Diagnosing Secondary Hypertension

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Secondary hypertension is elevated blood pressure that results from an underlying, identifiable, often correctable cause. Only about 5 to 10 percent of hypertension cases are thought to result from secondary causes. The ABCDE mnemonic can be used to help determine a secondary cause of hypertension: *A*ccuracy of diagnosis, obstructive sleep *A*pnea, *A*ldosteronism, presence of renal artery *B*ruits (suggesting renal artery stenosis), renal parenchymal disease (*B*ad kidneys), excess *C*atecholamines, *C*oarctation of the aorta, *C*ushing's syndrome, *D*rugs, *D*iet, excess *E*rythropoietin, and *E*ndocrine disorders. An algorithm showing the general strategy to help screen for factors involved in secondary hypertension is presented. Routine urinalysis, complete blood cell count, blood chemistry profile (potassium, sodium, creatinine, fasting glucose, fasting lipid levels), and a 12-lead electrocardiogram are recommended for all patients with hypertension. (Am Fam Physician 2003;67:67-74. Copyright© 2003 American Academy of Family Physicians)

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Patients with hypertension have some underlying mechanism that elevates their blood pressure. Conceptually, it is useful to think of patients with hypertension as having either essential hypertension (systemic hypertension of unknown cause) or secondary hypertension (hypertension that results from an underlying, identifiable, often correctable cause).[1] Although only about 5 to 10 percent of hypertension cases are thought to result from secondary causes, hypertension is so common that secondary hypertension probably will be encountered frequently by the primary care practitioner.[2-4]

The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI)[5] defines four goals for the evaluation of the patient with elevated blood pressure: detection and confirmation of hypertension; detection of target organ disease (e.g., renal damage, congestive heart failure); identification of other risk factors for cardiovascular disorders (e.g., diabetes mellitus, hyperlipidemia); and detection of secondary causes of hypertension. Physicians can use the mnemonic ABCDE to help determine secondary causes in the patient with elevated blood pressure (*Table 1*).

Diagnosis: ABCDE

A: ACCURACY, APNEA, ALDOSTERONISM

Accuracy. The first, most practical step in evaluating an elevated blood pressure reading is to investigate its accuracy. A blood pressure cuff that is too small, tight-fitting sleeves that are not removed, or a brachial artery that is noncompressible because of calcification (sometimes seen in the elderly) can cause falsely elevated readings. White-coat hypertension (blood pressure that is elevated in the physician's office but normal at other times) accounts for about 20 percent of patients with elevated readings.[3] JNC-VI recommends confirming high blood pressure readings outside of the office setting.

Apnea. Obstructive sleep apnea (OSA), a repetitive mechanical obstruction of the upper airway during sleep, is an independent risk factor for hypertension.[6] At least one half of patients with OSA have hypertension.[7] Treatment of OSA with surgery or nasal continuous positive air-

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TABLE 1
Findings That Suggest Secondary Hypertension

Findings	Disorder suspected	Further diagnostic studies
Snoring, daytime somnolence, obesity	Obstructive sleep apnea	Sleep study
Hypernatremia, hypokalemia	Aldosteronism	Ratio of plasma aldosterone to plasma renin activity, CT scan of adrenal glands
Renal insufficiency, atherosclerotic cardiovascular disease, edema, elevated blood urea nitrogen and creatinine levels, proteinuria	Renal parenchymal disease	Creatinine clearance, renal ultrasonography
Systolic/diastolic abdominal bruit	Renovascular disease	Magnetic resonance angiography, captopril (Capoten)-augmented radioisotopic renography, renal arteriography
Use of sympathomimetics, perioperative setting, acute stress, tachycardia	Excess catecholamines	Confirm patient is normotensive in absence of high catecholamines.
Decreased or delayed femoral pulses, abnormal chest radiograph	Coarctation of aorta	Doppler or CT imaging of aorta
Weight gain, fatigue, weakness, hirsutism, amenorrhea, moon facies, dorsal hump, purple striae, truncal obesity, hypokalemia	Cushing's syndrome	Dexamethasone-suppression test
Use of drug in Table 2	Drug side effect	Trial off drug, if possible
High salt intake, excessive alcohol intake, obesity	Diet side effects	Trial of dietary modification
Erythropoietin use in renal disease, polycythemia in COPD	Erythropoietin side effect	Trial off drug, if possible
Paroxysmal hypertension, headaches, diaphoresis, palpitations, tachycardia	Pheochromocytoma	Urinary catecholamine metabolites (vanillylmandelic acid, metanephrines, normetanephrines) Plasma free metanephrines
Fatigue, weight loss, hair loss, diastolic hypertension, muscle weakness	Hypothyroidism	TSH levels
Heat intolerance, weight loss, palpitations, systolic hypertension, exophthalmos tremor, tachycardia	Hyperthyroidism	TSH levels
Kidney stones, osteoporosis, depression, lethargy, muscle weakness	Hyperparathyroidism	Serum calcium, parathyroid hormone levels
Headaches, fatigue, visual problems, enlargement of hands, feet, tongue	Acromegaly	Growth hormone level

