NCC Pediatrics Continuity Clinic Curriculum:
Hypertension for Primary Care Pediatricians
Faculty Guide

Goals & Objectives:

Identify causes, evaluation and initial management of hypertension in children.

- Be able to correctly identify hypertension in a child based on age, gender and height
- Be able to formulate a differential diagnosis of secondary hypertension and initiate an appropriate diagnostic workup
- Describe the main modalities of management for essential hypertension
- Be familiar with the exercise recommendations for a patient with hypertension

Pre-Meeting Preparation:

- Hypertension in Childhood *(Pediatrics in Review, 2007)*
- USPSTF: Blood Pressure Screening Not Useful for Children *(Medscape 2013)*
    - Full Recommendation Statement in Pediatrics Oct 2013 *(skim)*

Conference Agenda:

- Complete Hypertension Cases
- **Discuss USPSTF Recommendations**: Do you agree or disagree? What are the pros and cons of blood pressure screening in pediatrics? Does this statement affect your practice?
    - *Faculty: Consider having residents pick sides and debate this topic.*

Post-Conference:

- *Board Review Q&A*

Extra Credit:

- Neonatal Hypertension *(Lebanese Medical Journal, 2010)*
- Ambulatory Blood Pressure Monitoring *(NEJM, 2006)*
- DASH Diet *(NEJM, 1997)*

Hypertension in Childhood

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Author Disclosure
Drs Feld and Corey did not disclose any financial relationships relevant to this article. The authors discuss all drugs used for hypertension, although all drugs do not have pediatric labeling and safety information.

Objectives

After completing this article, readers should be able to:

1. Describe the practical approach to confirming the diagnosis of hypertension.
2. Delineate the differential diagnosis and diagnostic approach for a child who has significant hypertension.
3. Discuss the role of the pediatrician in advising the parents and child/adolescent on the nonpharmacologic approach to treating hypertension.
4. List the primary classes of antihypertensive medications to treat hypertension in childhood.

Case Study

David is a 10-year-old boy who complains of frequent headaches. He generally is healthy, but he is overweight and has an anxiety disorder. There is a strong family history of hypertension. On physical examination, the seated blood pressure (BP) using a child-size cuff and an automated noninvasive blood pressure monitor is 140/85 mm Hg. Suspecting hypertension as the cause of the headache, his physician refers David to a pediatric nephrologist for additional investigation.

On the initial physical examination, the seated BP reading using an adult-size cuff and a manual aneroid manometer is 135/80 mm Hg. A second reading, taken 15 minutes later, is 122/72 mm Hg. His body mass index (BMI) exceeds the 95th percentile for age. The remainder of the physical examination findings are unremarkable.

Subsequently, a 24-hour ambulatory blood pressure monitor (ABPM) reveals that 35% of the daytime readings exceed the 95th percentile for age, sex, and height, confirming the diagnosis of hypertension. Echocardiography reveals mild left ventricular hypertrophy (LVH), but otherwise shows normal results, as do blood chemistries, urinalysis, plasma renin activity, catecholamine measurement, and renal ultrasonography. However, the plasma uric acid concentration is mildly elevated at 6.6 mg/dL (0.39 mmol/L).

Introduction

In the 3 decades since the first *Report of the Task Force on Blood Pressure Control in Children*, the guidelines for pediatric hypertension have been clarified, diagnostic evaluation has been refined, and therapeutic options have been expanded. Increasing evidence shows that the presence of hypertension in childhood and adolescence is not benign. There appears to be a good correlation among BMI, hypertension, LVH, and early coronary artery disease in the adolescent. In fact, children whose essential hypertension is untreated may have vascular injury (LVH and increased intima-media thickness of the carotid and femoral arteries) at the time of diagnosis. Because nearly one of every six Americans has or develops hypertension, pediatricians can play an important role in reducing the associated long-term cardiovascular morbidity and mortality through the early identification, evaluation, and treatment of this common disorder.

Diagnostic Evaluation

The *Fourth Report by the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents* provides guidelines for the diagnostic

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Table 1. Recommended Dimensions for Blood Pressure 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

*Calculated so that the bladder can encircle even the largest arm by at least 80%.

evaluation of the nearly 5% of children who have sustained hypertension. (1) These recommendations can be broken down into a four-step process using the mnemonic COST*:

1. *Confirm* the diagnosis of hypertension.
2. *Organize* a diagnostic approach.
3. Determine the *Severity* of the hypertension.
4. *Treat* the hypertension effectively. *Severe hypertension or hypertensive emergencies with significant symptoms of headache, epistaxis, diplopia, seizures, encephalopathy, hemiplegia, lethargy, or somnolence require hospitalization, a more aggressive evaluation, and intravenous antihypertensive therapy.

Confirm the Diagnosis of Hypertension

Accurate measurement of the BP may be difficult in children because the readings vary significantly with cuff size, patient positioning, clinical setting, equipment used (mercury sphygmomanometer versus oscillometric methods), and training of the observer. Dimensions for appropriate cuff size are presented in Table 1. Hyperten-

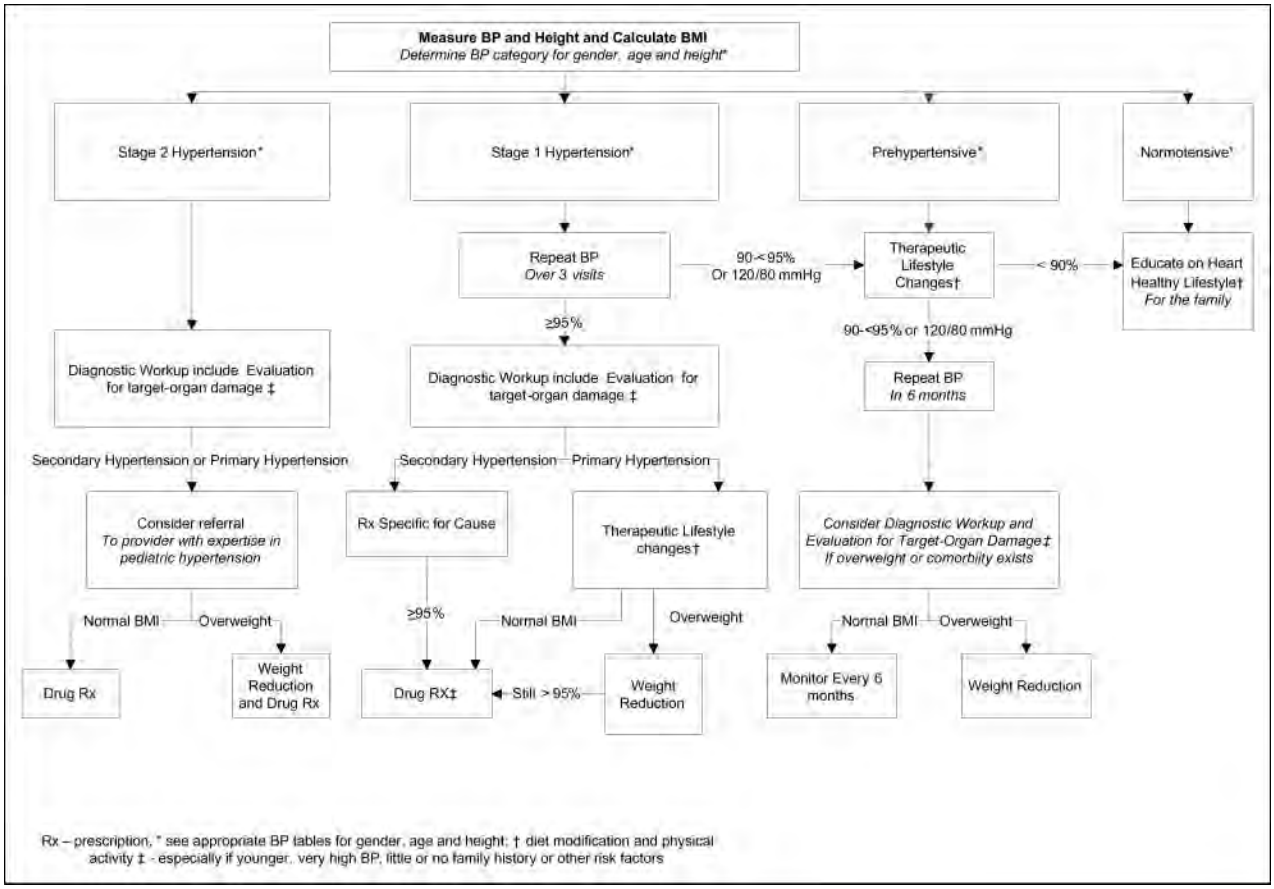

Figure 1. Algorithm for treatment of hypertension. BP=blood pressure, BMI=body mass index. Reproduced with permission from The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. *Pediatrics.* 2004;114:555–576.

