such as caffeine, may be iatrogenic causes or contributors to secondary hypertension.

Other etiologies are much less prevalent. Wilms tumor, neuroblastoma and, rarely, pheochromocytoma are childhood tumors associated with hypertension.

Table 2 | Prevalent causes of hypertension by age

Age group	Main causes
Neonates	Renal artery/vein thrombosis Congenital renal anomalies Coarctation of the aorta
<1 year	Coarctation of the aorta Renovascular disease Renal parenchymal disease
1–6 years	Renal parenchymal disease Renovascular disease Coarctation of the aorta
7–12 years	Renal parenchymal disease Renovascular disease Primary/essential hypertension
13–18 years	Primary/essential hypertension Medication or substance use Renal parenchymal disease

Williams syndrome is associated with renal artery stenosis, and Turner syndrome is associated with coarctation of the aorta. Endocrinopathies associated with hypertension include hypercortisolism, hyperthyroidism, hyperaldosteronism, and diabetes as well as rare metabolic conditions, such as congenital adrenal hyperplasia. These conditions unbalance normal homeostasis. Neurocutaneous syndromes, such as tuberous sclerosis and neurofibromatosis, can be associated with various pathophysiological mechanisms contributing to hypertension. Systemic lupus erythematosus can lead to renal parenchymal disease and hypertension.

Blood pressure measurement

General screening

Current guidelines recommend that all children over 3 years of age should have their blood pressure assessed as part of routine health maintenance.¹² The setting for assessment should be optimized to reduce distractions and stress, and the patient should be in a relaxed state. Although oscillometric devices are being more frequently used, auscultation and the use of a mercury column sphygmomanometer remains the recommended approach, and the method that was used to derive current normal values of blood pressure upon which cutpoints for decision-making are based.²⁹ Blood pressure measurements above the 90th percentile from oscillometric assessment should be reassessed with the auscultatory method, since normal values based on this method are not available. Elevated measurements demonstrated by either method should be confirmed by repeated assessment at a minimum of three different time points.

For either method, use of an appropriately sized cuff is important, and 80–100% of the inflatable bladder length should encircle the mid-portion of the upper arm. The right arm is preferred, with the child seated (infants can be supine). At least 40% of the arm from the olecranon to the acromion should be covered by the width of the inflatable bladder. Use of a cuff that is too small might falsely elevate readings. Particular care should be taken to ensure the appropriate cuff size when assessing overweight and obese patients. The head of the stethoscope

is placed over the brachial artery pulse, below the lower edge of the cuff. The arm should be relaxed and supported such that the cubital fossa is at the level of the heart. Systolic pressure is taken as the onset of the first Korotkoff sound; disappearance of Korotkoff sounds (the fifth Korotkoff sound) is taken as the diastolic pressure.²⁹ In some children, Korotkoff sounds are evident down to 0 mmHg. In this instance, the measurement should be repeated with less pressure on the head of the stethoscope; if the low pressure measurement persists, then the fourth Korotkoff sound or muffling may be recorded as the diastolic pressure.

Despite the current recommendation for using the fifth Korotkoff sound to indicate diastolic blood pressure, some evidence suggests that the fourth sound might be better. A meta-analysis of 50 cohort studies showed that tracking coefficients tended to be higher for the fourth versus fifth sound, although the difference was not significant.³⁰ Although tracking might be better for diastolic measurements based on the fourth versus the fifth sound, there are systematic differences in the values derived. An analysis of 129 surveys worldwide showed that diastolic blood pressure measured using the fourth sound was consistently 5 mmHg higher than when using the fifth sound.³¹ Successive previous recommendations have advocated use of the fourth sound,³² followed by use of the fourth sound in infants and young children, and the fifth sound in older children and adolescents,³³ followed by the current recommendation for sole use of the fifth sound, based on a growing body of normal values using the fifth sound from the NHANES studies.^{12,34} Current normal values and definitions of hypertension are based on the use of the fifth sound, and this should be taken into account if one uses the fourth sound for assessment. Although sphygmomanometric devices with auscultation are currently recommended for blood pressure measurement, automated devices have gained widespread popularity. These devices are easier to use, digit bias is eliminated, observer variation minimized, and they can be used when auscultation is difficult, particularly in very young children. In addition, these devices have been associated with stronger tracking coefficients.³⁰ However, current normal values and definitions of hypertension are based on the use of sphygmomanometry with auscultation, and this should be taken into account when measuring blood pressure with an automated device. Mercury manometers have been banned in some countries and many health-care institutions because of concerns about toxicity. Newer sphygmomanometric and oscillometric devices have not yet been fully validated, and normal values specific for measurement with these devices are not available. The potential for systematic errors requires further study.

