

## HYPERTENSION, AORTIC DISEASE, AND OTHER MEDICAL ILLNESSES WITH CARDIOVASCULAR EFFECTS

### Abbreviations

AAA	abdominal aortic aneurysm	LVH	LV hypertrophy
ACE	angiotensin-converting enzyme	MI	myocardial infarction
ARB	angiotensin receptor blocker	MRFIT	Multiple Risk Factor Intervention Trial
BP	blood pressure		
CAD	coronary artery disease	P <sub>2</sub>	pulmonic second heart sound
CHF	congestive heart failure	PA	pulmonary artery
CVD	cardiovascular disease	PPH	primary pulmonary hypertension
ECG	electrocardiogram	PVR	pulmonary vascular resistance
HBP	high blood pressure (hypertension)	RAA	renin-angiotensin-aldosterone (system)
HDL	high-density lipoprotein (cholesterol)	RA	right atrial
JNC	Joint National Committee	RBBB	right bundle branch block
LDL	low-density lipoprotein (cholesterol)	RV	right ventricle (ventricular)
LV	left ventricle (ventricular)	S <sub>3</sub>	third heart sound
LVEF	LV ejection fraction	S <sub>4</sub>	fourth heart sound
		TR	tricuspid valve regurgitation

### *Hypertension*

About 50 million Americans are hypertensive, and it seems that most of us will be. According to the Framingham study, those who are normotensive at age 55 years have a 90% chance of developing high blood pressure (HBP) at some time.<sup>1</sup> You who are in primary care medicine spend a lot of time treating hypertension, and I suggest a review of the latest Joint National Committee report, JNC 7.<sup>2</sup> It is comprehensive yet avoids excessive detail, and it summarizes the clinical trials that have substantially changed our approach since the JNC 6 report in 1997. Box 8.1 summarizes the key points.

The reason to treat HBP is to prevent end-organ damage, primarily cardiovascular disease (CVD). Declining mortality rates from stroke and coronary artery disease (CAD) over the last 40 years have been attributed to more effective antihypertensive therapy. In the 1960s the most common cause of congestive heart failure (CHF) was hypertensive heart disease; now it is CAD, probably because of

## Box 8.1 JNC 7 Summary

- Systolic BP is a better predictor of cardiovascular disease (CVD) than diastolic BP
- The risk of CVD doubles for each 20/10 mm Hg increase in BP, above 115/75 mm Hg
- New definition of prehypertension: 120–139/80–89 mm Hg. Lifestyle changes recommended
- Best initial therapy is a thiazide diuretic
- Other conditions are indications for other drug classes, even as monotherapy
- The goal of therapy is BP <140/90 mm Hg. With diabetes or kidney disease, the goal is 130/80 mm Hg
- Most patients require more than one drug to achieve goal
- If the baseline BP is >20/10 mm Hg above goal, start with two-drug therapy (one of them a thiazide)

better therapy for HBP. In clinical trials antihypertensive lowers the rate of stroke by 40%, myocardial infarction (MI) by 25%, and CHF by more than 50%.

Yet we are not doing as well as we should. In the early 1990s, a rule of halves was described for the United States and Western Europe based on population surveys: half the hypertensive population was undetected, half of those diagnosed were untreated, and half of those treated had inadequate control. It is slightly better now, yet 30% with HBP are not aware they have it.<sup>2</sup>

### Evaluating Hypertension

Blood pressure (BP) should be measured with the patient seated, at least 30 minutes after exposure to coffee or cigarettes. Smokers often stop for a last, furtive drag before coming into the office (attaching pejorative terms to this behavior seems unfair, but it is hard not to disapprove . . .). An elevated pressure should be reconfirmed in 5 to 10 minutes in the other arm. If still elevated, HBP should not be diagnosed until elevated pressure is confirmed with two subsequent visits. Have the office nurse check the pressure with the patient not scheduled to see the doctor; this may help avoid white coat hypertension. You and your staff should tell the patient what the BP measurement is.

JNC 7 provides a simplified classification for HBP, and introduces the prehypertension category (Table 8.1). The rationale for this is population data showing that increasing risk of CVD begins when BP is above 115/75 mm Hg, with the incidence of CVD doubling for each incremental increase of 20/10 mm Hg. Furthermore, those in the prehypertension category have a doubling of the risk of developing HBP. At lower levels, lifestyle modification is usually adequate. Both systolic and diastolic hypertension are indications for treatment, although elevated systolic pressure is a more potent risk factor for CVD.<sup>2</sup>

### Examination and Laboratory Studies

The goal of the initial evaluation is to gauge the risk of CVD, detect end-organ disease, and screen for correctible causes of HBP. Risk factors for CVD, particularly the metabolic syndrome, have been reviewed in Chapter 3.

Abnormalities on physical examination that are noteworthy include retinal arterial narrowing, thyromegaly, arterial bruit (carotid, abdominal, or femoral),

**Table 8.1 Classification and Management of Blood Pressure\***

Class	Systolic BP -or- Diastolic BP (mm Hg)		Treatment†
Prehypertension	120–139	80–89	Drug therapy only if another condition requires it (see Table 8.3)
Stage 1	140–159	90–99	Start with a thiazide, and add other drug(s) to reach BP goal†
Stage 2	≥160	≥100	Start two-drug therapy, including a thiazide

\*Adults over age 18.

†All should have lifestyle modification (see text).

