



Q/ Whom should you test for secondary causes of hypertension?

EVIDENCE-BASED ANSWER

A | **IT'S RECOMMENDED** that all children and adolescents with a new diagnosis of hypertension undergo renal ultrasound and laboratory evaluation for renal pathology (strength of recommendation [SOR]: **C**, consensus-based guidelines).

Specific diagnostic tests are recommended for newly diagnosed patients who have suspicious clinical findings suggestive of a secondary cause of hypertension

based on the initial history (excess daytime sleepiness, palpitations, tremor, sweating); physical examination (abdominal bruit, thyromegaly, malar rash); or laboratory analysis (elevated serum creatinine, low thyroid-stimulating hormone) (SOR: **C**, consensus-based guidelines).

Patients with undifferentiated resistant hypertension should receive further directed evaluation for secondary causes (SOR: **C**, consensus-based guidelines).

Evidence summary

The evidence for selecting which patients should undergo additional testing for potentially correctable secondary causes of hypertension is based on the prevalence of these causes in different age groups, case series of reversal of hypertension with effective treatment of the underlying cause, and clinical suspicion of a secondary cause that may be reversible. We found no prospective cohort studies or randomized trials evaluating diagnostic approaches or outcomes associated with particular selection criteria for conducting additional diagnostic evaluations in search of secondary causes. Therefore, our recommendations are based primarily on expert guidelines, which we summarize here.

When caring for children and adolescents with newly diagnosed hypertension...

Secondary hypertension is more prevalent in younger children and in children and adolescents with stage 2 hypertension (blood pressure [BP] >99th percentile for age and height plus 5 mm Hg).¹ Renoparenchymal and renovascular disease account for most cases of secondary hypertension in these children.²

The National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents recommends that all children and adolescents with hypertension have an additional diagnostic work-up. This is based on the observation that 70% to 85% of children <12 years and 10% to 15% of adolescents 12 to 18 years with hypertension have an underlying cause, most commonly renoparenchymal and renovascular disease.³

According to the National Institutes of Health (NIH), “the possibility that some underlying disorder may be the cause of the hypertension should be considered in every child or adolescent” with elevated BP, but the evaluation itself should be individualized.³

The NIH recommends more extensive evaluation for very young children, children with stage 2 hypertension, and children or adolescents who show clinical signs suggesting hypertension-linked systemic conditions. Such evaluation should include a renal ultrasound and laboratory testing (creatinine, urinalysis, and urine culture) to look for structural or functional anomalies.³

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CLINICAL INQUIRIES

TABLE

Secondary causes of hypertension: Identifying and evaluating suggestive findings¹²⁻¹⁴

History	Physical examination	Laboratory findings	Potential etiology	Diagnostic approach
Adults: Excessive daytime sleepiness, snoring, morning headache, witnessed apnea Children: Poor school performance, inattentiveness	Overweight/obese, large neck size, crowded oropharynx, adenotonsillar hypertrophy	None	Sleep apnea syndrome	Polysomnogram
Headache, muscle weakness, paresthesias, paralysis	Resistant hypertension, stage 2 hypertension	Hypokalemia, metabolic alkalosis, "incidentaloma" on CT scan	Primary aldosteronism	Plasma aldosterone-to-renin activity ratio; CT imaging of adrenal glands
Adults: African American, comorbid DM or atherosclerotic disease Children: Enuresis, family history of renal disease, fatigue, recurrent UTI	Abdominal mass, gross hematuria, growth restriction	Proteinuria, elevated creatinine	Renoparenchymal disease	24-hour urine for protein and creatinine; renal ultrasound
<Age 30 yr and female or >Age 50 yr and male	Abdominal bruit, flash pulmonary edema	Elevated creatinine (particularly after ACE-I or ARB use for hypertension)	Renovascular disease; fibromuscular dysplasia; atherosclerosis	MR or CT angiogram (normal renal function); MR angiogram or ultrasound of the kidneys (diminished renal function)
Muscle weakness, bruising, acne, edema, hirsutism, oligomenorrhea	Truncal obesity, abdominal striae, moon facies, ecchymosis	Hypokalemia, hyperglycemia	Cushing disease	Urinary free cortisol; dexamethasone suppression test; ACTH; CT/MRI of the pituitary and/or abdomen
Paroxysmal hypertension, headache, palpitations, tremor, flushing	Resistant hypertension, tachycardia, pallor	None	Pheochromocytoma	Plasma-free metanephrines; CT/MRI of the abdomen
None	Difference in right and left arm BP, diminished femoral pulses, heart murmur, lower BP in legs than arms	None	Coarctation of the aorta	Echocardiogram
Family history of thyroid disorder, heat intolerance, rash, sweating, pallor	Ophthalmopathy, tachycardia, thyromegaly, weight loss	Suppressed thyroid-stimulating hormone	Hyperthyroidism	Thyroid scan
Family history of autoimmune disease, fatigue, joint pain, rash	Friction rub, joint swelling, malar rash	Elevated white blood cell count	Rheumatologic disorder	Abnormal findings on autoimmune laboratory studies; elevated markers of inflammation

ACE-I, angiotensin-converting enzyme inhibitor; ACTH, adrenocorticotropic hormone; ARB, angiotensin II receptor blocker; BP, blood pressure; CT, computed tomography; DM, diabetes mellitus; MR, magnetic resonance; MRI, magnetic resonance imaging; UTI, urinary tract infection.