CT = computed tomography; COPD = chronic obstructive pulmonary disease; TSH = thyroid-stimulating hormone.

way pressure reduces hypertension in these patients.[8] Daytime somnolence, obesity, snoring, lower-extremity edema (secondary to the right-sided congestive heart failure that occurs after repetitive anoxic insults to the myocardium during sleep), morning headaches, and nocturia suggest OSA.[9] There is a high incidence of OSA in patients with chronic obstructive pulmonary disease (COPD). A formal sleep study usually is needed for diagnosis of OSA and determination of corrective interventions.

Aldosteronism. Primary hyperaldosteronism is defined as overproduction of aldosterone independent of its usual regulator, the renin-angiotensin system.[10] The resulting retention of excess salt and water suppresses renin levels (as opposed to elevating renin levels, which causes secondary hyperaldosteronism). Increased urinary excretion of potassium signals hyperaldosteronism, which should be suspected in all hypertensive patients with unprovoked (i.e., not diuretic-induced) hypokalemia.[11] The next diagnostic test should be demonstration of an elevated ratio of plasma aldosterone levels to plasma renin activity.[12]

B: BRUITS, BAD KIDNEYS (RENAL PARENCHYMAL DISEASE)

Bruits. Renovascular hypertension is defined as hypertension resulting from compromised arterial supply to the kidneys. About 65 percent of renovascular disease is secondary to atherosclerosis in the renal arteries, usually seen after age 50 in patients at risk for arterial compromise (e.g., smokers, patients with diabetes, patients with known atherosclerotic disease).[13] The remainder of patients will demonstrate fibromuscular dysplasia (FMD) and will tend to be younger (25 to 50 years of age) at the time of diagnosis.[13]

About one half of patients with renovascular hypertension will have an abdominal bruit identifiable on physical examination.[13] Bruits heard in both systole and diastole are more suggestive of renovascular hypertension than systolic bruits alone.[14] In unselected popula-

Increased urinary excretion of potassium signals hyperaldosteronism, which should be suspected in all hypertensive patients with unprovoked hypokalemia.

tions of hypertensive persons, the incidence of renovascular hypertension is less than 1 percent.[14] However, identification of this relatively small population can be important because surgery or angioplasty can reverse the hypertension, especially if performed early enough to prevent permanent renal damage.

Magnetic resonance angiography (MRA) is a noninvasive imaging modality with a sensitivity of 100 percent and a specificity of 70 to 90 percent compared with renal arteriography for detection of renal artery stenosis.[2,15] MRA best delineates the proximal renal vasculature and is therefore useful as an initial diagnostic tool for patients suspected of having atherosclerotic renal artery stenosis, which usually involves the proximal renal artery.[16] Patients suspected of having FMD, which tends to involve the distal renal artery, should undergo conventional angiography or computed tomographic angiography.[16]