Modified with permission from Chobanian AV, Bakris GL, Cushman WC, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7). *JAMA* 2003;289:2560–2572.

depressed lower extremity pulses or BP (coarctation of the aorta), a forceful cardiac apical impulse or  $S_4$  gallop, and an abnormal abdominal examination (bruit, enlarged aorta, masses).

As an exercise, try to justify each of the laboratory tests commonly recommended for newly diagnosed HBP. Do it before reading my explanation (and let me know if I miss something obvious).

*Urinalysis.* Urine glucose is a crude screen for diabetes. Albuminuria is a diagnostic criterion for kidney disease, even when serum creatinine is normal, and justifies a lower target BP (Box 8.1). Specifically, it is an indication for angiotensin converting enzyme (ACE) inhibitor therapy, which is antiproteinuric.<sup>3</sup> Proteinuria has also been identified as a risk factor for early CVD.

*Chemistries.* Serum *potassium* is especially important. When low off diuretics, it may indicate hyperaldosteronism, Conn's syndrome, as the cause of hypertension. Hypokalemia is a dangerous complication of diuretic therapy, and seems worse with thiazides than loop diuretics. Out-of-hospital cardiac arrest has been related to hypokalemia and to thiazide use. The MRFIT trial showed no mortality benefit with risk factor modification with early follow-up (there was a benefit later). There was an excess of sudden cardiac death (SCD) in the treated group that was later ascribed to thiazide therapy and hypokalemia.

*Sodium* measurement is less useful in patients with mild hypertension and who are otherwise healthy. In those with CHF, low sodium indicates poor prognosis and is a marker for high plasma renin activity (and increased sensitivity to ACE inhibition—start with low-dose therapy).

*Creatinine* and blood urea nitrogen are important as screens for underlying renal dysfunction, which changes the target BP (Box 8.1). *Glucose* is a better screen for diabetes when measured in a fasting state. Hyperglycemia may also be associated with secondary causes of HBP including Cushing's syndrome, pheochromocytoma, and primary aldosteronism.

*Lipid analysis* is a part of the CVD risk assessment. High triglycerides and low high-density lipoprotein (HDL) cholesterol are features of the metabolic syndrome (along with abdominal obesity, glucose intolerance and hypertension, Chapter 3). In this case the low-density lipoprotein (LDL) cholesterol level may be normal, but the LDL particles tend to be small and dense, and are more atherogenic.

*Calcium and phosphate* measurement is a screen for hyperparathyroidism, a potential cause of HBP. Uric acid may rise with diuretic therapy, and a baseline is useful.

The *hematocrit* has little direct relationship to HBP, but it is cheap and reasonable to screen for anemia if the patient is to have blood drawn.

The *ECG* is a crude tool. Its sensitivity for detecting LV hypertrophy (LVH) is less than 50%. The earliest sign of hypertensive heart disease is left atrial abnormality, usually a biphasic P wave in  $V_1$  (see Figure 7.2). If you suspect LVH based on the ECG or physical examination ( $S_4$  gallop or forceful apical impulse), get an echocardiogram to measure LV thickness. That is the gold standard, and increased thickness—LVH—indicates hypertensive heart disease. Making that diagnosis reinforces a need for aggressive BP control.

A *chest x-ray* is another sensible and relatively inexpensive screen for any middle aged person. It is relatively unreliable as a test for cardiac enlargement. Patients with LVH have concentric hypertrophy, with little chamber enlargement. Coarctation of the aorta may cause rib notching (collaterals vessels) and a “3” sign (dilated ascending aorta).

## Secondary Hypertension

Hypertension is a complication of a number of illnesses, many of them apparent from the screening evaluation (Table 8.2).<sup>4</sup> There is an element of uncertainty when deciding how much farther to go when looking for a correctible cause of HBP. It is the conflict between too much testing and not wanting to miss disease. JNC 7 helps by stating that “more extensive testing for identifiable causes is not indicated generally unless BP control is not achieved.”<sup>2</sup>

About 5% to 10% of HBP is secondary (Table 8.2). That does not seem like much, yet HBP is so common that we all see cases. In some series, renovascular hypertension accounts for 5%. Primary aldosteronism (0.5%), coarctation of the aorta (0.5%), pheochromocytoma (0.2%), and Cushing’s syndrome (0.1%) are much less common. Sleep apnea and excessive alcohol use are often overlooked, and BP control may depend on their correction.

## Treatment of Hypertension

The goals of therapy are aggressive and are based on clinical trials showing a reduction in CVD at these targets (Box 8.1). JNC 7 recommends focusing on the systolic BP; most patients reach the diastolic BP goal when the systolic pressure target is reached.<sup>1</sup>

**Table 8.2 Secondary Causes of Hypertension**

Disorder	Clinical Presentation	Laboratory Evaluation
Renal artery stenosis	HBP under age 20 New onset or worsening HBP in an older patient with increasing creatinine Abdominal/flank bruit	Magnetic resonance angiography Captopril augmented renal scan Angiography
Hyperaldosteronism	Hypokalemia, possibly hypernatremia	CT scan of adrenal glands
Sleep apnea	Snoring, daytime somnolence, obesity (thick neck)	Sleep study
Pheochromocytoma	Paroxysmal HBP, headache, flushing, tachycardia	Urinary catecholamine metabolites (metanephrines, VMA)
Hypothyroidism	Diastolic HBP, fatigue, weight loss, weakness	TSH level
Hyperthyroidism	Systolic HBP, heat intolerance, weight loss, tremor, new AF	TSH level
Hyperparathyroidism	Kidney stones, osteoporosis, weakness, lethargy	Serum calcium and parathyroid hormone levels
Chronic renal disease	Clinical setting	Creatinine clearance
Cushing's syndrome	Typical habitus	Dexamethasone suppression test
Coarctation of the aorta	Decreased or delayed femoral pulses, low leg BP	Chest x-ray findings, CT scan of the aorta
Excessive alcohol intake	Clinical history	Trial of abstinence
Drug side effects	Erythropoietin, cyclosporin, NSAIDs, COX-2 inhibitors, estrogen birth control pills, appetite suppressants, pseudoephedrine, monoamine oxidase inhibitors (Nardil), nicotine, amphetamines, testosterone	