Assessment of young children

For children aged 3 years or younger, blood pressure should be assessed if a secondary condition known to be associated with hypertension is present (Box 1).¹² Blood pressure measurement can be technically challenging in these patients, and the role of pulse palpation or Doppler devices has not been systematically defined. The use of

oscillometric devices might be acceptable. Interpretation of the measurements should take into account the level of cooperation or agitation of the child.

Measurement in the lower extremity

Blood pressure should be measured in the lower extremities when elevated systolic blood pressure is noted in the upper extremities or if congenital heart disease, particularly aortic coarctation, is suspected. The child should be supine, and comparison made to measurements in the upper extremities also obtained while supine. The cuff can be placed around the child's thigh, with auscultation or Doppler assessment of the popliteal artery, or around the calf, with assessment of the posterior tibial or dorsalis pedis artery. A large cuff is required and should cover at least 60% of the distance between either the perineum and the knee, or the knee and the ankle. Blood pressure in the upper extremity should not exceed that of the lower extremity. Distal pulse amplification, or a wide pulse pressure, may cause the lower extremity systolic blood pressure to exceed that of the upper extremity by an average of 5 mmHg in older children and adolescents, although these pressures equalize with exercise.³⁵

Ambulatory blood pressure monitoring

Ambulatory blood pressure monitoring (ABPM) has emerged as a useful modality for assessment of blood pressure in children and has been shown, in adults, to better predict cardiovascular disease and events and the risk of end-organ damage than blood pressure measurements obtained in a clinical setting.^{36,37} Recommendations for standard assessment and normative blood pressure values in children and adolescents exist.³⁸ ABPM is particularly useful in the evaluation of suspected 'white coat' hypertension and masked hypertension, to assess blood pressure variability, and to evaluate the effectiveness of drug therapy for hypertension. ABPM is indicated for evaluation of children with conditions associated with hypertension, including diabetes and unrepaired or repaired aortic coarctation, solid-organ transplantation recipients, and carriers of genes associated with polycystic ovary disease, Williams or Turner syndromes, or neurofibromatosis.¹²

ABPM should be performed by trained personnel using age-appropriate equipment with the correct cuff size on the nondominant arm. Calibration to resting clinic blood pressure measurements should be performed, and recordings made every 20–30 min while the patient is awake and 30–60 min while asleep. Valid interpretation requires an appropriate number of recordings, including a minimum of one reading per hour with at least 40 to 50 readings in total (representing at least 65% to 75% of all possible readings) over the 24 h period. Values that are considerably outside of the expected range should be deleted. Interpretation should be related to specific pediatric normative values for ABPM. The primary measure is the mean systolic and diastolic ambulatory blood pressure over the entire period, and separately for day time and night time. Additional important measurements include an indicator of blood pressure load, calculated as the

Box 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 transplantation
- Malignancy or bone marrow transplantation
- Treatment with drugs known to raise blood pressure
- Other systemic illnesses associated with hypertension (neurofibromatosis, tuberous sclerosis, etc.)
- Evidence of elevated intracranial pressure

Abbreviation: BP, blood pressure. Reproduced with permission from *Pediatrics* Vol. 114, Pages 555–576, © 2004 by the American Academy of Pediatrics.

Table 3 | Classification of hypertension in youth incorporating ABP*

Category	Clinic BP	Mean systolic ABP	Systolic BP load (%)
Normal	<95 th percentile	<95 th percentile	<25
'White coat' hypertension	>95 th percentile	<95 th percentile	<25
Masked hypertension	<95 th percentile	>95 th percentile	>25
Prehypertension	>95 th percentile	<95 th percentile	25–50
Ambulatory hypertension	>95 th percentile	>95 th percentile	25–50
Severe ambulatory hypertension	>95 th percentile	>95 th percentile	>50

*Relates clinic BP to normal values from the Fourth Report; relate ambulatory BP to normal values for ambulatory BP. Abbreviations: ABP, ambulatory blood pressure; BP, blood pressure. Adapted from Urbina, E. et al. *Hypertension* 52, 433–451 (2008).

percentage of readings that exceed the 95th percentile of normative ambulatory values. Night-time dipping is calculated as the percentage fall of mean night-time values versus mean day-time values,³⁹ and blunted dipping may be associated with nephropathy in patients with diabetes.^{40,41} Definitions of hypertension incorporating the contribution of ABPM are shown in Table 3.³⁸