Another initial diagnostic test is the captopril (Capoten)-augmented radioisotopic renogram.[17] This test is based on the fact that a kidney that is receiving an inadequate blood supply will activate the renin-angiotensin system. Therefore, a single dose of the angiotensin-converting enzyme (ACE) inhibitor captopril will abruptly reduce renal function in the ischemic kidney. A scan is considered positive if there is delayed or decreased uptake of the radioisotope in the stenotic kidney compared with the non-stenotic one, so this test is not as useful if stenosis is present bilaterally.[2]

Duplex ultrasound scanning is another diagnostic option, but it can be limited by its dependence on operator skill and experience. Renal arteriography remains the gold standard for defining the vessel anatomy but does not always correlate with postprocedural outcomes (i.e.,

surgical correction of the renal artery stenosis often does not resolve the hypertension).[13]

Bad Kidneys. Renal parenchymal disease can be a cause or consequence of hypertension. Progressive renal damage is caused by the mechanical and humoral effects of glomerular hypertension. The renal damage decreases the kidneys' ability to excrete salt and excess fluid (resulting in a low renin state, as opposed to the high renin state found in renovascular hypertension), and the hypertension worsens. As renal damage progresses, hyperparathyroidism develops and erythropoietin production increases, exacerbating the hypertension.[5,18] Thus, a vicious cycle of worsening renal function and hypertension begins.

Aggressive treatment of hypertension (particularly with ACE inhibitors) in patients with renal parenchymal disease can lower the blood pressure and slow the disease's progression, although it is difficult to effectively control hypertension in chronic renal disease. Early treatment of hypertension and diabetes, the two most common causes of end-stage renal disease, can lower the incidence of long-term renal complications.[18]

Diagnosis is based on loss of renal cortical function (demonstrated by elevated serum creatinine levels and decreased creatinine clearance), although it may be impossible to tell if the renal dysfunction is primary or secondary to the hypertension.[2]

C: CATECHOLAMINES, COARCTATION, CUSHING'S SYNDROME

Catecholamines. Excess catecholamine levels play a role in causing white-coat hypertension and hypertension in pheochromocytoma, OSA, and other diseases discussed in this article. Acute stress induces catecholamine release and often contributes to preoperative or postoperative hypertension. Over-the-counter or prescription decongestants can have sympathomimetic effects, as do nonprescription weight-loss preparations containing ephedra (ma huang).[19,20] The hypertensive effects of cocaine and amphetamines also are sympathomimetic.

Coarctation of the Aorta. Coarctation of the aorta is a congenital narrowing of the aortic lumen, most often occurring just distal to the origin of the left subclavian artery. Patients with less severe forms of the disorder may not be diagnosed until young adulthood but have a high incidence of premature death.[21] Diagnostic clues include decreased lower-extremity (femoral) pulses with upper-extremity hypertension, dyspnea on exertion, and chest radiographic findings of notched ribs (from dilated collateral vessels) and dilation of the aorta above and below the constriction (the "3" sign).[22]

Cushing's Syndrome. Cushing's syndrome can cause hypertension via the mineralocorticoid effects of excess glucocorticoids and is best screened for with a dexamethasone-suppression test.[23]

D: DRUGS, DIET

Drugs. Many prescription and nonprescription drugs can cause or exacerbate hypertension *(Table 2)*. Immunosuppressive agents such as cyclosporine (Sandimmune), tacrolimus (Prograf), and corticosteroids increase blood pressure in up to 80 percent of solid-organ transplant recipients.[5] Nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 (COX-2) inhibitors elevate blood pressure via their antiprostaglandin effects on the kidneys. Estrogen, in the dosages most often used in oral contraceptive pills (30 to 35 mcg), appears to have only a mild hypertensive effect and no increased risk for overall mortality or myocardial infarction (if