HBP, high blood pressure; CT, computed tomography; VMA, vanillylmandelic acid; NSAID, non-steroidal anti-inflammatory drug; COX, cyclooxygenase; CT, computed tomography; TSH, thyroid stimulating hormone.

It also emphasizes lifestyle modification, including weight loss, sodium restriction, physical activity, and reduced alcohol consumption. The Dietary Approach to Stop Hypertension (DASH) lowers the systolic BP about 10 mm Hg; it is rich in fruits and low-fat dairy products (and thus is high in potassium and calcium), and is low in saturated fats. The DASH diet plus a 1.6-g sodium intake is as effective as single drug therapy in reducing BP. We have little information about the long-term effects of popular low carbohydrate diets (e.g., the Atkins diet).

**Drug therapy**—Clinical trials evaluating CVD outcomes have continued to find no drug class superior to thiazide diuretics as initial treatment. Furthermore, diuretics enhance the actions of other drugs. One reason for failure of vasodilator therapy

is inadequate diuresis. Sodium retention is a normal response to vasodilatation—it is perceived by the kidney as hypovolemia. Control of pressure requires correction of the consequent hypovolemia.

Most patients require multiple drugs to reach the BP goal, and JNC 7 suggests starting with two if the baseline BP is more than 20/10 mm Hg above goal. Angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blocker (ARB), beta-blockers, and calcium channel blockers are effective antihypertensive agents, and all are reasonable as a second agent. The pharmacology of antihypertensives is the subject of standard texts and other reviews.<sup>6</sup>

Another illness often dictates the choice of therapy, which then has the dual purpose of lowering BP plus favorably influencing the progress of the disease (Table 8.3). Thus, a patient with known vascular disease should be on an ACE inhibitor for its vascular protective effects. Patients with a history of MI or heart failure with low LVEF have improved survival with beta blockade (as well as ACE inhibition and aldosterone blocking therapy). Diabetes is an indication for ACE inhibition. Prostatism is effectively treated with alpha blockers, although monotherapy in patients with CAD and a history of MI is associated with increased risk.<sup>5</sup>

**Table 8.3 Choice of Antihypertensive Therapy for Patients with Other Illnesses**

Condition	Drug Class Shown to Improve Outcome	Comments
Previous myocardial infarction	Beta-blocker, ACE inhibitor, aldosterone antagonist with low LVEF	The coronary event rate may be higher with alpha blockers and calcium channel blockers <sup>5</sup>
Congestive heart failure and low LVEF	Beta-blocker, ACE inhibitor, ARB, aldosterone antagonist (spironolactone)	Chapter 1; beta blockade has the most potent beneficial effect on survival
ASCVD	ACE inhibitor	See Chapters 4 and 5
Prior stroke	ACE inhibitor + thiazide	PROGRESS trial showed less recurrence of stroke <sup>2</sup>
Diabetes mellitus	ACE inhibitor or ARB, beta blocker, diuretics calcium blocker	All prevent CVD and stroke, and ACE inhibitors and ARBs reduce proteinuria and progression of nephropathy
Chronic renal disease	ACE inhibitor or ARB	Both lower the rate of progression, even for nondiabetic renal disease
Left ventricular hypertrophy	All classes reduce LVH, except direct vasodilators (hydralazine and minoxidil)	LVH is an independent risk factor for sudden cardiac death as well as CVD

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; CVD, cardiovascular disease including coronary artery disease, peripheral vascular disease and stroke; LVH, left ventricular hypertrophy; ASCVD, atherosclerotic CVD; LVEF, left ventricular ejection fraction.

A need for multiple drugs to treat these other illnesses may prevent the use of thiazides. If the pressure is still high after regulating the doses of other medicines, the diuretic can be added.

**Chronic renal disease**—Patients with kidney disease (creatinine >1.5 mg/dL for men, >1.4 mg/dL for women) tend to have a progressive decline in creatinine clearance. The rate of decline is slower when BP is lowered to 130/80 mm Hg or less. Multidrug therapy is usually needed, and should include blockade of the renin-angiotensin-aldosterone (RAA) system with an ACE inhibitor or ARB. The renal protective effect of RAA blockade applies to both nondiabetic and diabetic patients, and it is most pronounced for those with proteinuria. ACE inhibition reduces proteinuria. Those with mild renal dysfunction also have a higher incidence of CVD, and RAA blocking therapy lowers the rate of cardiac events.<sup>3</sup>

Renal dysfunction plus hyperkalemia is a contraindication to ACE inhibitors or ARBs. Monitoring serum potassium and creatinine is important for all patients, and I recheck a creatinine a couple days after starting RAA blocking therapy. A marked rise in serum creatinine during the first couple days of treatment suggests co-existing renal artery stenosis, which should be evaluated. If creatinine rises by less than 0.3 mg/dL, the ACE inhibitor or ARB can be continued with careful monitoring.