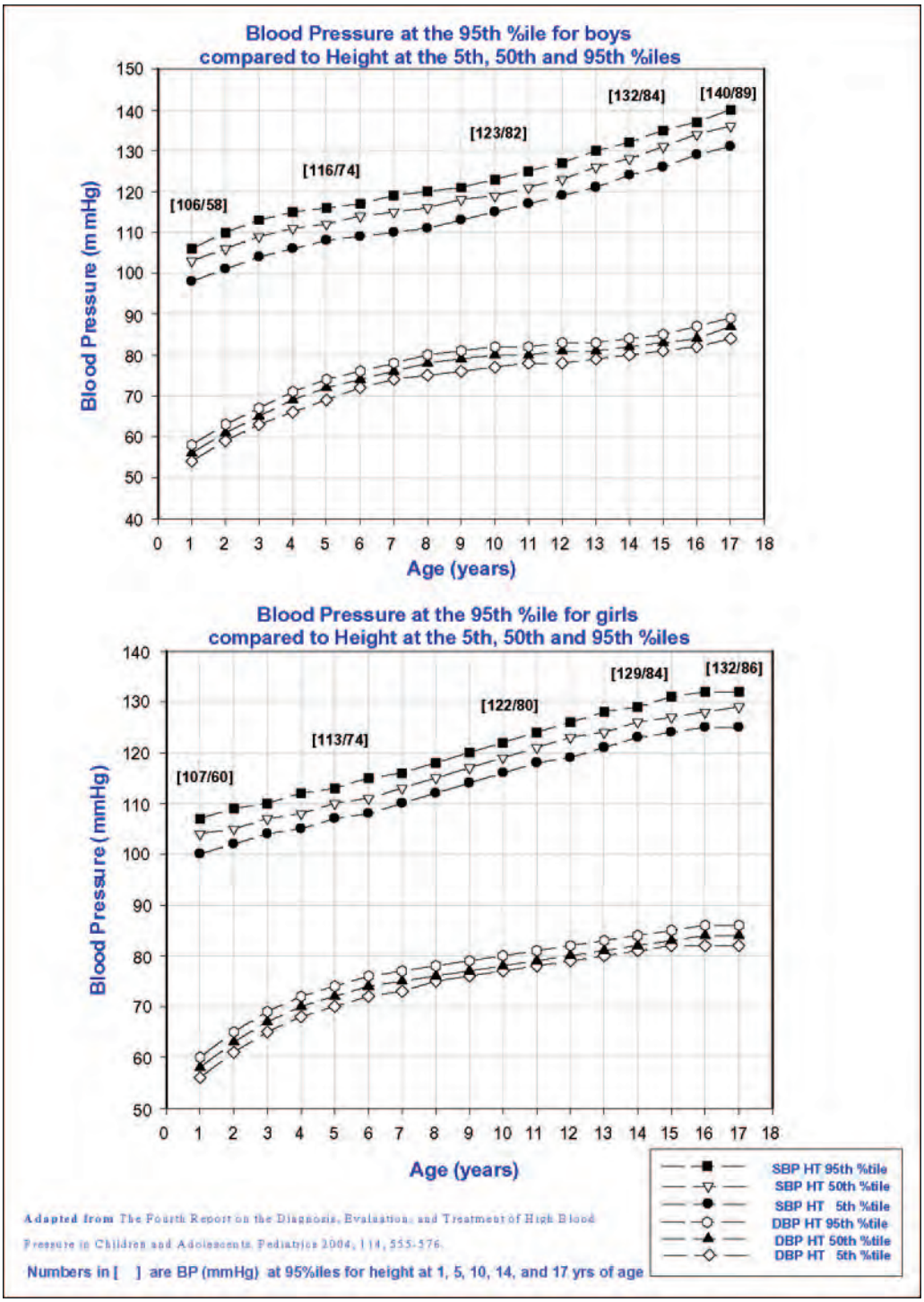

Figure 2. Blood pressure at the 95th percentile for boys and girls at height percentiles. Adapted from The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. *Pediatrics.* 2004;114:555–576.

sion may be suspected when the BP reading is high for the height, age, and sex of the child.

The diagnosis of hypertension is confirmed when a high reading is obtained at three or more separate office visits about 1 week apart (Figs. 1 and 2). If BP readings are normal outside of the office, the patient may have

Table 2. **Grades of Hypertension in Children**

Grade of Hypertension	Definition	Appropriate Next Step
"White-coat" hypertension	BP levels >95th percentile in a physician's office or clinic, but normotensive outside a clinical setting	Readings may be obtained at home with appropriate family training or with the assistance of a school nurse or with the use of ambulatory BP monitoring.
Prehypertension	Average SBP or DBP levels that are ≥90th percentile but <95th percentile; as with adults, adolescents who have BP levels ≥120/80 mm Hg should be considered prehypertensive	Additional readings may be obtained at home with appropriate family training or with the assistance of a school nurse.
Stage I hypertension	Average SBP or DBP that is ≥95th percentile	A diagnostic evaluation in a nonurgent, phased approach may be organized.
Stage II hypertension	Average SBP or DBP that is >5 mm Hg higher than the 95th percentile	A diagnostic evaluation over a short period of time in conjunction with pharmacologic treatment may be organized.
Hypertensive urgency and emergency	Average SBP or DBP that is >5 mm Hg higher than the 95th percentile, along with clinical signs or symptoms	Patient hospitalized and treated to lower the BP.

BP=blood pressure, SBP=systolic blood pressure, DBP=diastolic blood pressure. Modified from The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. *Pediatrics.* 2004;114:555–576.

"white-coat" hypertension. This form of stress-induced hypertension may be validated by BP monitoring at school, in the home, or in all locations with the use of an ABPM.

Some patients have borderline readings (systolic or diastolic readings between the 90th and 95th percentile), a state termed prehypertension. It is important to follow such patients over time and to implement lifestyle modifications such as weight reduction and increased physical activity. For those who have persistent elevations, the approach should be tailored to the magnitude of the elevation and the nature of concurrent signs or symptoms (Table 2). The use of an ABPM may aid in the diagnosis of hypertension by limiting inter-and intra-observer variability. Recent investigations provide normative reference values for ABPMs in children. (2)

Organize a Diagnostic Approach

A simple sequence or mnemonic to start the diagnostic process is MONSTER: *M*edications, *O*besity, *N*eonatal history, *S*ymptoms or *S*igns, *T*rends in the family, *E*ndocrine or *R*enal (Fig. 3). Some medications prescribed for other conditions may cause hypertension, such as amphetamines, corticosteroids, contraceptives, and cyclosporine, as might many over-the-counter medications (ie, allergy or cold medication) and licorice (glycyrrhizic acid).

During the evaluation, obesity and obstructive sleep apnea syndrome (OSAS) need to be considered. In the United States, more that 9 million children or youth older than 6 years of age are obese, (3) defined as having a BMI ≥95th percentile according to the age- and sex-specific Centers for Disease Control and Prevention BMI charts. Compared with nonobese children, those who are obese are approximately three to five times more likely to have hypertension. Additional consequences of obesity include glucose intolerance, insulin resistance, type 2 diabetes mellitus, dyslipidemia, hepatic steatosis, cholelithiasis, sleep apnea, and orthopedic problems.

OSAS affects 1% to 3% of the preschool population. Patients who have OSAS diagnosed by polysomnography have significantly higher diastolic BPs during both wakefulness and sleep. (4) The degree of the hypertension appears to correlate with the severity of obstructive sleep apnea and the BMI. Although the mechanism for hypertension is unknown, it probably is similar to that described in adults: sympathetic nervous system activation due to arousal, hypoxemia, and possibly to changes in cardiac output caused by intrathoracic pressure swings.

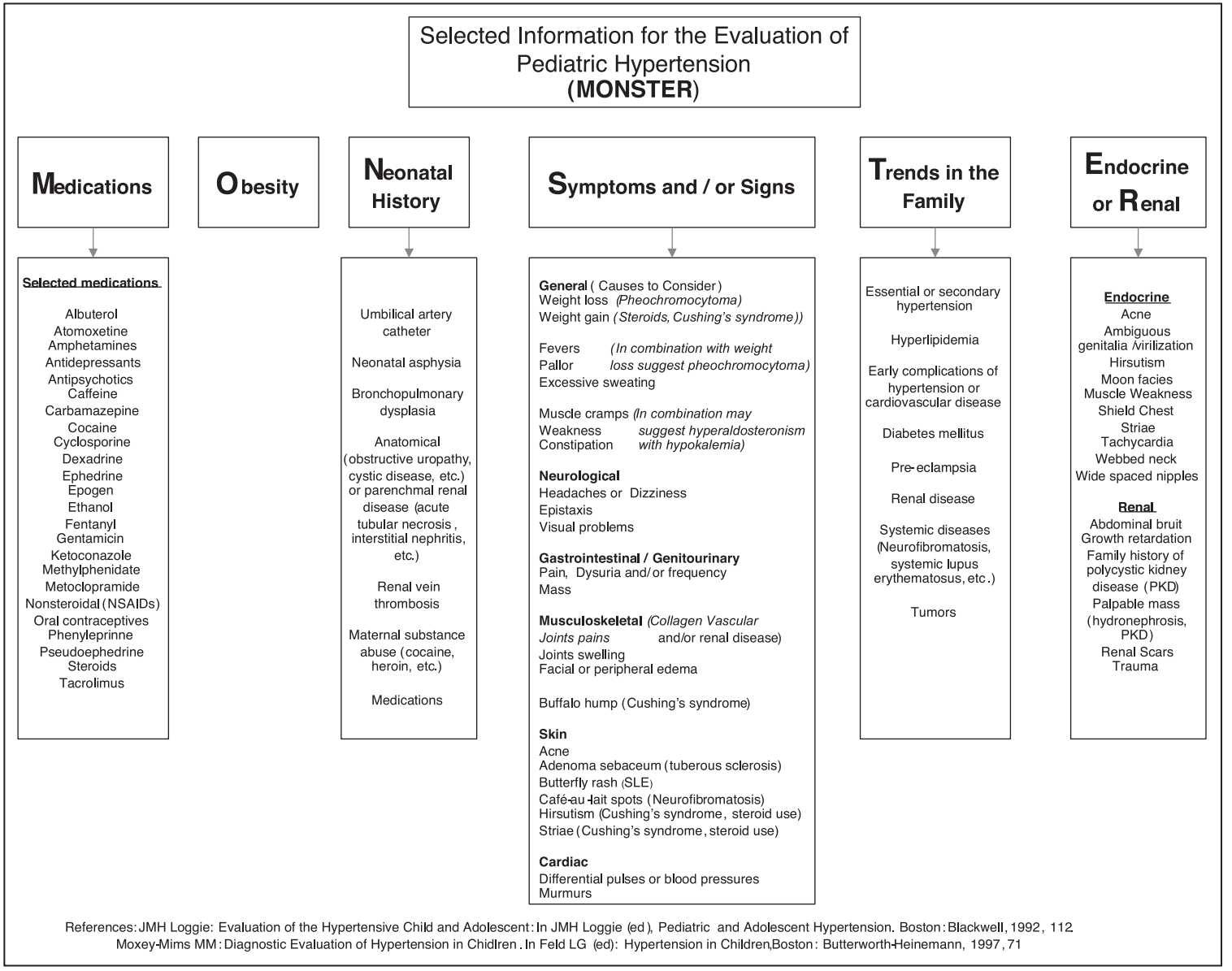

Figure 3. Selected information for evaluation of hypertension (MONSTER). Data from Loggie JMH. Evaluation of the hypertensive child and adolescent. In: *Pediatric and Adolescent Hypertension*. Boston, Mass: Blackwell; 1992:112 and Moxey-Mims MM. Diagnostic evaluation of hypertension in children. In: Feld LG, ed. *Hypertension in Children*. Boston, Mass: Butterworth-Heinemann; 1997:71.