Diagnostic evaluation

Clinical evaluation of patients with prehypertension and hypertension begins with a thorough history and physical examination. The focus of this assessment is to detect symptoms and signs that might be associated with a secondary etiology or reveal the presence of other cardiovascular risk factors or high-risk conditions. A detailed family history should focus on cardiovascular risk factors and disease, and inheritable conditions. Past and current medical history should include a review of medications, substances, and dietary supplements. Symptoms and signs specifically related to hypertension are rare in childhood and usually only evident if hypertension is severe. Symptoms and signs in neonates are nonspecific, and include irritability, lethargy, poor weight gain, respiratory distress, congestive heart failure (tachypnea, tachycardia, hepatomegaly), and seizures. Additional symptoms noted in children and adolescents include fatigue, headache, and visual

Table 4 | Laboratory testing for hypertension in youth

Evaluation	Main diagnostic utility
General	
Urinalysis	Renal disease
Urine culture	Chronic pyelonephritis
Renal ultrasound	Structural renal anomalies, renal scar, malignancy
Blood chemistries (creatinine, urea nitrogen, uric acid, electrolytes, calcium)	Chronic renal failure, endocrinopathies
Complete blood count	Anemia associated with chronic renal failure
Echocardiography	Left ventricular hypertrophy (coarctation of the aorta)
Fasting lipid profile, glucose	Obesity-related metabolic comorbidities
Etiology-specific	
Radionuclide renal scan	Renovascular disease
Renovascular imaging	Renovascular disease
Plasma renin profiling	Mineralocorticoid-related disease, genetic disorders of renal sodium handling
Plasma and urine catecholamines, metanephrines	Catecholamine-mediated hypertension, pheochromocytoma
Plasma and urine steroids	Steroid-mediated hypertension

disturbances. A careful and complete review of systems is essential for identification of symptoms that suggest a specific secondary etiology. Lifestyle assessment should also be included, with detailed evaluation of nutritional intake and dietary behaviors (with attention to sodium, potassium, and calcium intake), physical activity habits, time spent in sedentary pursuits, and smoking, or smoke exposure. A sleep history or assessment is particularly important for obese patients.

Physical examination, in addition to careful assessment of blood pressure, should be focused on assessing cardiovascular risk and detecting signs suggestive of secondary causes. Height and weight should be measured and plotted, and BMI calculated and plotted. Although retinal vasculopathy and papilledema are rare, ophthalmological examination is indicated in patients with severe hypertension. Physical signs of secondary causes can be subtle, such as tachycardia, abdominal bruits, café au lait spots, or thyromegaly, and the assessment should be thorough.

Laboratory evaluation is aimed at screening and evaluation for secondary causes, assessment for associated cardiovascular risk factors, and identification of target-organ damage. Use of testing should be tiered, with some tests included as part of general screening, while more specialized tests are used if a clinical suspicion is present for a specific underlying cause based on history, physical examination, and screening tests. More specialized tests may also be indicated for patients, with stage 1 or 2 hypertension, persistent or worsening hypertension despite treatment, and hypertension in neonates and infants. Particularly with more severe hypertension, the presence of obesity should not preclude more specialized assessment, despite the higher likelihood that the hypertension is primary in nature. A strategy and indication for

general assessment versus specific assessment is shown in Table 4. LVH is the main target-organ damage evident in children and adolescents, and echocardiography is the primary modality for assessment. Left ventricular mass is calculated from measurements made from standardized echocardiographic views using the equation of Devereux and colleagues.⁴² Left ventricular mass must be indexed to body size (lean body mass) and height ($m^{2.7}$).¹² A cutpoint of $51 \text{ g}/m^{2.7}$ (99th percentile) has been used to define LVH, although this is somewhat arbitrary, as the relationship to outcomes for children is unknown. Age-specific reference values for left ventricular mass index in children and adolescents have been reported.⁴³

Management of hypertension in youth

Management of hypertension in children and adolescents should be directed toward the underlying etiology, exacerbating factors, and the magnitude of the blood pressure abnormality. For both primary and secondary hypertension, exacerbating factors, such as poor dietary and physical activity habits, smoking, stress, sleep disturbance, and obesity, should be addressed and minimized. The goal of management is to reduce blood pressure to within the normal range while preventing or reversing target-organ damage. The balance of the risks of therapy versus the benefits should be considered, given that there is no direct evidence to confirm that reducing hypertension in youth affects the patient's cardiovascular health in adulthood; however, indirect evidence exists and is increasing, and is informing the imperative to treat.⁴⁴ The Fourth Report Task Force outlines a general algorithm for management (Figure 2).¹² Uncomplicated primary prehypertension and hypertension can be effectively evaluated and managed by primary-care providers. Pediatric patients with secondary hypertension usually require evaluation and management by a specialist in the particular underlying etiology. Patients with primary hypertension who require pharmacological management might benefit from consultation with and management by a physician with specific expertise in pediatric hypertension, usually a nephrologist or cardiologist.