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➤ **Renal ultrasound and laboratory evaluation for renal pathology are recommended for all children and adolescents with a new diagnosis of hypertension.**

What about newly diagnosed adults with suspected secondary causes?

Secondary hypertension reportedly occurs in 5% to 10% of hypertensive patients.^{4,5} The only prospective study completed in a primary care setting evaluated 1020 patients at a general outpatient clinic in Yokohama, Japan. The investigators reported that 9.1% of the patients had an endocrinologic or renovascular cause contributing to their hypertension.⁶ The 5 most common causes were primary aldosteronism (6%), Cushing syndrome (1%), preclinical Cushing syndrome (1%), pheochromocytoma (0.6%), and renovascular disease (0.5%).⁶

According to the Institute for Clinical Systems Improvement (ICSI), patients at highest risk for secondary hypertension have no family history of hypertension; abrupt onset, symptomatic, or crisis hypertension; stage 2 hypertension; sudden loss of hypertensive control; and drug-resistant hypertension.⁷

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommends that patients with the following characteristics undergo further directed evaluation for a secondary cause:⁸

- younger than 30 years with no family history of hypertension
- older than 55 years with new hypertension
- abdominal bruit with diastolic component

- sudden worsening of BP control
- recurrent flash pulmonary edema
- renal failure with abnormal urinary sediment or proteinuria
- acute renal failure after administration of an ACE inhibitor or ARB.

These patients should receive particular scrutiny

Patients with resistant hypertension (BP > 140/90 mm Hg despite taking optimal doses of 3 antihypertensive medications, one of which is a diuretic) should receive particular scrutiny for an identifiable secondary cause, according to the ICSI.⁷

In a retrospective analysis of 141 patients with resistant hypertension referred to a university hypertension center in Chicago in 2005, 5% of patients had an identifiable secondary cause.⁹ A chart review of 436 patients presenting to a tertiary hypertension clinic in Japan identified 91 with resistant hypertension. A secondary cause was identified in 9.1%.¹⁰

Careful history and examination should identify patients suffering from uncontrolled hypertension because of noncompliance, suboptimal antihypertensive regimen, inaccurate BP readings, antagonizing substances, and white coat hypertension.¹¹ The **TABLE** summarizes common presentations of, and workup for, secondary causes of hypertension.¹²⁻¹⁴

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References

1. 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*. Rockville, MD: National Heart, Lung, and Blood Institute, US Department of Health and Human Services; May 2005. NIH Publication No. 05-5267.
2. Hansen ML, Gunn PW, Kaelber DC. Underdiagnosis of hypertension in children and adolescents. *JAMA*. 2007;298:874-879.
3. Brady TM, Feld LG. Pediatric approach to hypertension. *Semin Nephrol*. 2009;29:379-388.
4. Taler SJ. Secondary causes of hypertension. *Prim Care Clin Office Pract*. 2008;35:489-500.
5. Chiong JR, Aronow WS, Khan IA, et al. Secondary hypertension: current diagnosis and treatment. *Int J Cardiol*. 2008;124:6-21.
6. Omura M, Saito J, Yamaguchi K, et al. Prospective study on the prevalence of secondary hypertension among hypertensive patients visiting a general outpatient clinic in Japan. *Hypertens Res*. 2004;27:193-202.
7. Luehr D, Woolley T, Burke R, et al. Institute for Clinical Systems Improvement. Hypertension Diagnosis and Treatment. Available at: <http://bit.ly/Hypertension1112>. Updated November 2012. Accessed January 7, 2010.
8. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension*. 2003;42:1206-1252.
9. Garg JP, Elliott WJ, Folker A, et al; Rush University Hypertension Service. Resistant hypertension revisited: a comparison of two university-based cohorts. *Am J Hypertens*. 2005;185:619-626.
10. Yakovlevitch M, Black HR. Resistant hypertension in a tertiary care clinic. *Arch Intern Med*. 1991;151:1786-1792.
11. O'Rourke JE, Richardson WS. What to do when hypertension is difficult to control. *BMJ*. 2001;322:1229-1232.
12. Rossi GP, Seccia TM, Pessina AC. Clinical use of laboratory tests for the identification of secondary forms of arterial hypertension. *Crit Rev Clin Lab Sci*. 2007;44:1-85.
13. Riley M, Bluhm B. High blood pressure in children and adolescents. *Am Fam Physician*. 2012;85:693-700.
14. Viera AJ, Neutze DM. Diagnosis of secondary hypertension: an age based approach. *Am Fam Physician*. 2010;82:1471-1478.