The neonatal history or selected findings can provide important information regarding possible complications during or in the early postnatal course, such as asphyxia, use of an umbilical artery catheter, occurrence of a renal vein thrombosis, maternal substance abuse, disparities between upper extremity and lower extremity pulses or blood pressures, abdominal bruits, abnormal urinalysis findings (hematuria, proteinuria), abdominal masses (hydronephrosis/obstructive uropathy), and bronchopulmonary dysplasia.

Although essential hypertension is becoming more prevalent in children, a secondary cause should be sought, especially in the preadolescent. The evaluation is guided by history and physical examination findings to identify symptoms or signs of hypertension that may direct specific evaluation and avoid unnecessary and invasive testing (Figs. 3 and 4). The data gathered through history and physical examination allow the clinician to select the most appropriate laboratory investigations in the next phase of evaluation.

Biochemical and imaging studies are used to address three primary organ systems: endocrine, renal, and cardiovascular. Although high plasma renin activity or direct renin measurements suggest renal vascular disease, a low value may be even more significant because it implies endocrine or genetic causes of hypertension. Low renin concentrations are present in the following disorders: steroidogenic enzyme defects (steroid 11-beta-hydrozylase deficiency, steroid 11-alpha-hydrozylase deficiency/17, 20-lyase deficiency), hyperaldosteronism (primary aldosteronism, adrenocortical hyperplasia, idiopathic primary aldosteronism, glucocorticoid-remediable aldosteronism), apparent mineralocorticoid excess, and nonsteroidal defects (Liddle syndrome, pseudohypoaldosteronism II or Gordon syndrome). (5)(6) In these disorders, overactivity of the epithelial sodium channel (ENaC), either as a primary or secondary effect, leads to salt retention, volume expansion, and hypertension. Although these specific disorders are uncommon, polymorphisms of the ENaC may be common and have been implicated in promoting essential hypertension. (7) In these entities, specific therapy with amiloride, glucocorticoids, or spironolactone may normalize the BP.

Because renal disorders are among the most common causes of secondary hypertension in children, many studies are used to investigate the possibility of renal parenchymal or vascular disease. For example, a complete blood count may detect anemia of chronic renal disease, urinalysis provides an index of both glomerular (protein, blood) and tubular function (pH, specific gravity, glucose), and the plasma blood urea nitrogen (BUN) and creatinine values assess the glomerular filtration rate (mL/min/1.73 m^2), calculated as length in cm $\times$ K/plasma creatinine concentration (K is the coefficient of 0.45 for <1 to 12 months of age; 0.55 for 2 to 13 years of age, and 0.7 for 14 to 18 years of age via the Schwartz Formula). In addition, renal ultrasonography with Doppler provides information about size, location, echogenicity, and vascular flow of the kidney. Small renal scars can cause hypertension.

Cardiovascular disorders, such as coarctation of the aorta and the mid-aortic syndrome, are important and often overlooked causes of hypertension in children. Investigations such as the measurement of serum lipids and echocardiography provide essential information about key cardiovascular risk factors to guide therapeutic intervention. For example, cardiac hypertrophy is a major indication for hypertensive therapy, even for patients who have only borderline high BP readings.

Two recent studies have provided additional information on the predictive role of serum uric acid concentration in the development of hypertension. In the Bogalusa Heart Study, a high plasma uric acid concentration was associated with high BP readings in childhood that may persist into adulthood. (8) Feig and Johnson, in a study of 125 children, observed a strong relationship between serum uric acid concentrations and essential hypertension. (9) Interestingly, a serum uric acid value higher than 5.5 mg/dL (0.33 mmol/L) was found in 89% of children who had primary hypertension but only in about 30% of those who had secondary forms of hypertension. None of the controls or patients who had white-coat hypertension had elevated values. The possible mechanisms for the relationship between hyperuricemia and hypertension remain unclear.

Additional information may be obtained by a urine drug screen or polysomnography based on the initial review of systems.

There is no consensus on the best modality for renal vascular imaging, except that the gold standard is digital subtraction or conventional angiography with differential renal vein renin sampling. Other imaging modalities have limitations and may fail to detect intrarenal vascular lesions. Magnetic resonance angiography, computed tomographic angiography (CTA), isotope or renal nuclear medicine scanning, and renal ultrasonography with color Doppler may provide normal results in the face of significant segmental renal arterial disease. Despite the radiation and use of intravenous contrast, CTA may be considered in a nonemergent situation in lieu of other radiologic testing such as renal ultrasonography and renal nuclear

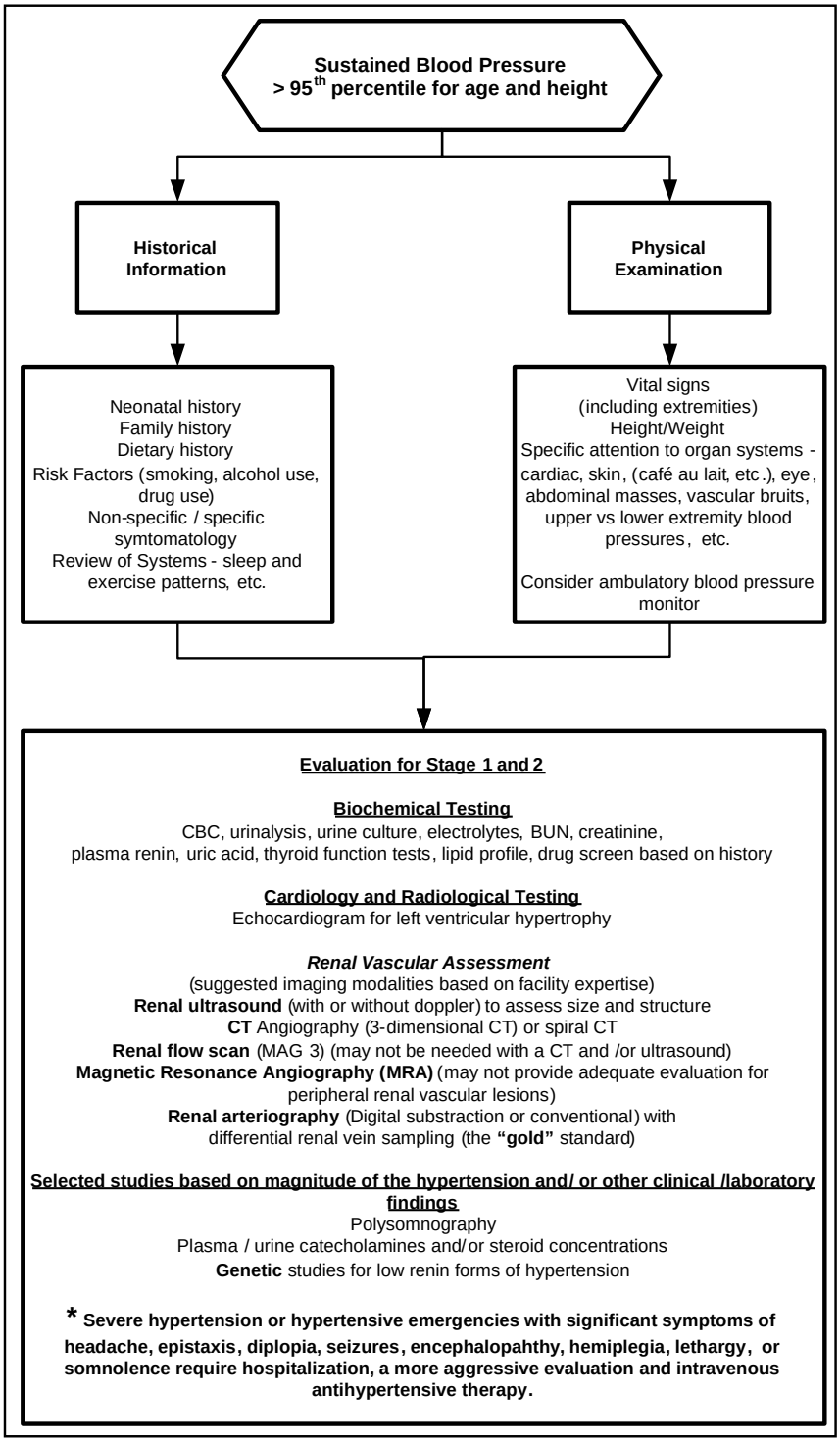

Figure 4. Suggested evaluation of hypertension in children. Modified with permission from Moxey-Mims MM. Diagnostic evaluation of hypertension in children. In: Feld LG, ed. *Hypertension in Children*. Boston, Mass: Butterworth-Heinemann; 1997:74 and The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. *Pediatrics*. 2004;114:555–576.