When the creatinine is above 1.5 mg/dL, thiazides are less effective and loop diuretics are needed. Diuretics and reduced sodium intake are especially important, as sodium retention is a common feature of renal dysfunction. Nonsteroidal anti-inflammatory drugs may provoke renal vasoconstriction and further lower glomerular filtration, leading to salt retention and possibly to hyperkalemia. They and potassium containing salt substitutes should be avoided.

**Black patients**—As a group, they have earlier onset HBP and are more likely to have severe (stage 2) disease. For years we thought that the RAA system played a minor role when compared with other racial groups. This was based upon the relative ineffectiveness of ACE inhibitors as monotherapy, when compared with diuretics and calcium channel blockers. The critical observation, however, is that monotherapy with any drug is ineffective for this group, and especially with ACE inhibitors or beta-blockers.

With appropriate combination therapy, both ACE inhibition and beta blockade are effective for black patients. The African-American Study of Kidney Disease (AASK) trial compared ramipril, metoprolol and amlodipine plus diuretic therapy in patients with moderate renal dysfunction (glomerular filtration rate 20 to 60 mL/min). The BP response was identical in the ramipril and amlodipine arms, but the rate of decline of renal function was substantially better with ramipril therapy.<sup>3</sup> Thus, for persons of color 1) ACE inhibition is as effective as calcium channel blockade in lowering BP when used as part of a multidrug regimen, and 2) it provides the best protection of renal function and thus should be the first choice of therapy. The study underscores an important management principle: drug therapy is about more than lowering BP. The other actions of drugs independent of BP effects—for example, renal or vascular protection—are as important.

Table 8.4 Causes of Inadequate Response to Antihypertensive Therapy	
Pseudoresistance	White coat hypertension Use of a regular cuff on an obese arm
Noncompliance to therapy	
Unrecognized secondary causes of hypertension	Table 8.2
Volume overload	Excess salt intake Fluid retention from vasodilator therapy and <i>inadequate diuresis</i>
Drug-related causes	Doses too low or incorrect dosing schedule Wrong type of diuretic (i.e., thiazide in a patient with advanced renal disease) Drug effects: Sympathomimetics, nasal decongestants, appetite suppressants, cocaine, oral contraceptives, adrenal steroids, cyclosporine, erythropoietin, antidepressants, nonsteroidal anti-inflammatory drugs
Associated conditions	Sleep apnea Smoking Increasing obesity Insulin resistance/hyperinsulinemia Alcohol intake >1 oz per day Arteritis with vasoconstriction Chronic pain

**Elderly patients**—As noted, most people older than 65 years have HBP. This is a group that is undertreated. Blood pressure goals, the workup, and choice of drugs are no different than those with younger patients. An abrupt and substantial rise in BP suggest atherosclerotic renal artery stenosis, especially when there is an increase in creatinine.

Postural hypotension is more common in older patients, and you may want to start with lower dose therapy to avoid this side effect. Volume depletion is a common cause. For this reason, targeting therapy to an upright BP makes sense for older patients. If the BP is borderline, measure it after a walk down the hall and while standing.

**Women**—Oral contraceptives raise BP, and this effect increases with the duration of therapy. Hormone replacement therapy, with its lower dose of estrogen, has no effect on BP (a broader discussion of hormone replacement is in Chapter 3).

During pregnancy, ACE inhibitors and ARBs should not be used because of fetal toxicity (avoid them if there is a chance of pregnancy). Methyldopa and nifedipine are safe. Beta-blockers may be used late in pregnancy, but can slow fetal growth.<sup>3</sup> Thiazides may be used, but furosemide may be embryotoxic.

**Resistance to drug therapy**—An inability to lower BP despite multiple drug therapy should prompt reconsideration of secondary hypertension (Table 8.2), or



noncompliance with the medicine regimen. In the absence of these, consider other causes of drug resistance are outlined in Table 8.4. The most common of these in my experience are inadequate diuretic therapy, use of nonsteroidal anti-inflammatory drugs, excessive alcohol intake, and failure to recognize sleep apnea.

## *Diseases of the Aorta*

---

### **Abdominal Aortic Aneurysm**

About three fourths of aortic aneurysms are limited to the abdomen, originating below the renal arteries and usually sparing the visceral circulation. The size of the abdominal aortic aneurysm (AAA) determines the chance of rupture. There is a 50% chance of rupture in 1 year with a diameter greater than 6 cm, 15% to 20% when the AAA measures 5 to 6 cm, and less than 2% with a diameter less than 4 cm. Without surgery, the 5-year mortality rate with an aneurysm larger than 6 cm is at least 90%.

Most AAAs are detected during abdominal examination or with ultrasound screening studies. Because of the high mortality risk with undetected, large aneurysms, routine screening has been advocated for those older than 60 years of age.<sup>7</sup> There are few clinical trials data to support widespread screening, and it is not (yet) the standard of care, but patients are beginning to ask for it.

AAA is an atherosclerotic illness, and cigarette smoking, male gender, and family history are the major risk factors. Recall that wall tension = intraluminal pressure  $\times$  radius (Laplace's law). Thus, hypertension—high intraluminal pressure—contributes to aneurysm growth. Because expansion occurs in 80% of patients, time is another risk factor for rupture. Gradual expansion is the rule, with only 20% enlarging rapidly (more than 0.5 cm per year).