Nonpharmacological management

Healthy behavioral changes are the primary management tool for treating hypertension and, particularly, prehypertension. However, the main role of lifestyle changes is to prevent and address other cardiovascular risk factors, particularly those that cluster in association with the metabolic syndrome. Given that overweight and obesity both cause primary hypertension and exacerbate primary and secondary hypertension, weight reduction or maintenance is important. Specific health behaviors that should be targeted include dietary modifications, increasing levels of physical activity while decreasing time spent in sedentary pursuits, and eliminating exposure to tobacco smoke. Measures to address stress and disordered sleep should be incorporated as indicated.

Dietary modifications aimed at overweight and obesity could include reduction of cholesterol and fat intake, particularly saturated fat, reducing intake of sweetened

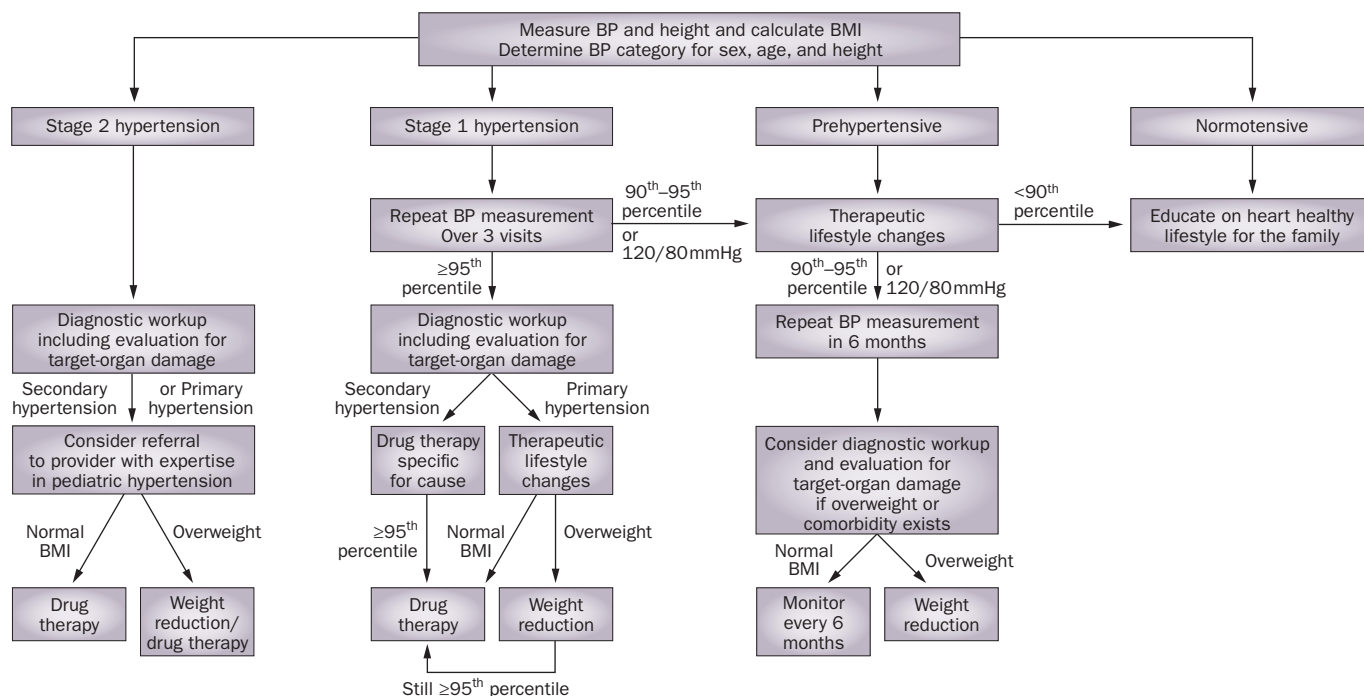


Figure 2 | Management algorithm for blood pressure categories in children and adolescents. Abbreviation: BP, blood pressure. Reproduced with permission from *Pediatrics* Vol. 114, Pages 555–576, © 2004 by the American Academy of Pediatrics.