Table 3. **Public Health Considerations**

Environment	Suggestions
Healthy Marketplace/Media	Promote healthy foods and beverages with nutrition product packaging; limit or prohibit direct marketing to children (selected foods, tobacco, and alcohol)
Schools/Communities/Built Environment	Subsidize or extend school meal funding for children at risk of obesity, limit fast food in schools, and prohibit soft drinks and vending machines in schools Encourage and build environments for increased physical activity and provide physical activity report cards
Home	Encourage family dinners and limit fast foods and non-nutritious snacks; limit television and handheld and computer gaming; promote physical behaviors, with parents serving as role models for stopping smoking and limiting alcohol consumption.

From Institute of Medicine. *Preventing Childhood Obesity: Health in Balance.* Washington, DC: National Academics Press; 2005.

scans to exclude renal vascular disease. (10) The therapeutic interventions for renal artery stenosis include angioplasty, use of stenting, or surgical revascularization with a graft to bypass the lesion.

In cases of suspected pheochromocytoma, 24-hour urinary measurement of catecholamines (fractionated metanephrine, epinephrine, norepinephrine) or plasma catecholamines is appropriate. For functional localization of the neural crest tissue, nuclear imaging with I^{123} or I^{132} metaiodobenzylguanidine (MIBG scan) is performed.

Other causes of hypertension include anemia (systolic hypertension), hyperthyroidism (systolic hypertension), Williams syndrome (elfin facies), Turner syndrome (webbed neck, wide spaced nipples), Cushing syndrome, neurofibromatosis, and lower extremity traction.

Determine the Severity of the Hypertension

The combination of the magnitude of the BP elevation and presence of LVH on echocardiography are proof of sustained hypertension. The finding of LVH suggests risk for future cardiovascular disease, which underscores the importance of recognizing and treating BP elevation in children and adolescents. (11)

Treat the Hypertension Effectively

Nonpharmacologic Therapy

Lifestyle modifications or environmental changes must be implemented or at least attempted. The Institute of Medicine's approach to prevention of childhood obesity addresses nonpharmacologic interventions for hypertension, including reducing sodium intake (no added salt diet, ~2 to 3 g/d or 88 to 132 mEq/d), increasing activity, stopping smoking, reducing alcohol intake, and intervening in other public health areas (Table 3). (3) Three easy steps to reduce salt intake include limiting grocery purchases of salt-added foods, limiting meals from fast-food restaurants/take-outs, and not adding salt to cooking. A referral to a dietitian may improve compliance through education and follow-up re-evaluations.

Physical activity should be encouraged to reduce obesity, improve BP, and prevent children from becoming handicapped or stigmatized. Before encouraging a child to participate in sports, the following questions should be asked: Is there a history of exercise-associated syncope; light-headedness; chest pain; dyspnea; or family history of sudden death, dysrhythmias, or hypertrophic cardiomyopathy? (12)

In general, BP responds to different types of activity in different ways. During brisk dynamic exercise (swimming, running, cycling), peripheral vascular resistance decreases, resulting in an increase in systolic BP, a moderate rise in mean arterial pressure, and a fall in the diastolic value. In static exercise, large intramuscular forces develop with a limited change in muscle length. In contrast to dynamic exercise, static or isometric exercise (weight or strength training) causes significant increases in systolic, mean, and diastolic BP with no change in total peripheral resistance. The magnitude of the increase in BP during static exercise can exceed values for dynamic exercise significantly. Most physical activities and sports have both static and dynamic components, and a few basic rules can guide exercise: (12)(13)

- Decisions to restrict participation should be based on the cardiovascular demands of the activity and the demands of the practice, training, or preparation for that activity.

Table 4. Guidelines, Principles, and Response to Therapy

Suggested Guidelines to Improve Compliance of Therapy[1]

- Be aware of inadequate intake of medications
- Provide written instructions and blood pressure guidelines (high and low) for when to call the physician
- Make patient/family aware that the goal is the normalization of blood pressure
- Maintain phone contact with patient/family
- Implement home/school blood pressure monitoring
- Use nonpharmacologic therapy in combination with antihypertensive therapy
- Communicate and monitor adverse effects
- Provide feedback and validation of success
- Obtain laboratory studies on a reasonable schedule
- Contact patients who do not return for follow-up

Suggested Principles of Therapy[2]

- Consider starting with one drug and maximizing dose before adding a second agent to achieve normalization or near-normalization of blood pressure (this may improve compliance, but the approach needs to be individualized)
- Provide written instructions with clear blood pressure limits (high and low) when to call the physician
- Be considerate of patient and family routines (daily dosing if possible)
- Select agent(s) that have the lowest adverse effect profile

Possible Causes of Inadequate Response to Therapy[3]

- Errors with the equipment or measuring technique
- Noncompliance with therapy
- Progression of underlying disease
- Unacceptable adverse effects
- Selection of drug inappropriate for the suspected cause of hypertension
- Drug interactions (eg, steroids, cyclosporine, caffeine, sympathomimetics)
- Drug metabolism
- Rapid inactivation (eg, rapid acetylator with hydralazine)
- Slow bioactivation of prodrug (eg, angiotensin receptor blockers)

[1]Adapted with permission from Kaplan NM. Systemic hypertension: an overview of the problem. *Semin Nephrol.* 2005;25:191.
[2]Adapted from Choi KL, Bakris GL. Hypertension treatment guidelines: practical implications. *Semin Nephrol.* 2005;25:198.
[3]Adapted with permission from Blowey DL. Approach to the pharmacologic treatment of pediatric hypertension. In: Portman RJ, Sorof JM, Ingelfinger JR, eds. *Pediatric Hypertension.* Totowa, NJ: Humana Press; 2004:429.

• Children and adolescents who have significant essential or severe hypertension should avoid weight/power lifting, body building, and strength training. Those who have secondary causes of hypertension or severe essential hypertension should avoid strenuous static exercise and restrict competitive sports to those of low intensity (low dynamic/low static demands) such as bowling, golf, cricket, curling, or riflery, until an evaluation is performed and target organ damage is excluded.

• Exercise restriction should be based on the possibility that an abrupt increase in BP may place the child or adolescent at a higher risk of a catastrophic event, exacerbate the BP effect on end-organ damage significantly, or contribute to sustained BP elevation.

Pharmacologic Therapies

The goal of therapy is the normalization or near-normalization of BP based on age, sex, and height, using a drug regimen that causes minimal adverse effects. It also is important to appreciate the guidelines for and principles of drug therapy as well as the causes of inadequate response to therapy in treating children who have hypertension (Table 4). The physician experienced in managing hypertension can employ numerous approaches to improve adherence to therapeutic regimens, but it is equally important to appreciate reasons that lead to a poor response to therapy, such as drug interactions, unacceptable adverse effects, and inaccuracies in the BP measurements.

The approach to antihypertensive therapy is based on whether the patient has primary (essential) or secondary (identifiable cause) hypertension (Table 5). Many antihypertensive drugs are available for children, although clinical trials are limited, and most recommendations are based on extrapolation from adult dosage recommendations or clinical experience. Because the drug compendium is extensive, only practitioners experienced with their use should prescribe these medications. In our

Table 5. Antihypertensive Drugs for Outpatient Management of Hypertension in Children 1 to 17 Years of Age*

Class	Drug	Dose (Interval)	Common Adverse Effects/Special Considerations of Each Class
Angiotensin Converting Enzyme Inhibitor (ACEi)	Captopril§	Initial: 0.3 to 0.5 mg/kg per dose (tid) Maximum: 6 mg/kg per day	All ACEis are contraindicated in pregnancy Periodically measure serum creatinine and potassium concentrations Cough and angioedema are less common with new ACEis Some agents can be made into a suspension United States Food and Drug Administration (FDA) approval is limited to children ≥6 yrs of age and creatinine clearances ≥30 mL/min per 1.73m^2 Consider for renoprotective effect for renal disease with proteinuria and diabetes mellitus
	Enalapril§	Initial: 0.08 mg/kg per day up to 5 mg/d (once daily-bid) Maximum: 0.6 mg/kg per day up to 40 mg/d	
	Benazepril	Initial: 0.2 mg/kg per day up to 10 mg/d Maximum: 0.6 mg/kg per day up to 40 mg/d	
	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	
	Fosinopril	Children >50 kg: Initial: 5 to 10 mg/d Maximum: 40 mg/d	
	Quinapril	Initial: 5 to 10 mg/d Maximum: 80 mg/d	
Angiotensin Receptor Blocker (ARB)	Irbesartan	6 to 12 y: 75 to 150 mg/d (once daily) ≥13 y: 150 to 300 mg/d	All ARBs are contraindicated in pregnancy Periodically measure serum creatinine and potassium concentrations Losartan can be made into a suspension FDA approval is limited to children ≥6 y of age and creatinine clearances ≥30 mL/min per 1.73m^2
	Losartan	Initial: 0.7 mg/kg per day up to 50 mg/d (once daily) Maximum: 1.4 mg/kg per day up to 100 mg/d	
Calcium Channel Blocker	Amlodipine§	Children 6 to 17 y: 2.5 to 5 mg once daily	Amlodipine and isradipine can be compounded into stable extemporaneous suspensions Felodipine and extended-release nifedipine tablets must be swallowed whole May cause tachycardia and edema
	Felodipine	Initial: 2.5 mg/d Maximum: 10 mg/d	
	Isradipine§	Initial: 0.15 to 0.2 mg/kg per day (tid-qid) Maximum: 0.8 mg/kg per day up to 20 mg/d	
	Extended-release nifedipine	Initial: 0.25 to 0.5 mg/kg per day (once daily-bid) Maximum: 3 mg/kg per day up to 120 mg/d	
Alpha and Beta Blocker	Labetalol§	Initial: 1 to 3 mg/kg per d (bid) Maximum: 10 to 12 mg/kg per day up to 1,200 mg/d	Asthma and overt heart failure are contraindications Heart rate is dose-limiting May impair athletic performance Should not be used in those who have insulin-dependent diabetes
Beta Blocker	Atenolol§	Initial: 0.5 to 1 mg/kg per day (once daily-bid) Maximum: 2 mg/kg per day up to 100 mg/d	Noncardioselective agents (propranolol) are contraindicated in those who have asthma and heart failure Heart rate is dose-limiting May impair athletic performance Should not be used in those who have diabetes mellitus
	Metoprolol§	Initial: 1 to 2 mg/kg per day (bid) Maximum: 6 mg/kg per day up to 200 mg/d	
	Propranolol§	Initial: 1 to 2 mg/kg per day (bid-tid) Maximum: 4 mg/kg per day up to 640 mg/d	