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smokers over age 35 are excluded).[24] The lower doses of estrogen used in postmenopausal hormone-replacement regimens actually can have some antihypertensive effect.[25] Nicotine in cigarettes, smokeless tobacco, and cigars causes transient (30 minutes or less) increases in blood pressure, although transdermal nicotine preparations do not appear to have this effect.[26] Because patients who smoke often have a cigarette just before coming into the physician's office, blood pressure should be rechecked after 30 minutes if initial readings are elevated. Although caffeine can raise blood pressure acutely, tolerance develops rapidly, and there appears to be no direct relationship between caffeine intake and chronic hypertension.[27] Chronic overuse of alcohol is a potentially reversible cause of hypertension.[4]

Diet. Excess consumption of dietary sodium is linked to chronic hypertension, although the lower limit of "excess" can be difficult to define. Blacks, the elderly, patients with diabetes, and patients with essential hypertension appear to be particularly sensitive to dietary sodium intake.[5] Low intake of potassium, calcium, and magnesium can have a similar but less pronounced effect.[5] Dietary patterns that cause obesity also can cause hypertension. Sustained weight reduction lowers blood pressure—often to normal levels—in at least one half of obese patients.[28] A loss of 5 to 10 percent of body weight can significantly reduce blood pressure.

E: ERYTHROPOIETIN, ENDOCRINE DISORDERS

Erythropoietin. Elevated erythropoietin levels can be endogenous (as in response to the chronic hypoxia of COPD) or exogenous (administered to alleviate the anemia seen in chronic renal failure). High erythropoietin levels can elevate blood pressure either via a polycythemia/hyperviscosity mechanism or by direct pressor effects.[7]

Endocrine Disorders. Hypothyroidism can cause decreased cardiac output with a compensatory increase in vascular tone, resulting in a more prominent rise in diastolic blood pressure than in systolic blood pressure.[7] Conversely, hyperthyroidism induces increased cardiac output and compensatory decreased vascular tone, causing a greater increase in systolic blood pressure.[7] A thyroid-stimulating hormone level is the best diagnostic screening test for thyroid disorders.

Hyperparathyroidism (primary or secondary to chronic renal insufficiency) is a potentially reversible cause of hypertension. Its incidence in hypertensive patients is about 1 percent, compared with a 0.1 percent incidence in the general population.[29] However, only 30 to 40 percent of patients with hyperparathyroidism have hypertension, and parathyroidectomy does not reliably resolve hypertension in patients with this disorder.[29] It is unclear how hyperparathyroidism increases blood pressure, because there is no direct correlation with parathyroid hormone or calcium levels.

TABLE 2

Drugs That Can Raise Blood Pressure

Drug class	Drug examples
Immunosuppressive agents	Cyclosporine (Sandimmune), tacrolimus (Prograf), corticosteroids
Nonsteroidal anti-inflammatory drugs	Ibuprofen (Motrin), naproxen (Naprosyn), piroxicam (Feldene)
COX-2 inhibitors	Celecoxib (Celebrex), rofecoxib (Vioxx), valdecoxib (Bextra)
Estrogens	30- to 35-mcg estrogen oral contraceptives
Weight-loss agents	Sibutramine (Meridia), phentermine (Adipex), ma huang (ephedra)
Stimulants	Nicotine, amphetamines
Mineralocorticoids	Fludrocortisone (Florinef)
Antiparkinsonian	Bromocriptine (Parlodel)
Monoamine oxidase inhibitors	Phenelzine (Nardil)
Anabolic steroids	Testosterone
Sympathomimetics	Pseudoephedrine (Novafed)

COX-2 = cyclooxygenase-2.

Pregnancy-induced hypertension has an incompletely understood neurohumoral mechanism (possibly initiated by inadequate establishment of blood supply to the developing placenta) and occasionally can develop in the immediate postpartum period.