drinks and processed and fast foods, and increasing intake of fresh vegetables, fruits, and whole grain products. Eating behaviors to target include limitations on portion sizes and snacking, elimination of meal skipping, and increases in the number of meals eaten as a family. Reduction of sodium intake and increase in potassium intake has been advocated as a strategy for reducing hypertension.⁴⁵ Although sodium restriction is difficult to achieve for children, avoiding processed foods, paying attention to sodium content as noted on food labels, and not adding salt to foods is feasible. A recent meta-analysis of 10 controlled trials, including 966 children, concluded that a modest reduction in salt intake was associated with significant reductions in systolic and diastolic blood pressure.⁴⁶ Dietary counseling with a dietician or nutritionist should be family-based and include techniques in motivational interviewing that promote behavioral changes. Online resources, such as “Dietary Approaches to Stop Hypertension” or DASH from the US National Heart, Lung and Blood Institute,⁴⁷ can be useful educational adjuncts. The DASH approach advocates reducing intake of saturated fat and refined sugar, while increasing intake of fruits and vegetables, high fiber foods, and low-fat dairy products. The DASH dietary approach has recently been studied in hypertensive adolescents and been shown to effectively lower systolic blood pressure with improvements in nutritional intake.⁴⁸

Physical activity has also been advocated as an important management tool.¹² A meta-analysis of clinical trials in children and adolescents showed a 1% reduction in systolic blood pressure and 3% reduction in diastolic blood pressure with exercise interventions, although these findings were not statistically significant.⁴⁹

Nonetheless, increases in physical activity, both through aerobic exercise and noncompetitive resistance training, has been recommended for the treatment and prevention of obesity, hypertension, and other cardiovascular risk factors in youth.⁵⁰ A caveat is that patients with uncontrolled stage 2 hypertension should be restricted from participation in competitive sports. At least 60 min of moderate to vigorous daily physical activity, together with a reduction in sedentary pursuits to less than 2 h per day, should be the goal.⁵¹

Pharmacological management

Pharmacological management is reserved for patients with stage 1 or 2 hypertension (Box 2). The presence of other cardiovascular risk factors, such as hyperlipidemia, could be a further indication for pharmacological intervention given the exponential increase in cardiovascular risk associated with multiple risk factors. The goal of pharmacological management is to reduce blood pressure to below the 95th percentile and to prevent target-organ damage. If target-organ damage is present, or the patient has diabetes or chronic renal failure, then the goal is to reduce blood pressure to below the 90th percentile.^{12,52} Several classes of drugs are suitable for nonemergent management, including angiotensin-converting-enzyme (ACE) inhibitors, angiotensin-receptor blockers, β-blockers, calcium-channel blockers, and diuretics. A review by Flynn and Daniels gives pediatric dosing information for these medications.⁵² Many of these drugs used to treat hypertension in adults now have a pediatric indication supported by an appropriate clinical trial.^{52,53} However, none of the studies investigating pharmacological management of hypertension in

Box 2 | Indications for pharmacological management

- Persistent hypertension despite nonpharmacological management
- Secondary hypertension
- Presence of hypertension-related symptoms
- Presence of target-organ damage
- Presence of associated diabetes

children and adolescents have had a cardiovascular end point, and none have compared different drugs in children. In addition, there have been several negative clinical trials, highlighting the need for careful attention to differences in pharmacology between adults and children, pediatric formulations, and appropriate primary end points.⁵⁴ These trials have also been short-term in nature; therefore, long-term and comparative efficacy and safety remain unknown.⁵⁵ As a result, guidelines about the use of specific agents to use have been necessarily vague,^{12,52} and compliance in practice has been suboptimal.^{56–58}

The choice of initial drug remains at the discretion of the patient's care provider. In some circumstances, the choice of drug might be directed by the underlying pathophysiological mechanism. An ACE inhibitor or angiotensin-receptor blocker might be recommended for patients with diabetes and microalbuminuria or proteinuric renal diseases. A clinical trial of intensified blood pressure control with ramipril in hypertensive children with chronic renal disease showed a benefit in terms of freedom from worsening renal function.⁵⁹ A calcium-channel blocker or β -blocker might be recommended for patients with associated migraine headaches, and a β -blocker might be preferred for patients with hypertension after repair of aortic coarctation.⁵² Patients with hypertension primarily associated with obesity, particularly those with higher renin levels, may benefit from an ACE inhibitor.⁵² Those obese patients with low renin levels may benefit from a diuretic. The chosen agent should be started at the lowest dose and titrated as tolerated on the basis of adverse effects and treatment response. A stepped-care approach individualized to the patient has been recommended.⁵² Patients who do not respond to their initial drug may be switched to another drug in that class or to a drug in a different class. Some patients require an additional drug from a different class,

usually one with a complementary mechanism of action. Ongoing monitoring is important, and should address blood pressure response, adverse effects, compliance with both pharmacological and nonpharmacological management, assessment for target-organ damage, and resolution or exacerbation of additional cardiovascular risk factors. Hypertensive emergencies are rare in children and are usually related to underlying renal disease or after repair of aortic coarctation, characterized by severe and symptomatic hypertension with blood pressure above the 99th percentile, and should be treated carefully with intravenous antihypertensive medications.⁶⁰