Class	Drug	Dose (Interval)	Common Adverse Effects/Special Considerations of Each Class
Central Alpha Blocker	Clonidine	Children ≥12 y: Initial: 0.2 mg/d (bid) Maximum: 2.4 mg/d	May cause dry mouth or sedation Transdermal preparation is available Sudden cessation of therapy can lead to severe rebound hypertension
Vasodilator	Hydralazine[§]	Initial: 0.75 mg/kg per day (qid) Maximum: 7.5 mg/kg per day up to 200 mg/d	Tachycardia and fluid retention are common Contraindicated with pericardial effusion, supraventricular tachycardia, and tachydysrhythmias Hydralazine can cause lupus-like syndrome Prolonged use of minoxidil can cause hypertrichosis Minoxidil usually is reserved for patients who have hypertension that is resistant to multiple drugs
	Minoxidil[§]	Children <12 y: Initial: 0.2 mg/kg per day (once daily-tid) Maximum: 50 mg/day Children ≥12 y: Initial: 5 mg/kg per day (once daily-tid) Maximum: 100 mg/day	
Diuretics	Hydrochlorothiazide	Initial: 1 mg/kg per day (once daily) Maximum: 3 mg/kg per day up to 50 mg/day	All patients taking diuretics should have electrolytes monitored after initiation of therapy and periodically Potassium-sparing diuretics (spironolactone, triamterene) may cause severe hyperkalemia, especially in conjunction with ACEi or ARB Furosemide is useful adjunctive therapy for patients who have renal disease Some agents may be useful in low renin forms of hypertension
	Furosemide	Initial: 0.5 to 2 mg/kg per day (once daily-bid) Maximum: 6 mg/kg per day	
	Spironolactone[§]	Initial: 1 mg/kg per day (once daily-bid) Maximum: 3.3 mg/kg per day up to 100 mg/d	
	Triamterene	Initial: 1 to 2 mg/kg per day (bid) Maximum: 3 to 4 mg/kg per day up to 300 mg/d	

Modified from The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. *Pediatrics.* 2004;114:555–576.
*Check pediatric labeling and safety information on all agents. Also, see http://www.fda.gov/oc/opt/default.htm for complete United States Food and Drug Administration labeling and levels of evidence for dosing recommendations. Comments apply to all members of each drug class except where otherwise stated. The table does not include all available drugs in each category. Some drugs require adjustment for renal disease or specific glomerular filtration rates. These medications should be used by physicians experienced in the treatment/management of children who have hypertension.
[§]Extemporaneous formulations (liquid) may be prepared by a pharmacy.

opinion, the preferable adverse effect and compliance profiles support the use of angiotensin-converting enzyme inhibitors (ACEis), angiotensin receptor blockers (ARBs), and calcium channel blockers (CCBs) as first-line therapy. Although beta blockers (propranolol, atenolol), an alpha and beta blocker (labetalol), direct vasodilators (hydralazine, minoxidil), and central alpha agonists (clonidine) have been used in pediatrics, they should not be considered first-line medications except under specific circumstances (ie, clonidine patch to improve compliance in adolescents).

ANGIOTENSIN-CONVERTING ENZYME INHIBITORS. ACEis block the conversion of angiotensin I to angiotensin II and inhibit kininase II, an important participant in the kinin/kallikrein system, resulting in increased circulating concentrations of vasodilatory bradykinins. The predominant antihypertensive effect is the inhibition of angiotensin II production. There is a renal protective effect in addition to the antihypertensive effects of ACEis that adds to their value as first-line antihypertensive medications. (14)

Captopril and enalapril were the first ACEis used in children. Pediatric dosing and adverse effect profiles are well described for these drugs (Table 5). Captopril and enalapril can be used in neonates and young children, employing formulations that improve the ability to titrate doses. For older patients maintained on stable doses, the use of daily dosing intervals is preferred over more frequent doses of the shorter half-life formulations.

The adverse effects of ACEis in children do not differ from those in adults. Renal impairment, hyperkalemia, neutropenia, anemia, dry cough, and angioedema have

been reported in children. (14) The use of an ACEi is contraindicated in patients who have bilateral renal artery stenosis, hyperkalemia, or pregnancy. If renal impairment occurs with ACEi therapy, it generally is reversible with discontinuation of the drug. Hyperkalemia may be related to medication-induced renal failure but may occur in patients who have relatively normal renal function because of aldosterone inhibition. We suggest measuring BUN, creatinine, and electrolytes within 1 week after starting an ACEi, with any dosage changes, and every 3 to 6 months for the patient receiving therapy. Hematologic complications are rare and are reversible when the drug is discontinued.

In contrast to adults, the dry, nonproductive cough (not dose-related) is a rare complication in children and adolescents. The mechanism causing the cough may be related to kininase inhibition resulting in increased bradykinin production. If a cough occurs, it improves with discontinuation of the ACEi. It is important to ask about the cough because parents and patients may attribute coughing to asthma or upper respiratory tract infection or they may take the medication less frequently than recommended to avoid symptoms.

ACEis are contraindicated in pregnancy. Maternal use of such drugs during pregnancy can result in fetal hypotension, anuria, renal tubular dysplasia, and death. Infants who have only first-trimester exposure to ACEis have an increased risk of major congenital malformations (ie, cardiac). (15)

ANGIOTENSIN RECEPTOR BLOCKERS. ARBs directly block the action of angiotensin II on their cell membrane receptors. Although there are fewer adverse effects (eg, dry cough), the laboratory monitoring, contraindications in pregnancy, and risk of renal impairment are similar to the ACEis. The use of ARBs in combination with ACEis has increased recently for patients who have chronic renal failure as a renoprotective regimen to reduce proteinuria and delay progression of renal disease. Based on extensive experience, ACEis and ARBs are the drugs of choice for patients who have diabetes mellitus and chronic glomerular disease.

CALCIUM CHANNEL BLOCKERS. CCBs act as direct vasodilators by inhibiting calcium transport into vascular smooth muscle and other contractile cells, thereby limiting contractility and vasoconstriction. (14) The major class of CCBs used in pediatrics for hypertension is the dihydropyridines (nifedipine, nicardipine, isradipine, felodipine, amlodipine) because of the relative selectivity for arteriolar smooth muscle. The nondihydropyridines (phenylalkylamines, benzothiazepines), such as verapamil and diltiazem, have more effects on cardiac conduction and contractility than do the dihydropyridines.

Pediatric experience with CCBs demonstrates safety and efficacy with an acceptable adverse effect profile. They are used as first-line therapy and have particular usefulness in those patients for whom ACEis are contraindicated and in children who have renal disease in whom ACEis/ARBs alone are inadequate to control the hypertension. As the dose of CCBs approaches the maximal range, the incidence of adverse effects, particularly peripheral edema, increases significantly. Due to their formulations, nicardipine (intravenous) and isradipine (can be compounded into stable suspensions) are used in the emergency and intensive care settings. Rapid, safe, and effective reductions in BP have been achieved with continuous infusions, providing an alternative to nitroprusside or intravenous labetalol.

Some controversy continues to surround the use of nifedipine (sublingual or immediate-release dosage forms) to treat hypertensive emergencies in children due to the reported cerebrovascular and cardiovascular adverse events associated with aggressive treatment of increased BP by the use of sublingual nifedipine in adults. The most commonly observed adverse effects of CCBs are peripheral edema, dizziness, nausea, headache, flushing, weakness, and transient postural hypotension. (14) These effects are uncommon with sustained-release preparations and rarely necessitate discontinuing the drug.

BETA-ADRENERGIC ANTAGONISTS (BETA BLOCKERS). These drugs are among the first and most widely used antihypertensive medications in children. Several mechanisms for their antihypertensive effect have been proposed, including decreased cardiac output, decreased peripheral vascular resistance, inhibition of renin secretion, decreased circulating plasma volume, and inhibition of central nervous system (CNS) sympathetic activity. (14) The relative importance of each of these mechanisms is unclear and may depend on which particular drug from the class is being used.

Several characteristics distinguish one beta blocker from another, including cardioselectivity, intrinsic sympathomimetic activity, alpha-adrenergic antagonism, and relative hydrophilic and lipophilic characteristics. Use of the prototype beta blocker propranolol is limited by its lack of selectivity for cardiovascular $beta_1$ receptors. Because of effects on peripheral $beta_2$ receptors, manifested

as bronchoconstriction, impaired glucose tolerance, and altered lipid profiles, drugs that have relative cardioselectivity were created.

Intrinsic sympathomimetic activity is characteristic of some, but not all, drugs in the class. This characteristic may be of benefit for several reasons, including reduced impairment of left ventricular function, reduced compromise of peripheral vasculature, and minimized effects on lipid profiles.

Labetalol and carvedilol (not approved by the United States Food and Drug Administration in children and used primarily for congestive heart failure) essentially have beta-blocking effects and peripheral alpha-adrenergic antagonism. This vasodilatory effect on peripheral vasculature provides synergistic antihypertensive efficacy.

Many patients treated with beta blockers experience significant CNS effects; newer formulations have been developed to limit CNS absorption through alterations in hydrophilicity and lipophilicity. Each of these characteristics–cardioselectivity, intrinsic sympathomimetic activity, alpha-adrenergic antagonism, and hydrophilicity/lipophilicity–can be individualized when selecting a beta blocker for a particular patient.