Pheochromocytoma is another endocrine cause of hypertension. The classic symptoms include headache, diaphoresis, palpitations, and paroxysmal hypertension. The syndrome can vary depending on the types of catecholamines being produced, the amount and frequency of their release into the circulation, and other factors. The usual screening test has been urinary measurement of catecholamine metabolites (vanillylmandelic acid, metanephrines, normetanephrines).[30] Determination of plasma free metanephrines might be the test of first choice for diagnosis of this tumor, although availability of this test at
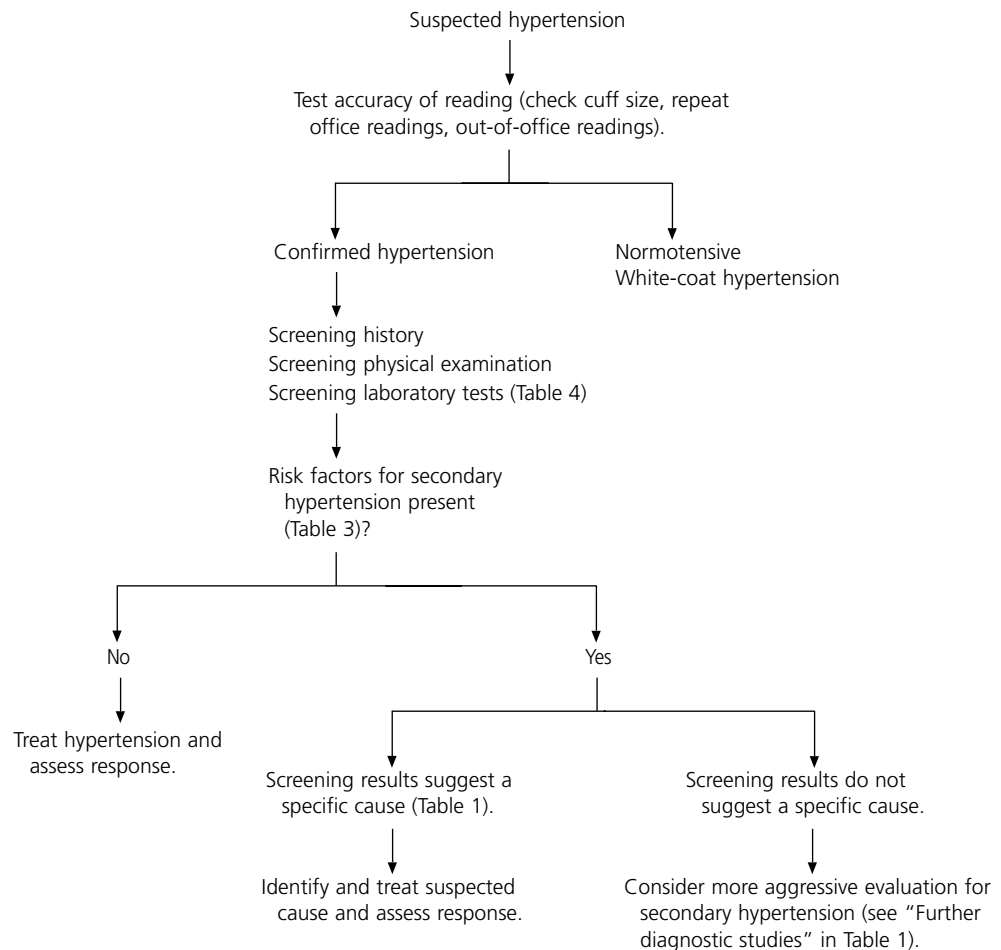
Evaluation for Secondary Causes of Hypertension

Suspected hypertension

↓

Test accuracy of reading (check cuff size, repeat office readings, out-of-office readings).

Confirmed hypertension → Normotensive White-coat hypertension

↓

Screening history
Screening physical examination
Screening laboratory tests (Table 4)

↓

Risk factors for secondary hypertension present (Table 3)?

No / Yes

No:
Treat hypertension and assess response.

Yes:
Screening results suggest a specific cause (Table 1).
↓
Identify and treat suspected cause and assess response.

Screening results do not suggest a specific cause.
↓
Consider more aggressive evaluation for secondary hypertension (see "Further diagnostic studies" in Table 1).

FIGURE 1. General strategy for diagnosing a secondary cause of hypertension.

hospital and reference laboratories is limited.[31] Pheochromocytoma is very rare, and routine screening in hypertensive patients is not recommended.