Conclusions

Adult hypertension often begins in childhood. However, prehypertension and hypertension are distinctly different in children and adolescents than they are in adults, and require evaluation and management reflecting differences in the underlying pathophysiology and the developmental aspects of these conditions. Although manifest cardiovascular disease related to hypertension is rare during childhood, early onset of this condition undoubtedly contributes to an acceleration of cardiovascular disease and target-organ damage, particularly in the presence of the clustering of risk factors associated with obesity. Public-health strategies need to be aimed toward childhood obesity and hypertension if a future epidemic of cardiovascular disease is to be prevented. Such initiatives should be based on an expanded evidence base derived from longitudinal cohort studies, mechanistic studies, and randomized clinical trials of interventions that utilize noninvasive markers of atherosclerosis as vascular end

Review criteria

The majority of the recommendations included in this Review are derived from the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents, published in 2004 from work of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, National Heart, Lung and Blood Institute, National Institutes of Health.¹² Literature from 2004 to 2009 was derived from a Medline search using the terms "blood pressure" and "hypertension" limited to the pediatric age groups. References cited in pertinent review articles and guidelines were also included.

points.

1. Berenson, G. S. *et al.* Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. *N. Engl. J. Med.* **338**, 1650–1656 (1998).
2. McGill, H. C. Jr *et al.* Effects of nonlipid risk factors on atherosclerosis in youth with a favorable lipoprotein profile. *Circulation* **103**, 1546–1550 (2001).
3. Homma, S. *et al.* Histopathological modifications of early atherosclerotic lesions by risk factors—findings in PDAY subjects. *Atherosclerosis* **156**, 389–399 (2001).
4. Sorof, J. M., Alexandrov, A. V., Cardwell, G. & Portman, R. J. Carotid artery intimal–medial thickness and left ventricular hypertrophy in children with elevated blood pressure. *Pediatrics* **111**, 61–66 (2003).
5. Lande, M. B., Carson, N. L., Roy, J. & Meagher, C. C. Effects of childhood primary hypertension on carotid intima media thickness: a matched controlled study. *Hypertension* **48**, 40–44 (2006).
6. Aggoun, Y. *et al.* Impaired endothelial and smooth muscle functions and arterial stiffness appear before puberty in obese children and are associated with elevated ambulatory blood pressure. *Eur. Heart J.* **29**, 792–799 (2008).
7. Mahoney, L. T. *et al.* Coronary risk factors measured in childhood and young adult life are associated with coronary artery calcification in young adults: the Muscatine Study. *J. Am. Coll. Cardiol.* **27**, 277–284 (1996).
8. Daniels, S. R., Loggie, J. M., Khoury, P. & Kimball, T. R. Left ventricular geometry and severe left ventricular hypertrophy in children and adolescents with essential hypertension. *Circulation* **97**, 1907–1911 (1998).
9. 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* **113**, 328–333 (2004).