Most pediatric experience with beta blockers involves the use of propranolol, but the unacceptable adverse effects, as well as the availability of equally efficacious and better-tolerated alternatives, have limited its use as a first-line treatment for pediatric hypertension. Other beta blockers used in pediatrics include atenolol (cardioselective, no intrinsic sympathomimetic activity), labetalol (not cardioselective, no intrinsic sympathomimetic activity, significant alpha antagonism), and metoprolol (cardioselective, no intrinsic sympathomimetic activity). Review of the pediatric literature shows minimal new research on the use of beta blockers in pediatric hypertension.

No direct comparisons of beta blockers with diuretics or with CCBs or ACEis as first-line pediatric antihypertensives have been published. Clinical practice and experience, rather than direct comparison, seems to have relegated beta blockers to a second or third choice for treating essential hypertension. However, these agents may be particularly useful when combined with vasodilators that produce reflex tachycardia or in patients for whom ACEis or CCBs are contraindicated.

The most common adverse effects of beta blockers include cardiovascular changes (bradycardia, syncope, fluid retention), CNS effects (lightheadedness, ataxia, dizziness, sleepiness, irritability, hearing and visual disturbances, vivid dreams/nightmares, weakness, fatigue, depression), gastrointestinal changes (nausea, diarrhea, cramping, constipation), hematologic effects (transient eosinophilia, idiosyncratic cytopenia), and impotence. (14) Beta blockers are contraindicated in patients who have asthma, Raynaud phenomenon, cystic fibrosis, bronchopulmonary dysplasia, uncompensated congestive heart failure, hyperactive airway disease, bradycardia or heart block, or cardiogenic shock (14) as well as in athletes (may affect performance and prevent potassium retry into the cells on strenuous exercise).

CENTRAL ALPHA AGONIST OR SYMPATHOLYTIC AGENT (CLONIDINE). The mechanism of action of the central sympatholytic (CA) agents is based on modulation of CNS centers for cardiovascular control. Clonidine acts as an agonist of CNS alpha-adrenoceptors (primarily alpha-2). (14) The initial dose may be associated with a transient increase in blood pressure, suggesting that clonidine also stimulates peripheral (vasoconstrictive) alpha receptors in addition to its primary mechanism of CA activity.

To increase compliance, especially in adolescents, the use of a transdermal clonidine preparation can be considered. A steady-state concentration is achieved in about 2 to 3 days, and patches are changed weekly. (14) The possible benefits of this formulation are stable serum concentrations, fewer adverse effects, and reduction in the incidence of rebound hypertension when the medication is discontinued. Skin reactions (allergic, irritation) are observed in up to 20% of patients. Although clonidine may be considered second-tier treatment for symptoms of attention-deficit/hyperactivity disorder, its effect is less than that of stimulants and is associated with many adverse effects, including sedation, dry mouth, fatigue, hallucinations /nightmares, and rebound hypertension on abrupt discontinuation.

VASODILATORS. The typical use of vasodilators is treatment of hypertensive emergencies. Hydralazine acts primarily to dilate the arteriolar resistance vessels, with a less pronounced effect on the venous capacitance vessels. (14) In the acute setting, hydralazine is an effective antihypertensive, although its long-term effectiveness has been limited by the body's compensatory responses to its actions (increased cardiac output, fluid retention), by development of tolerance, and by adverse effects. Minoxidil use as an antihypertensive medication is limited to refractory cases. In these cases, concurrent therapy with other medications (eg, diuretics) often is necessary. The common pediatric adverse effects of vasodilators include headache, palpitations, tachycardia, flushing, fluid

Table 6. **Selected Combinations of Drug Products***

Combination	Some Available Preparations
ACEi plus CCB	
Benazepril/Amlodipine	10 mg/2.5 mg; 10 mg/5 mg; 20 mg/5 mg
ACEi plus Diuretic	
Benazepril/Hydrochlorothiazide	5 mg/6.25 mg; 10 mg/12.5 mg; 20 mg/12.5 mg
Captopril/Hydrochlorothiazide	25 mg/15 mg; 25 mg/25 mg
Enalapril/Hydrochlorothiazide	5 mg/12.5 mg; 10 mg/25 mg
Lisinopril/Hydrochlorothiazide	10 mg/12.5 mg; 20 mg/12.5 mg
ARB plus Diuretic	
Losartan/Hydrochlorothiazide	50 mg/12.5 mg; 100 mg/12.5 mg
Irbesartan/Hydrochlorothiazide	150 mg/12.5 mg; 300 mg/12.5 mg

ACEi=angiotensin-converting enzyme inhibitor, CCB=calcium channel blocker, ARB=angiotensin receptor blocker

* Check pediatric labeling and safety information on all agents. These drug combinations do not have specific pediatric testing or indications but are recommended on the basis of clinical experience primarily in adolescents and young adults. See http://www.fda.gov/oc/opt/default.htm for complete FDA labeling and levels of evidence for dosing recommendations.

and sodium retention, and lupus-like syndrome (hydralazine). Minoxidil has caused pericardial effusion, congestive heart failure, and hypertrichosis (leads to poor compliance). Pediatric contraindications to the use of minoxidil include congestive heart failure and the presence or suspicion of pheochromocytoma. (14)

DIURETICS. Diuretics are safe, effective, first-line therapy for hypertension. Thiazide diuretics are the preferred choice to treat essential hypertension in adults. In children, there is no consensus on the best or preferred medications due to the lack of data. Clinicians are guided by their own experience, except in cases where there are clear advantages or contraindications to other classes of drugs. With the development of alternatives to diuretics such as ACEis, ARBs, and CCBs, some practitioners have limited the use of diuretics as first-line medications. Such decreased use may relate to their adverse effects. In some situations, diuretics can be synergistic with other agents, such as ACEis and ARBs, and are included in combination products (Table 6).

Diuretics exert their action on the kidney by inhibiting absorption of solute, resulting in decreased reabsorption of water and enhanced urine flow. (14) The classification of diuretics is based on the mechanism of their inhibition of solute reabsorption. Due to the potential adverse effect of hypokalemia, serum potassium concentrations should be monitored regularly. Common adverse effects include fluid and electrolyte disturbances (hypokalemia, volume depletion/hypotension, hypomagnesemia, hypercalcemia); metabolic disturbances (decreased glucose tolerance, hyperlipidemia, hyperuricemia); gastrointestinal effects (anorexia, gastric irritation, nausea/vomiting, cramping, diarrhea, intrahepatic cholestatic jaundice, pancreatitis); and ototoxicity in patients receiving furosemide, particularly when combined with other ototoxic medications. (14)

Potassium-sparing diuretics (spironolactone, triamterene, amiloride) are used primarily when diuretics are needed, but there is concern about hypokalemia. The diuretic effect of spironolactone results from its action as a competitive antagonist of aldosterone. It is efficacious in children who have increased plasma aldosterone concentrations because of conditions such as hyperaldosteronism, congestive heart failure, or hepatic disease. (14) Amiloride and triamterene have utility in low renin forms of hypertension. As noted, diuretics generally are used as adjunctive therapy with other drugs to improve blood pressure control.

Continuation of Case Study

The obese child who had hypertension underwent an extensive evaluation without discovery of a secondary cause of his hypertension, aided by the use of the appropriate cuff size and ABPM. His elevated serum uric acid concentration was strongly predictive of essential hypertension. Due to the LVH and the magnitude of the hypertension, he was a candidate for concomitant nonpharmacologic and pharmacologic therapy to reduce his risk factors for coronary artery disease. He was referred to a nutritionist to assist in nonpharmacologic treatment (dietary modifications of calories, lipids, and sodium). Initial pharmacologic therapy was hydrochlorothiazide (12.5 mg/day with monitoring of his electrolytes). Over the next 12 months under close follow-up, his hypertension was controlled. Because of significant weight loss, his diuretics were discontinued, and his blood pressure was normal at the 50th percentile for age and height. Subsequent echocardiography demonstrated normal left ventricular wall thickness.

Conclusion

The evaluation and treatment of hypertension in childhood has continued to evolve over the past 4 decades. The genetic verification of selected forms of hypertension, newer imaging modalities, and improved antihypertensive drugs have provided a more focused approach to

pediatric hypertension. Despite these advances, the basic requirements for detecting and evaluating the hypertensive youth remain a thorough history and physical examination.

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USPSTF: Blood Pressure Screening Not Useful for Children

Lara C. Pullen, PhD | October 07, 2013

The US Preventive Services Task Force (USPSTF) has concluded that "the current evidence is insufficient to assess the balance of benefits and harms of screening for primary hypertension in asymptomatic children and adolescents to prevent subsequent cardiovascular disease in childhood or adulthood."

The recommendation stands in contrast to the endorsement from the American Academy of Pediatrics of the National High Blood Pressure Education Program 2004 recommendations that children aged 3 years or older have their blood pressure measured at least once at every "health care episode."

The USPSTF published their recommendation statement online October 7 in both the *Annals of Internal Medicine* and *Pediatrics*. Task force members reviewed studies published since 2003 and could not find any clear evidence that justified blood pressure screening in the general pediatric population.

The recommendations, which are an update to 2003 recommendations, relate specifically to children and teenagers who do not have an underlying health problem and have no signs or symptoms of high blood pressure and encourage clinicians to consider each patient specifically and make an individual decision for each patient.

As the childhood obesity rate has increased, so has the prevalence of high blood pressure in children and teenagers. The prevalence of hypertension among US children and adolescents ranges from 1% to 5%. The prevalence of hypertension among obese children is 11%.

Some clinicians have proposed that screening for hypertension in children and adolescents may allow for interventions to reduce blood pressure, thereby reducing the risk for cardiovascular events and death in adulthood. However, the task force could not find evidence to substantiate this hypothesis.