Acromegaly (elevated growth hormone) is a rare endocrine cause of hypertension.

Recommendations

A more aggressive evaluation for secondary causes of hypertension should be considered in certain clinical situations *(Table 3)*.[5,32,33] A diagnostic algorithm for secondary hypertension is presented in *Figure 1*.[34,35] However, there is little objective evidence that following these recommendations would significantly benefit patients. Despite this uncertainty, it would seem reasonable for the physician to follow the recommendations in the JNC-VI *(Table 4)* for routine medical history, physical examination, and laboratory testing. Doing so would screen for most of the secondary causes of hypertension discussed in this article, along with signs of target organ disease and comorbid factors. Although it is not one of the JNC-VI recommendations, obtaining fasting low-density lipoprotein cholesterol levels and triglyceride levels makes sense, because recent

The classic symptoms of pheochromocytoma include headache, diaphoresis, palpitations, and paroxysmal hypertension.

treatment recommendations by the National Cholesterol Education Program (NCEP-III) are based on these findings.[36]

REFERENCES

1. O'Rorke JE, Richardson WS. Evidence based management of hypertension: what to do when blood pressure is difficult to control. BMJ 2001;322:1229-32.
2. Wofford MR, King DS, Wyatt SB, Jones DW. Secondary hypertension: detection and management for the primary care provider. J Clin Hypertens 2000;2:124-31.
3. Setaro JF. An update on the diagnostic evaluation of the hypertensive patient. J Clin Hypertens 2000;2:25-32.

TABLE 3
Risk Factors for Secondary Hypertension

Poor response to therapy (resistant hypertension)

Worsening of control in previously stable hypertensive patient

Stage 3 hypertension (systolic blood pressure > 180 mm Hg or diastolic blood pressure >110 mm Hg)

Onset of hypertension in persons younger than age 20 or older than age 50

Significant hypertensive target organ damage

Lack of family history of hypertension

Findings on history, physical examination, or laboratory testing that suggest a secondary cause (Table 1)

Information from references 5,32, and 33.

TABLE 4
Routine Screening Laboratory Tests for Hypertension

Urinalysis

Complete blood count

Blood chemistries (potassium, sodium, creatinine, fasting glucose)

Fasting lipid profile (LDL, HDL, triglycerides, total cholesterol)

12-lead electrocardiogram

LDL = low-density lipoprotein; HDL = high-density lipoprotein.

Information from Joint National Committee. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.

4. Oparil S, Calhoun DA. Managing the patient with hard-to-control hypertension. Am Fam Physician 1998;57:1007-14.

5. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.

6. Silverberg DS, Oksenberg A. Essential and secondary hypertension and sleep-disordered breathing: a unifying hypothesis. J Hum Hypertens 1996;10:353-63.

7. Kaplan NM. Other forms of secondary hypertension. In: Kaplan NM, Lieberman E, eds. Clinical hypertension. 7th ed. Baltimore: Williams & Wilkins, 1998:395-406.

8. Stradling JR, Partlett J, Davies RJ, Siegwart D, Tarassenko L. Effect of short term graded withdrawal of nasal continuous positive airway pressure on systemic blood pressure in patients with obstructive sleep apnea. Blood Press 1996;5:234-40.

9. Victor LD. Obstructive sleep apnea. Am Fam Physician 1999;60:2279-86.

10. Gordon RD. Mineralocorticoid hypertension. Lancet 1994;344:240-3.

11. Ganguly A. Primary aldosteronism. N Engl J Med 1998;339:1828-34.

12. Gordon RD, Stowasser M, Tunny TJ, Klemm SA, Rutherford JC. High incidence of primary aldosteronism in 199 patients referred with hypertension. Clin Exp Pharmacol Physiol 1994;21:315-8.

13. Kaplan NM. Renal vascular hypertension. In: Kaplan NM, Lieberman E, eds. Clinical hypertension. 7th ed. Baltimore: Williams & Wilkins, 1998: 301-21.