10. McNiece, K. L. *et al.* Left ventricular hypertrophy in hypertensive adolescents: analysis of risk by 2004 National High Blood Pressure Education Program Working Group staging criteria. *Hypertension* **50**, 392–395 (2007).
11. Lande, M. B. *et al.* Left ventricular mass index in children with white coat hypertension. *J. Pediatr.* **153**, 50–54 (2008).
12. The National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics* **114** (2 Suppl.), 555–576 (2004).
13. Centers for Disease Control and Prevention. National Center for Health Statistics. CDC Growth Charts. [online], <http://www.cdc.gov/growthcharts> (2009).
14. National Heart Lung and Blood Institute, NIH. Information for health professionals, interactive tools and resources. [online], <http://www.nhlbi.nih.gov/health/prof/other/index.htm> (2009).
15. Falkner, B., Gidding, S. S., Portman, R. & Rosner, B. Blood pressure variability and classification of prehypertension and hypertension in adolescence. *Pediatrics* **122**, 238–242 (2008).
16. Ostchega, Y. *et al.* Trends of elevated blood pressure among children and adolescents: data from the National Health and Nutrition Examination Survey 1988–2006. *Am. J. Hypertens.* **22**, 59–67 (2009).
17. Chen, X. & Wang, Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. *Circulation* **117**, 3171–3180 (2008).
18. Joffres, M. R., Hamet, P., MacLean, D. R., L'Italien, G. J. & Fodor, G. Distribution of blood pressure and hypertension in Canada and the United States. *Am. J. Hypertens.* **14**, 1099–1105 (2001).
19. Grebla, R. C., Rodriguez, C. J., Borrell, L. N. & Pickering, T. G. Prevalence and determinants of isolated systolic hypertension among young adults: the 1999–2004 US national health and nutrition examination survey. *J. Hypertens.* doi:10.1097/HJH.0b013e328331b7ff.
20. Chirinos, J. A., Franklin, S. S., Townsend, R. R. & Raji, L. Body mass index and hypertension hemodynamic subtypes in the adult US population. *Arch. Intern. Med.* **169**, 580–586 (2009).
21. Maffei, C. *et al.* Insulin resistance is a risk factor for high blood pressure regardless of body size and fat distribution in obese children. *Nutr. Metab. Cardiovasc. Dis.* (in press).
22. Amin, R. S. *et al.* Twenty four hour ambulatory blood pressure in children with sleep-disordered breathing. *Am. J. Respir. Crit. Care Med.* **169**, 950–956 (2004).
23. Amin, R. *et al.* Activity-adjusted 24-hour ambulatory blood pressure and cardiac remodeling in children with sleep disordered breathing. *Hypertension* **51**, 84–91 (2008).
24. Robinson, R. F., Batisky, D. L., Hayes, J. R., Nahata, M. C. & Mahan, J. D. Body mass index in primary and secondary pediatric hypertension. *Pediatr. Nephrol.* **19**, 1379–1384 (2004).
25. Ingelfinger, J. R. The molecular basis of pediatric hypertension. *Pediatr. Clin. North Am.* **53**, 1011–1028 (2006).
26. Sugiyama, T. *et al.* Dietary and lifestyle factors associated with blood pressure among US adolescents. *J. Adolesc. Health* **40**, 166–172 (2007).
27. Flynn, J. T. & Alderman, M. H. Characteristics of children with primary hypertension seen at a referral center. *Pediatr. Nephrol.* **20**, 961–966 (2005).
28. Bartosh, S. M. & Aronson, A. J. Childhood hypertension. An update on etiology, diagnosis, and treatment. *Pediatr. Clin. North Am.* **46**, 235–252 (1999).
29. Ostchega, Y. *et al.* National Health and Nutrition Examination Survey 1999–2000: effect of observer training and protocol standardization on reducing blood pressure measurement error. *J. Clin. Epidemiol.* **56**, 768–774 (2003).
30. Chen, X., Wang, Y., Appel, L. J. & Mi, J. Impacts of measurement protocols on blood pressure tracking from childhood into adulthood: a meta-regression analysis. *Hypertension* **51**, 642–649 (2008).
31. Brotons, C., Singh, P., Nishio, T. & Labarthe, D. R. Blood pressure by age in childhood and adolescence: a review of 129 surveys worldwide. *Int. J. Epidemiol.* **18**, 824–829 (1989).
32. Blumenthal, S. *et al.* Report of the task force on blood pressure control in children. *Pediatrics* **59** (5 2 Suppl.), I–II, 797–820 (1977).
33. Report of the Second Task Force on Blood Pressure Control in Children—1987. Task Force on Blood Pressure Control in Children. National Heart, Lung, and Blood Institute, Bethesda, Maryland. *Pediatrics* **79**, 1–25 (1987).
34. 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. National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. *Pediatrics* **98** (4 Pt 1), 649–658 (1996).
35. Knecht, S. K., Mays, W. A., Gerdes, Y. M., Claytor, R. P. & Knilians, T. K. Exercise evaluation of upper- versus lower-extremity blood pressure gradients in pediatric and young-adult participants. *Pediatr. Exerc. Sci.* **19**, 344–348 (2007).