Randomized trials have compared surveillance vs. early surgery for small AAA, and found no advantage with surgery for aneurysms less than 5.5 cm.<sup>8,9</sup> In addition to AAA size, the patient's general medical condition also influences the timing of surgery. When the general health is good, surgery is recommended for an AAA 5.5 cm or larger. On the other hand, a patient with multiple medical problems who is considered a poor surgical candidate may have repair delayed until the aneurysm approaches 6 cm. Mortality with elective surgery in the ADAM trial was just 1.8%, substantially better than that a decade ago.<sup>8</sup> Surgical mortality is higher with rapidly expanding aneurysms (5% to 15%), while surgery during acute rupture has a mortality risk closer to 40%.<sup>7</sup>

The newest approach is endovascular aneurysm repair using stents. The first devices were introduced in the early 1990s, and current models have been tested in more than 1000 patients. With proper patient selection stenting works well and appears a durable solution to AAA. Its role in treating rupture is uncertain.

The medical therapy of small AAA begins with risk factor modification and BP control. Beta blockade has not been found to have special benefits.<sup>7</sup> Reducing vascular

inflammation may help, and trials of statins and antibiotics (doxycycline) therapy are in progress.

### Thoracic Aortic Aneurysm

In young patients the usual cause is Marfan's syndrome, while older patients have atherosclerotic disease. Expanding aneurysms tend to cause pain or compression symptoms—hoarseness, cough, dysphagia, or the superior vena cava syndrome.

A diameter greater than 7 cm indicates a high risk of rupture. Surgery is recommended when thoracic aneurysms reach 6 cm. High surgical risk would favor delaying surgery in the absence of symptoms. Expansion tends to be slow with aneurysms smaller than 5 cm, and annual CT or MRI imaging is adequate. Above 5 cm, the expansion rate increases fourfold, and twice-yearly imaging is needed.

Medical therapy includes risk factor modification and control of hypertension. Beta blockade has a special role, because reducing the velocity of LV ejection protects the aorta. This has been proven for those with Marfan's syndrome, and beta blockade makes sense as initial antihypertensive treatment for all with thoracic aneurysm. (Small studies of AAA showed no benefit with beta blockade; the shearing force of LV ejection apparently dissipates by the time it reaches the distal aorta.)

Marfan's syndrome is the most common cause of thoracic aortic aneurysm in young people. Pregnancy increases the risk of dissection and should be avoided if the proximal aorta is larger than 4.0 cm.

Survival with elective surgery is above 90%. Inadvertent interruption of the vascular supply to the spine leads to paralysis in more than 5%. Decompression with spinal fluid drainage before surgery may lower the risk of paraplegia.<sup>7</sup>

### Thoracic Aortic Dissection

Risk factors for dissection are poorly controlled hypertension, advanced age, and medial disease. A number of aortic diseases may cause it including Marfan's and Ehlers-Danlos syndromes, coarctation, bicuspid aortic valve, arteritis and Turner and Noonan syndromes.<sup>10</sup> Men are more commonly affected. Over age 50, hypertension is the usual etiology; under age 40, Marfan's syndrome is the most common cause.<sup>10</sup> While those with an aneurysm are at increased risk for dissection, not all dissections begin with a large aneurysm.

The standard classification of dissection is based on location: type A dissection begins in the proximal aorta, just above the aortic valve, and accounts for three fourths of cases. A type A dissection may extend all the way around to the distal aorta (DeBakey class 1), or may be limited to the proximal aorta (DeBakey class 2). Type B dissection (DeBakey class 3) begins distal to the left subclavian artery and involves the distal aorta (25% of cases).

Dissection causes chest pain. The diagnosis is often missed, as this is a less common cause of chest pain than CAD. The pain may be mid chest, and radiation

to the back occurs in less than half of cases. The most useful diagnostic feature is that the pain is at maximum intensity at its onset (more than 80% of cases, and this figures into board questions routinely).<sup>10</sup> In contrast, the pain of MI starts slowly and crescendos.

The dissection may occlude major branches of the aorta. For example, chest pain plus stroke (carotid occlusion) suggests dissection. On physical examination, indications of limb ischemia, including diminished pulses or unequal BPs is evidence for dissection. Acute inferior MI with ST-segment elevation on the ECG may occur if the dissection occludes the right coronary ostium. Occlusion of the left coronary ostium is possible, but most with this complication die suddenly. Proximal dissection may cause aortic regurgitation. Neck vein distension suggests rupture into the pericardium and tamponade.

Diagnosis requires a transesophageal echocardiogram or imaging with CT or MRI. All are sensitive and specific, and the choice of technique is based on speed and availability. Abdominal ultrasound is a screening test for AAA, and it is not useful for the evaluation of possible dissection of the aorta (nor is transthoracic echocardiography). The mediastinum and/or aorta appear widened on chest x-ray in 80% to 90% of patients with thoracic dissection, making this a useful but not diagnostic test.

Management is aimed at stopping the progression of dissection. Medical therapy includes 1) decreasing the systolic BP to 100 to 120 mm Hg if there is adequate perfusion of vital organs (nitroprusside is the intravenous vasodilator of choice); 2) beta blockade to counter the shearing force of LV ejection, which may increase with vasodilator therapy; and 3) pain control.

Indications for emergency surgery are severe aortic regurgitation, threatened rupture, occlusion of a branch artery and persistent, uncontrollable pain.<sup>10</sup> In addition, surgery improves survival for those with proximal, type A dissection. It is no better than medical management for those with stable distal dissection. With type B dissection, a patient who 90% as survived the acute phase and has no indication for emergency surgery has a 1-year survival rate with both medical and surgical therapy.