14. Pohl M. Renal artery stenosis, renal vascular hypertension, and ischemic nephropathy. In: Schrier RW, Gottschalk CW, eds. Diseases of the kidney. 6th ed. Boston: Little, Brown, 1997:1367-423.

15. Cohen DL, Townsend RR. How to manage complex hypertension. Emerg Med 2001;33:20-9.

16. Yucel EK. MRA of the aorta, visceral and peripheral arteries. In: Higgins CB, Hricak H, Helms CA, eds. Magnetic resonance imaging of the body. 3d ed. Philadelphia: Lippincott-Raven, 1997:1383-99.

17. Aitchison F, Page A. Diagnostic imaging of renal artery stenosis. J Hum Hypertens 1999;13:595-603.

18. Kaplan NM. Renal parenchymal hypertension. In: Kaplan NM, Lieberman E, eds. Clinical hypertension. 7th ed. Baltimore: Williams & Wilkins, 1998: 281-99.

19. Phenylpropanolamine and other OTC alpha-adrenergic agonists. Med Lett Drugs Ther 2000;42:113.

20. Morelli V, Zoorob RJ. Alternative therapies: part I. Depression, diabetes, obesity. Am Fam Physician 2000;62:1051-60.

21. Perloff JK. Congenital heart disease in adults. In: Braunwald E, ed. Heart disease: a textbook of cardiovascular medicine. 5th ed. Philadelphia: Saunders, 1997:963-87.

22. Steiner RM. Radiology of the heart. In: Braunwald E, ed. Heart disease: a textbook of cardiovascular medicine. 5th ed. Philadelphia: Saunders, 1997: 204-39.

23. Fitzgerald PA. Endocrinology. In: Tierney LM, ed. Current medical diagnosis and treatment, 2001. 40th ed. New York: Lange/McGraw-Hill, 2001: 1088-160.

24. Oral contraception. In: Speroff L, Glass RH, Kase NG, eds. Clinical gynecologic endocrinology and infertility. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 1999:867-945.

25. Menopause and the perimenopausal transition. In: Speroff L, Glass RH, Kase NG, eds. Clinical gynecologic endocrinology and infertility. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 1999:643-724.

26. Kaplan, NM. Treatment of hypertension: nondrug therapy. In: Kaplan NM, Lieberman E, eds. Clinical hypertension. 7th ed. Baltimore: Williams & Wilkins, 1998:323-44.

27. Basic metabolism and physiologic effects of the methylxanthines. In: Spiller GA, ed. Caffeine. Boca Raton, Fla.: CRC Press, 1998:225-31.

28. Alexander D. Obesity and coronary heart disease. In: Alpert MA, Alexander JK, eds. The heart and lung in obesity. Armonk, N.Y.: Futura, 1998:213-38.

29. Dluhy RG, Williams RH. Endocrine hypertension. In: Williams RH, Wilson JD, eds. Williams Textbook of endocrinology. 9th ed. Philadelphia: Saunders, 1998:729-49.

30. Williams GH. Approach to the patient with hypertension. In: Braunwald E, ed. Harrison's Principles of internal medicine. 15th ed. New York: McGraw-Hill, 2001:211-4.

31. Lenders JW, Pacak K, Walther MM, Linehan WM, Mannelli M, Friberg P, et al. Biochemical diagnosis of pheochromocytoma: which test is best? JAMA 2002;187:1427-34.

32. Health care guideline: Hypertension diagnosis and treatment. Retrieved November 2002, from www.icsi.org/guide/HTN.pdf.

33. Krijnen P, van Jaarsveld BC, Steyerberg EW, Man in 't Veld AJ, Schalekamp MA, Habbema JD. A clinical prediction rule for renal artery stenosis. Ann Intern Med 1998;129:705-11.

34. Hall WD. A rational approach to the treatment of hypertension in special populations. Am Fam Physician 1999;60:156-62.

35. Oparil S. Arterial hypertension. In: Cecil RL, Goldman L, Bennett JC, eds. Cecil Textbook of medicine. 21st ed. Philadelphia: Saunders, 2000:258-73.

36. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486-97.