36. Metoki, H. *et al.* Prognostic significance of nighttime, early morning, and daytime blood pressures on the risk of cerebrovascular and cardiovascular mortality: the Ohasama Study. *J. Hypertens.* **24**, 1841–1848 (2006).
37. Lin, J. M., Hsu, K. L., Chiang, F. T., Tseng, C. D. & Tseng, Y. Z. Influence of isolated diastolic hypertension identified by ambulatory blood pressure on target organ damage. *Int. J. Cardiol.* **48**, 311–316 (1995).
38. Urbina, E. *et al.* Ambulatory blood pressure monitoring in children and adolescents: recommendations for standard assessment: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the council on cardiovascular disease in the young and the council for high blood pressure research. *Hypertension* **52**, 433–451 (2008).
39. Lurbe, E. *et al.* Diurnal blood pressure curve in children and adolescents. *J. Hypertens.* **14**, 41–46 (1996).
40. Lurbe, E. *et al.* Increase in nocturnal blood pressure and progression to microalbuminuria in type 1 diabetes. *N. Engl. J. Med.* **347**, 797–805 (2002).
41. Ettinger, L. M., Freeman, K., DiMartino-Nardi, J. R. & Flynn, J. T. Microalbuminuria and abnormal ambulatory blood pressure in adolescents with type 2 diabetes mellitus. *J. Pediatr.* **147**, 67–73 (2005).
42. Devereux, R. B. *et al.* Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am. J. Cardiol.* **57**, 450–458 (1986).
43. Khoury, P. R., Mitsnefes, M., Daniels, S. R. & Kimball, T. R. Age-specific reference intervals for indexed left ventricular mass in children. *J. Am. Soc. Echocardiogr.* **22**, 709–714 (2009).
44. Mensah, G. A. High blood pressure in children and adolescents: to treat or not to treat is not the question. *J. Clin. Hypertens. (Greenwich)* **10**, 889–893 (2008).
45. Appel, L. J. *et al.* Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. *Hypertension* **47**, 296–308 (2006).
46. He, F. J. & MacGregor, G. A. Importance of salt in determining blood pressure in children: meta-analysis of controlled trials. *Hypertension* **48**, 861–869 (2006).
47. National Heart Lung and Blood Institute, NIH. Your guide to lowering blood pressure. Lower your blood pressure by eating right [online], http://www.nhlbi.nih.gov/health/public/heart/hbp/hbp_low/hbp_low.pdf (2003).
48. Couch, S. C. *et al.* The efficacy of a clinic-based behavioral nutrition intervention emphasizing a DASH-type diet for adolescents with elevated blood pressure. *J. Pediatr.* **152**, 494–501 (2008).
49. Kelley, G. A., Kelley, K. S. & Tran, Z. V. The effects of exercise on resting blood pressure in children and adolescents: a meta-analysis of randomized controlled trials. *Prev. Cardiol.* **6**, 8–16 (2003).
50. Flynn, M. A. *et al.* Reducing obesity and related chronic disease risk in children and youth: a synthesis of evidence with 'best practice' recommendations. *Obes. Rev.* **7** (Suppl. 1), 7–66 (2006).
51. Strong, W. B. *et al.* Evidence based physical activity for school-age youth. *J. Pediatr.* **146**, 732–737 (2005).
52. Flynn, J. T. & Daniels, S. R. Pharmacologic treatment of hypertension in children and adolescents. *J. Pediatr.* **149**, 746–754 (2006).
53. Flynn, J. T. Pediatric hypertension: recent trends and accomplishments, future challenges. *Am. J. Hypertens.* **21**, 605–612 (2008).
54. Benjamin, D. K. Jr *et al.* Pediatric antihypertensive trial failures: analysis of end points and dose range. *Hypertension* **51**, 834–840 (2008).
55. Hanevold, C. D. Concepts guiding therapy for hypertension in children. *Expert Rev. Cardiovasc. Ther.* **7**, 647–657 (2009).
56. Boneparth, A. & Flynn, J. T. Evaluation and treatment of hypertension in general pediatric practice. *Clin. Pediatr. (Phila.)* **48**, 44–49 (2009).
57. Yoon, E. Y., Davis, M. M., Rocchini, A., Kershaw, D. & Freed, G. L. Medical management of children with primary hypertension by pediatric subspecialists. *Pediatr. Nephrol.* **24**, 147–153 (2009).
58. Sinaiko, A. R. Antihypertensive therapy in children: implications for future studies. *Hypertension* **52**, 201–202 (2008).
59. Wuhl, E. *et al.* Strict blood-pressure control and progression of renal failure in children. *N. Engl. J. Med.* **361**, 1639–1650 (2009).
60. Patel, H. P. & Mitsnefes, M. Advances in the pathogenesis and management of hypertensive crisis. *Curr. Opin. Pediatr.* **17**, 210–214 (2005).

Acknowledgments

Désirée Lie, University of California, Orange, CA, is the author of and is solely responsible for the content of the learning objectives, questions and answers of the MedscapeCME-accredited continuing medical education activity associated with this article.