"We call on the research community to strengthen the evidence base linking screening and treatment of high blood pressure in children and teens to their long-term cardiovascular health," said USPSTF member Kirsten Bibbins-Domingo, MD, PhD, in a USPSTF news release.

Full conflict-of-interest information is available on the journal's Web sites.

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Send comments and news tips to news@medscape.net.

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Hypertension Cases:

Case 1:
A four-month-old presents to your clinic for a well visit, and because a murmur is heard incidentally, a blood pressure of 104/82 is obtained.

How do you determine whether this blood pressure is in the normal range for this child?

- *Norms for neonates and infants are listed in reference tables in Harriet Lane*
- *Four point blood pressures in a calm infant with appropriate cuff and technique will give the most accurate information*

What pertinent questions do you want to ask about the child's medical history?

- *Includes prematurity, UAC line, prior UTI, growth, urination pattern, family history*

What is your differential diagnosis for hypertension in a young patient?

- *Coarctation, obstructive uropathy or reflux, inherited or congenital renal disease*

What further workup would you choose for this child?

- *Careful exam to include attention to pulses; workup as guided by history and exam may include four-point BPs, EKG, echo; electrolytes with BUN, Cr, Ca; CBC, UA and renal ultrasound*

Case 2:
A ten-year-old child presents to your clinic with a chief complaint of headaches and tiredness, and vital signs reveal a blood pressure of 132/84. Exam is otherwise normal.

At what age should screening blood pressures begin for all pediatric patients?

- *Age three for asymptomatic children; earlier if any reason for heightened concern*
- *Norms based on age, height and gender are listed in reference tables in Harriet Lane*

What are the symptoms of chronic hypertension?

- *Headache, difficulty falling asleep, fatigue, chest pain, abdominal pain, poor concentration, decreased school performance.*

What is the differential diagnosis for hypertension?

- *Secondary hypertension can be divided into three main categories:*
  - ***Renovascular**: includes renal parencheymal disease, renovascular disease (renal artery stenosis), reflux or UTI, renal scarring, and kidney failure*
  - ***Cardiac**: coarctation*
  - ***Neuroendocrine**: includes pheochromocytoma, neuroblastoma, excess mineralocorticoid states. Increased intracranial pressure can also cause hypertension.*

What further questions would you like to ask in your interview?

- *Includes duration, timing and severity of symptoms; growth history; skin lesions suggestive of NF-1 or tuberous sclerosis; family history;(history of otitis media – masking VUR and renal scarring)*

What further workup would you choose for this child?

- *Let your history and physical guide your workup: a reasonable baseline of studies includes electrolytes with Bun, Cr, Ca; CBC, UA, TFTs and renal ultrasound. For rarer diagnostic possibilities, choose testing in consultation with a pediatric nephrologist.*

Case 3:

An obese adolescent boy presents for a sports physical and has no complaints, other than being extremely nervous about being examined "down there" while at the office visit. Vital signs reveal a blood pressure of 145/84.

Is one blood pressure reading sufficient to diagnose hypertension?

- *Three elevated readings are necessary. If white-coat hypertension is a concern, consider having readings done by the school nurse, or doing ambulatory blood pressure monitoring, which can get readings during sleep as well.*
- *>95th percentile for age is hypertension; 90-95th percentile or readings above 120/80 are considered pre-hypertension.*
- *Make sure appropriate cuff size is used; a cuff that is too small can falsely elevate a reading. Appropriate size cuff: bladder of cuff fits all the way around the circumference of the arm; cuff length is two-thirds the length of the humerus.*
- *If a child has been running around the waiting room and the BP is high, have them rest for ten minutes and then measure it again.*

What are some transient causes of hypertension?

- *Pain, stress, medications; anxiety (teens may be anxious about the genital exam)*

What questions would you like to ask? What physical findings will you be looking for?

- *Includes family history of hypertension, obesity, diabetes, heart disease, kidney disease or dialysis; history of medications, supplements, or recreational drugs; history indicating obstructive sleep apnea*

What workup is necessary before making essential hypertension your working diagnosis?

- *Essential hypertension is a diagnosis of exclusion. Most doctors would begin with a RFP, UA, and CBC. Based on your history and physical, consider fasting lipids and glucose, drug screen, serum uric acid, and/or renal ultrasound.*
- *Echo can be helpful in documenting LVH, which can be a marker of an ongoing hypertensive state*
- *Serum uric acid has been shown to be frequently high in essential hypertension in adults.*

What medications can cause hypertension?

- *Amphetamines, steroids, OCPs, cyclosporine, allergy and cold medications*

How is essential hypertension managed?

- *Reduction of salt intake to 2-3 gm per day*
- *Increased dynamic physical activity, while avoiding static exercise activities (assuming there is no history of exertional symptoms or concerning cardiac family history)*
- *Smoking cessation and alcohol reduction*
- *Medications prescribed in conjunction with a pediatric nephrologist or cardiologist*

Can he play football? Can he lift weights? What exercise restrictions, if any, are appropriate?

- *Adolescents with essential hypertension can be cleared for sports, but should not participate in activities with high static demand, such as weight lifting, power lifting, bodybuilding and high static component sports.*

Hypertension Board Review:

1) You are seeing a 14-year-old girl who presents for follow up of a previously elevated blood pressure measurement. There is no history of headaches. Her body mass index is at the 95th percentile and her heart rate is 82 beats/min. The systolic and diastolic blood pressure taken in the right arm is between the 90th and 95th percentile for her age and height. Physical examination findings are normal. Pulse rates are equal in all extremities and there is no pulse delay between the brachial and femoral arteries.

Of the following, the MOST appropriate next step is to:

A) initiate oral angiotensin-converting-enzyme inhibitor therapy
B) measure lower extremity blood pressures
C) obtain urine electrolytes
D) obtain urine 24-hour catecholamine levels
E) recommend increased physical activity and diet modification

Systemic hypertension is a major cause of morbidity and mortality in adults. It is uncommon in infants and children, with a prevalence of less than 1%, but, when present, is usually secondary to another disease process. Essential hypertension (no underlying cause) during childhood may persist into adulthood, as demonstrated in several studies. About 50% of adults who have hypertension have a blood pressure greater than the 90th percentile during childhood.

Accurate blood pressure (BP) measurement may be difficult, especially in larger children. A wide variety of cuff sizes should be available. The cuff should completely cover the upper part of the arm to ensure a uniform compression; the inflatable bladder should cover at least two-thirds of the upper arm length and 80% to 100% of its circumference. A cuff that is too short or too narrow will erroneously result in higher measurements.

Hypertension may be suspected when a BP reading is elevated for the child's height, age, and sex. The diagnosis is established when a high reading is obtained at 3 or more office visits separated by about 1 week. The patient described in the vignette has a borderline BP reading (systolic and diastolic pressures between 90th and 95th percentile). This state is called pre-hypertension. It is important to follow this patient's BP over time and to implement lifestyle modifications, such as weight reduction and increased physical activity.

For those who have persistent elevations, the approach should focus on the management of the elevation and the nature of concurrent signs or symptoms (Item C38). The use of an ambulatory BP monitor may aid in the diagnosis of hypertension by limiting intraobserver and interobserver variability.

Initiation of angiotensin-converting-enzyme inhibitor therapy is not indicated because the patient does not fulfill criteria for hypertension. If coarctation of the aorta is suspected, measuring the BP in all 4 extremities is useful. Those who have coarctation exhibit hypertension and discrepant or delayed upper-to-lower extremity pulse relationship; these findings were not present in the girl in the vignette.

Given that renal disorders are among the most common causes of secondary hypertension in children, a renal workup may be initiated to investigate for renal parenchymal or vascular disease. A complete cell blood cell count may detect anemia of chronic renal disease, and urine analysis provides an index of both glomerular (protein and blood) and tubular function (pH, specific gravity, and glucose). Urine electrolytes alone would not be a specific diagnostic test to ascertain a renal etiology in a patient who is pre-hypertensive.

Collection of catecholamines from a 24-hour urine sample can be helpful when one suspects that hypertension is caused by an adrenal tumor. However, patients with adrenal tumors generally have tachycardia, headaches, and hypertension: findings not exhibited by the patient in the vignette.

2) A 3-year-old girl presents to the emergency department with irritability and weakness that was followed by the development of nausea and vomiting and finally a seizure. Her mother reports that earlier in the day she found the girl playing in the medicine cabinet but did not see her take any pills. Physical examination reveals a toxic-appearing, febrile child who has hypertension, tachycardia, dilated pupils, hyperreflexia, reduced muscle strength, and abdominal tenderness. You order a toxicology panel.

Of the following, the MOST likely cause of the child's clinical findings is an overdose of:

A) acetaminophen
B) amphetamines
C) barbiturates
D) digoxin
E) narcotics

The girl described in the vignette is hypertensive and exhibits other typical signs and symptoms of an amphetamine overdose. Amphetamines are powerful central nervous system stimulants that also have peripheral adrenergic actions. The acute toxic effects due to overdose include hyperactive reflexes, dilated pupils, talkativeness, irritability, weakness, and fever. In addition, the patient may experience palpitations, tachycardia, hypertension, nausea, vomiting, diarrhea, and abdominal cramps. Severe overdose is associated with seizure, coma, and stroke. A wide variety of prescription drugs (eg, corticosteroids, combined oral contraceptives), over-the-counter drugs (eg, cough and cold medicines, nonsteroidal anti-inflammatory drugs) and supplements (eg, caffeine-containing products, ginseng) can elevate blood pressure.

Hepatotoxicity is the primary and most dangerous adverse effect of acetaminophen overdose. Barbiturates are central nervous system sedative-hypnotic agents that primarily depress the level of consciousness. They may cause normal or small pupils and uncommonly result in hypotension. Digoxin has a narrow therapeutic index, and overdose is not uncommon at the higher end of the prescribed dose range. Toxic effects may include palpitations due to atrial and ventricular arrhythmias, nausea and vomiting, and visual disturbances that include blurred vision and xanthopsia (a disturbance of color vision involving yellow and green). Electrocardiographic findings may include bradycardia, atrioventricular block, and a highly reproducible change that results in slurring of the upstroke of the PR interval. Narcotic ingestion causes sedation, analgesia, respiratory depression, pinpoint pupils, hypotension, nausea, and vomiting.