Operative mortality ranges from 5% to as high as 70%, with highest risk predicted by cardiac tamponade, renal or visceral ischemia, the site of the tear, coexisting lung disease, and delayed time to surgery.<sup>10</sup> Tissue adhesives are now used to join the separated layers of aorta, eradicating the false lumen in more than half the cases.<sup>10</sup> Glue aortoplasty results in less bleeding, fewer postoperative complications, and probably improved survival (there have been no randomized studies, as there never are when a new surgical technique clearly makes things better).

Endovascular stenting has been tested in small numbers of patients who were poor surgical candidates, usually with descending aortic dissection (type B). Predictably, outcomes have been poor, and at this time stenting is considered a palliative procedure for those whose symptoms are from lower extremity ischemia.<sup>10</sup> Based on experience with most endovascular procedures, watch for the indications for stenting to expand with more experience and better equipment.

Residual aortic disease requires surgery within 10 years in 20% to 30% of patients who survive aortic dissection, with or without initial surgical therapy. Aggressive medical therapy is needed (risk factor and BP control, beta blockade, statins). They should have follow-up CT or MRI imaging at 3-month intervals for a year, then twice yearly, depending on the size of the aorta and rate of expansion.

### **Aortic Trauma**

The most common cause is sudden high-speed deceleration during a motor vehicle accident. This creates shearing forces that are greatest where mobile and fixed portions of the aorta meet, most commonly, the aortic isthmus where the ligamentum arteriosum inserts (the former ductus arteriosus just beyond the left subclavian artery).

The diagnosis may be masked by other injuries. Localized hematoma can cause dyspnea or stridor, dysphagia or the superior vena cava syndrome. There may be an interscapular bruit on exam. The chest x-ray is abnormal in 90% (opacification between the aorta and pulmonary artery [PA] or mediastinal widening). Contrast CT or MRI confirms the diagnosis. Surgical correction is usually successful and may prevent sudden death.

## ***Cardiac Complications of Other Medical Illnesses***

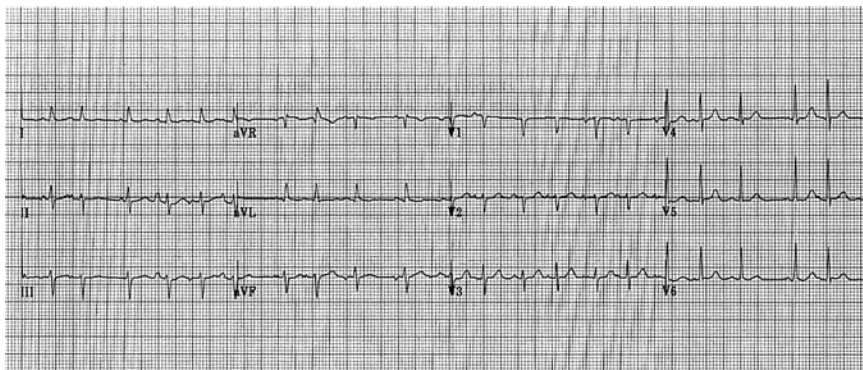
---

### **Chronic Lung Disease (Cor Pulmonale)**

Lung disease can cause pulmonary hypertension, leading to right heart failure. The three mechanisms are *hypoxic vasoconstriction* (especially with chronic bronchitis, cystic fibrosis, obesity hypoventilation—sleep apnea—and other hypoventilation syndromes), *obstruction of the vascular bed* (pulmonary embolism, primary pulmonary hypertension [PPH], sickle cell disease), and *obliteration of lung parenchyma* with loss of vascular surface area (emphysema, bronchiectasis, cystic fibrosis, interstitial lung disease).<sup>11</sup>

Hypoxia is a potent pulmonary vasoconstrictor. When prolonged, there is an increase in the thickness of the walls of small PA branches. These changes become permanent over time. A patient with chronic lung disease plus hypoxia, typically the blue bloater with bronchitis, is more prone to cor pulmonale than another with emphysema and equally severe airway obstruction, but with normal arterial oxygen saturation (the pink puffer). One of the indications for home oxygen therapy is right heart failure, because correction of hypoxemia relieves pulmonary hypertension.

Not everyone with bronchitis develops cor pulmonale. Some patients are susceptible but most are not. That also appears to be the case with some patients with left heart failure but predominantly right side CHF. A minority of those with mitral stenosis, atrial septal defect, or cardiomyopathy presents with edema (right heart failure) but no pulmonary congestion.



**Figure 8.1** Multifocal atrial tachycardia. The rhythm is irregular, and there is variable P wave morphology. (Reproduced by permission from Taylor GJ. 150 Practice ECGs, 2nd ed. Boston: Blackwell Science, 2002:196. Copyright © 2002, Blackwell Science, Inc.)

It is a conundrum—how can the cause of right heart failure be left heart failure if there is no left heart failure? My impression is that there is a percentage of the population with hyperreactive pulmonary vasculature. When stressed with hypoxia (COPD) or hemodynamic overload (left side CHF), these patients develop pulmonary hypertension. Because the PA clamps down, the left heart is protected, and the clinical picture is isolated right heart CHF.

**Clinical and laboratory findings**—The syndrome is right heart failure—peripheral edema—in a patient with lung disease. The chest x-ray shows no pulmonary congestion, and the echocardiogram confirms normal LV function. Dyspnea is usual but is caused by the lung disease. Palpitations and atrial arrhythmias are common, especially atrial flutter and multifocal atrial tachycardia (Figure 8.1).

Other cardiac findings of right heart failure are subtle, and may be hard to detect when the chest exam is grossly abnormal.  $P_2$  is accentuated with pulmonary hypertension. There may be a right ventricular (RV) lift and a right-side  $S_3$  gallop (audible during inspiration). Jugular venous distension is a prominent finding. If there is also a V wave, consider tricuspid regurgitation (see Chapter 7). With RV failure, there may be an inspiratory increase in jugular venous pressure (Kussmaul's sign) and pulsus paradoxus.

Although the chest examination is abnormal with lung disease, a normal exam does not exclude cor pulmonale. Other causes such as sleep apnea, PPH, and recurrent pulmonary embolus may not affect the chest examination.

The chest x-ray findings of PPH and cor pulmonale are enlargement of the RV and central pulmonary arteries. Decreased vessel markings at the periphery in contrast to the large central vessels produce a pruned tree appearance.

The ECG is a nonspecific test. There may be RV hypertrophy and P pulmonale (Table 8.5, Figure 8.2), but their absence does not exclude cor pulmonale.

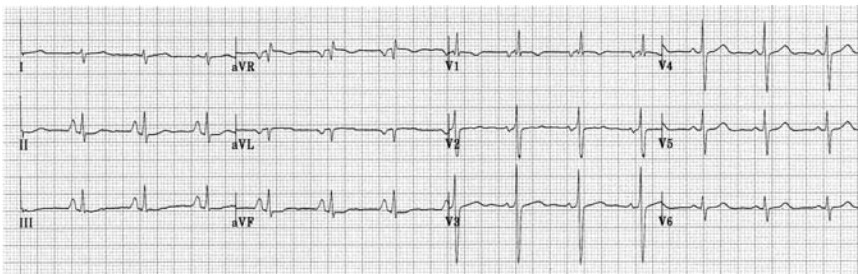
Criteria	R/S in $V_1 \geq 1$ , <i>or</i> R in $V_1 \geq 7$ , <i>or</i> R in $V_1 + S$ in $V_5$ or $V_6 > 10.5$
Supportive findings	Right axis deviation $> 110$ degrees Right atrial abnormality (inferior P waves $> 2.5$ mm) ST depression + T wave inversion in $V_1$ or $V_2$ (RV strain)

\*These findings are relatively nonspecific. For example right bundle branch block is a common ECG finding, and most patients with right bundle branch block do not have right ventricular hypertrophy; yet they have a tall R in  $V_1$  and associated T inversion.

Low voltage is common with emphysema as is delay in R wave progression. Right bundle branch block (RBBB) or incomplete RBBB are nonspecific signs of RV overload, but they may also result from conduction system disease unrelated to the state of the RV.

The echocardiogram is the key test, detecting RV and possibly right atrial (RA) enlargement. RA measurement is not precise, but there may be a qualitative assessment. Both chambers are enlarged with cor pulmonale. RV wall thickness is difficult to measure, so the echo is not reliable for the diagnosis of RV hypertrophy. Most with pulmonary hypertension have mild tricuspid regurgitation (TR, often without a murmur), and the TR jet is used for Doppler estimation of PA pressure. The echocardiogram also excludes other causes of pulmonary hypertension such as occult mitral stenosis or left heart failure (systolic or diastolic). In many patients with advanced lung disease, the cushion of air between the echo transducer and the heart prevents good imaging. Transesophageal echocardiogram is an alternative, but slightly riskier in those with severe lung disease. The clinical diagnosis of cor pulmonale usually is sufficient, and a transesophageal echocardiogram is unnecessary.

An occasional patient has right heart catheterization. The major finding is elevated PA pressure. The pulmonary wedge pressure—e.g., left ventricular (LV) filling



**Figure 8.2** Right ventricular hypertrophy. The R wave is tall in  $V_1$ , and the S wave persists in  $V_{5-6}$ . There is right axis deviation, and a right atrial abnormality (P waves taller than 2.5 mm in inferior leads). (Reproduced by permission from Taylor GJ. The cardiology rotation. Boston: Blackwell Science, 2001:282. Copyright © 2001, George J. Taylor.)

pressure—is normal unless there is LV dysfunction. Normally the PA diastolic pressure is equal to the wedge pressure; during diastole the PA, pulmonary capillary bed, pulmonary veins, left atrium, and LV are in open communication. Pulmonary vascular resistance (PVR) is elevated with cor pulmonale. Thus, PA diastolic pressure is higher than a LA pressure (or pulmonary wedge pressure).

I indicated that cor pulmonale is pulmonary hypertension in the face of normal LV diastolic pressures; it is the lung disease and not left heart failure that causes right heart failure. Smokers get CAD and have MIs, so many with cor pulmonale have coexisting left heart disease. In such cases the pulmonary wedge pressure is high, but the PA diastolic pressure is even higher. This transpulmonary gradient defines elevated PVR and is a constant finding of cor pulmonale.

Other laboratory testing may be needed to determine the etiology. When there is no apparent lung disease, evaluate the patient for pulmonary embolus. A sleep study may be needed to diagnose sleep apnea. In such cases, bradyarrhythmias during sleep are common. Last month I consulted on a 70-year-old patient with edema who had 3.5-second sinus pauses on telemetry, while asleep. The QRS duration and PR intervals were normal. Rather than an urgent pacemaker, we documented sleep apnea and treated his arrhythmia and right heart failure with nocturnal positive-pressure ventilation.