3) A 6-year-old girl presents for a health supervision visit that was scheduled as a follow-up appointment after she had an elevated blood pressure at an urgent care facility during an evaluation for abdominal pain. Her abdominal pain has resolved. Her mother recalls the blood pressure in the urgent care center as 135/90 mm Hg. The girl has had two urinary tract infections with fever in the past, and her father had hypertension diagnosed at age 45 years. On physical examination, the girl's temperature is 37.3°C, heart rate is 90 beats/min, respiratory rate is 20 breaths/min, and blood pressure is 146/86 mm Hg. A repeat blood pressure reading is 142/88 mm Hg. The four limb blood pressures are: 142/88 mm Hg in the right arm, 144/84 mm Hg in the left arm, 156/100 mm Hg in the right leg, and 160/96 mm Hg in the left leg. You find no cardiac murmurs, abdominal bruits, or edema. Femoral pulses are 2+ and symmetrical bilaterally. Renal ultrasonography shows the left kidney to be 8.5 cm with normal corticomedullary differentiation and the right kidney to be 5.5 cm with increased echogenicity.

Of the following, the MOST likely cause for this patient's elevated blood pressure is:

A) coarctation of the aorta
B) essential hypertension
C) renal artery stenosis
D) renal hypoplasia/dysplasia
E) renal scarring from prior pyelonephritis

The 6-year-old girl described in the vignette presents with hypertension that was initially observed in an urgent care facility and confirmed on two measurements in the clinic. Her past history is notable for two febrile urinary tract infections (UTIs), and her physical examination findings are essentially unremarkable. Of note, femoral pulses are present and blood pressures are higher in the legs than in the arms, observations that make coarctation of the aorta highly unlikely. Essential hypertension is a diagnosis of exclusion, often presenting with mild hypertension in adolescent patients who are overweight and have a positive family history of hypertension. The family history of hypertension in this patient's father is likely insignificant, based on his age of onset. Renal artery stenosis is a rare cause of hypertension in the pediatric patient and may have associated abdominal bruits on examination and a small kidney on ultrasonography. Although this girl does have a small kidney on ultrasonography, the increased echogenicity suggests renal parenchymal injury, which would not be expected in renal artery stenosis. Renal hypoplasia/dysplasia can be associated with an isolated small kidney, but hypertension is uncommon in this setting. The most likely cause of the hypertension in this child is renal scarring from prior pyelonephritis.

Vesicoureteral reflux (VUR) is discovered in 30% to 50% of children evaluated for febrile UTI. VUR can cause renal parenchymal damage in the form of renal scarring, which is known as reflux nephropathy. A recent study revealed renal scarring in infants who had VUR that increased with increasing severity of reflux: 7%, 21%, and 43% for grades III, IV, and V reflux, respectively. Hypertension can occur in up to 20% of patients who have reflux nephropathy and may take up to 8 years to develop. Conversely, 30% to 40% of pediatric patients who have secondary hypertension have renal scars from VUR. This is one of the reasons why febrile UTIs are evaluated aggressively with renal imaging in the hopes of uncovering VUR at an early age. In addition to increased risk for hypertension, reflux nephropathy also can cause end-stage renal disease later in life. Prospective studies are ongoing to evaluate the effectiveness of prophylactic antibiotics in the prevention of renal scars. The current recommendations are to use prophylactic antibiotics in children who have a febrile UTI and VUR. Patients usually respond well to angiotensin-converting enzyme inhibitors for the treatment of hypertension associated with renal scarring. Such therapy should be used with caution in females of childbearing age due to risks of teratogenicity.

4) You are seeing a 9-year-old prepubertal boy for the first time for a health supervision visit. The father mentions that the boy is playing competitive tennis, and his coach would like him to start a strength training program to improve his sports performance. The child has a past history of a murmur, but the father does not know any further details. The boy is currently asymptomatic and his examination findings are normal.

Of the following, the MOST appropriate advice to provide the father about strength training is that:

A) evidence shows that strength training affects growth plates adversely and impairs linear growth
B) specific strength-training exercises should be learned initially with no or low resistance
C) the most commonly reported adverse affects of strength training are injuries to joint structures such as ligaments
D) the risk of injury to children in supervised strength training programs exceeds the risk of injury in team sports
E) to be effective, the athlete must participate in strength training four or more times per week

Even as obesity and sedentary lifestyles become common, participation in competitive sports is increasing among youth. Coaches or athletes may see strength training as a method to enhance performance and prevent or rehabilitate injuries. Pediatricians have been concerned that resistance training might prove harmful, particularly to prepubertal children. However, an increasing body of literature demonstrates that resistance training, when pursued with proper technique and appropriate supervision, can be used successfully and safely by both adolescents and preadolescents to increase muscle strength. Evidence that this type of training is effective in preventing or lessening the severity of injury is limited, and no evidence indicates that it prevents catastrophic sports injury.

Strength training can begin once the child has developed appropriate balance and postural support, generally at age 7 or 8. All such training should be performed with close, appropriately trained, and (optimally) certified supervision. Initially, training should begin with no or low resistance until technique is perfected. Weight load can be added and subsequently increased in 10% increments. Sessions should last 20 to 30 minutes and occur two to three times per week; four or more sessions per week provide no additional benefit and may be associated with overuse injuries. Strength training should be coupled with aerobic conditioning, and appropriate warm up and cool down is encouraged. Of course, performance-enhancing drugs must not be used. With appropriate supervision, the risk of injury is low for strength training, accounting for less than 1% of sports-related injuries among school-age children in one study. By contrast, football contributed 19%, basketball 5%, and soccer 2% of injuries. Most strength training-related injuries were muscle strains rather than joint injuries, with low back pain being the most common complaint among high-school students in several studies.

Although the risk from appropriately performed resistance training is limited, certain children require more in-depth medical evaluation before they embark on such a program. Among those who require clearance before participation are: 1) children/teens who have uncontrolled hypertension; 2) patients who have undergone chemotherapy with anthracyclines (because of the drugs' cardiotoxicity); 3) patients who have cardiomyopathies, particularly hypertrophic cardiomyopathy; 4) youth who have moderate-to-severe pulmonary hypertension; 5) those who have Marfan syndrome with a dilated aortic root; and 6) children and teens who have seizure disorders that are not well controlled. Being skeletally immature is not a contraindication because there is no evidence that resistance training affects growth plates or linear growth.

5) A 14-year-old girl presents with periorbital swelling for the past week that is worsening. She had upper respiratory tract symptoms approximately 10 days ago. She denies itching at her eyes. Otherwise, she has been well. On physical examination, she is afebrile with a pulse rate of 76 beats/minute, a respiratory rate of 16 breaths/minute, and blood pressure of 136/86 mm Hg. Her examination is remarkable for bilateral periorbital edema with normal conjunctivae. She also has pitting edema from her pretibial region to the level of her knees. You suspect that the patient may have nephrotic syndrome. The following are results of her urinalysis:

Urine test strip:
- Specific gravity, 1.025
- pH, 7
- 3+ protein
- 1+ blood

Of the following, the laboratory finding that is MOST likely to indicate a poor renal prognosis for this girl is:

A) serum albumin of 1.4 g/dL (14 g/L)
B) serum complement component 3 (C3) of 40
C) serum creatinine of 0.7 mg/dL (61.88 μmol/L)
D) urine microscopy of 10 to 20 red blood cells/HPF
E) urine protein to creatinine ratio of 14

The patient in the vignette presents with edema, hypertension, 3+ proteinuria, and 1+ hematuria. While this patient has features of nephrotic syndrome, there are some features that challenge this potential diagnosis. While the majority of children with minimal change nephrotic syndrome (MCNS) are normotensive and lack microscopic hematuria, approximately 15% to 20% of children with MCNS have hypertension, and 20% to 25% have microscopic hematuria. By contrast, hypertension is present in approximately 40% of children with focal segmental glomerulosclerosis (FSGS) or membranoproliferative glomerulonephritis (MPGN), and microscopic hematuria is seen in 50% to 60% of children with these glomerular lesions.

The nephrotic syndrome is defined as marked proteinuria (3+ to 4+), hypoalbuminemia, and edema. Most often, the child has normal blood pressure and minimal microscopic hematuria. Unusual features would include gross hematuria, azotemia, and hypocomplementemia. When unusual features are present, the clinician should consider referral or discussion with a pediatric nephrologist because a renal biopsy could be considered. However, although a renal biopsy may better define the histologic lesion, the clinician should have a working diagnosis before proceeding with a biopsy with the understanding that the information gathered by a renal biopsy would alter the medical management. Another predictor of a histologic lesion is hypocomplementemia, which would raise the question of membranoproliferative glomerulonephritis (MPGN) or lupus nephritis.

The most important determination of renal prognosis is based on whether the nephrotic syndrome is steroid responsive (ie, responding to a prednisone dosage of 60 mg/m2/day over 4 to 6 weeks). Because the patient in the vignette demonstrates features of nephrotic syndrome, the presence of hypoalbuminemia, marked proteinuria, and normal serum creatinine would be very much expected and would not predict a poor renal prognosis. Again, microscopic hematuria can be seen in nearly 25% of children with MCNS, which tends to be steroid responsive; therefore, the presence of 10 to 20 red blood cells per high-power field would likewise not predict a poor renal prognosis. By contrast, a complement component 3 (C3) of 40 would indicate hypocomplementemia. In this setting, a renal biopsy would be warranted to look for MPGN, which is a chronic form of glomerulonephritis and carries a more guarded long-term prognosis.