**Treatment**—Improving oxygenation relieves pulmonary vasoconstriction. The usual indication for home oxygen is hypoxemia, but cor pulmonale is an additional indication in those with borderline oxygen saturation.<sup>12</sup> The goal is a PaO<sub>2</sub> greater than 60 mm Hg. Pulmonary hypertension may improve with part-time, overnight oxygen therapy. However, clinical trials have shown improved survival with continuous therapy for the general population needing oxygen for chronic lung disease, and those results would apply to patients with cor pulmonale. Supplemental oxygen must be used cautiously when there is chronic hypercarbia and respiratory acidosis. Vigorous treatment of the lung disease is critical.

Specific treatment of the heart failure is of limited benefit. Edema requires diuretic therapy. When there is splanchnic congestion, consider using the loop diuretics that are best absorbed (torsemide and bumetanide rather than furosemide; see Chapter 1). Vasodilator therapy has little effect on PVR when there is parenchymal lung disease, so afterload reduction therapy is not indicated, nor does beta blockade help.

Digoxin may be used for treatment of right heart failure, but it is less effective for controlling the ventricular rate when there are atrial tachyarrhythmias. Those with cor pulmonale are more susceptible to digitalis toxicity. Verapamil is a better choice for rate control. The successful treatment of atrial arrhythmias, like heart failure, requires control of the lung disease. Cardioversion may be considered for atrial flutter, but maintaining sinus rhythm is unlikely unless pulmonary function improves.

**Primary pulmonary hypertension**—This rare illness is marked by pulmonary vasoconstriction, intimal proliferation, and thrombosis in situ.<sup>11</sup> It is probably caused by endothelial dysfunction. Although more common in young women, others

may be afflicted. They usually present with dyspnea, and other symptoms include chest pain, edema (right heart failure), light-headedness, and syncope. It is a fatal illness, with survival determined by the response to vasodilators.

All patients should receive anticoagulation therapy. Digoxin may relieve the symptoms of right heart failure.<sup>11</sup> Vasodilator therapy is critical. Calcium channel blockade is effective for some patients; in one study a favorable response led to a 94% 5-year survival, compared with 36% in those who did not respond.<sup>11</sup>

Prostacyclin is a vasodilator produced by the endothelium that is deficient in some patients with PPH. It has been shown to increase survival and relieve symptoms, even in those with advanced PPH (functional class 3–4). On average, patients have at least a 50% reduction in PVR, and the effect persists with chronic therapy. Epoprostenol (Flolan) is given by constant infusion through a permanent central catheter using an ambulatory pump.<sup>11</sup> A few patients have been on it 10 years. Oral and subcutaneous prostacyclins are being developed. More recently, bosentan, an endothelin receptor blocker, has been approved and as the first oral medicine available for PPH.<sup>13</sup> High dose sildenafil (Viagra) has been shown to improve exercise tolerance and other symptoms.<sup>14</sup>

## Other Medical Conditions and their Cardiac Effects

A brief review text must focus on the big picture, and what is in that picture requires picking and choosing. To flesh out this overview—perhaps to jog your memory—Table 8.6 summarizes the cardiac effects of a number of medical illnesses that are not covered in detail.

Condition	Cardiovascular Effects/Comment
<b>Endocrine Disorders</b>	
Cushing's syndrome	HBP in 80%. Diagnose with a dexamethasone suppression test.
Hyperaldosteronism (Conn's syndrome)	Expanded extracellular volume, moderate diastolic HBP, hypokalemia resistant to replacement therapy. Treat HBP with spironolactone (or resection of the adrenal adenoma).
Adrenocortical insufficiency	Chronic syndrome (Addison's disease): asthenia, fatigue, hypotension and a small heart on x-ray. Acute syndrome (Waterhouse-Friderichsen's syndrome with sepsis): shock
Hyperparathyroidism	Hypercalcemia and hyperphosphatemia. HBP common in elderly patients. Thiazides may aggravate the hypercalcemia.
Pheochromocytoma	HBP, sustained in 60% of cases, although labile. Half have paroxysms of flushing and HBP that can resemble anxiety attacks.

(Continued)



**Table 8.6 (Continued)**

Condition	Cardiovascular Effects/Comment
<b>Endocrine Disorders</b>	
Chronic hypocalcemia (hypoparathyroidism)	Long QT interval.
Diabetes insipidus	Polyuria and polydipsia, an inability to concentrate the urine. If the patient cannot drink, volume depletion and hypotension soon develop.
Hyperthyroidism	Increased heart rate, decreased systemic vascular resistance, high systolic BP (and low diastolic BP with wide pulse pressure), atrial fibrillation (a common presenting sign in the elderly), high-output heart failure.
Hypothyroidism	Low heart rate, reduced LV contractility (though CHF is rare and function improves with treatment), increased diastolic BP in 20% but low systolic BP (a narrow pulse pressure), large and slowly accumulating pericardial effusion.
<b>Connective Tissue Disease</b>	
Systemic lupus erythematosus	Pericardial effusion (tamponade and constriction are possible). Atypical endocarditis (Libman-Sacks endocarditis, with valve nodules at autopsy that rarely cause valvular dysfunction). Cardiomyopathy and coronary artery lesions are possible, but rare.
Polyarteritis nodosa (PAN)	Segmental, necrotizing arteritis of small-medium vessels, including coronary arteries. MI and conduction system disease are possible but uncommon. Renal arteritis causes HBP and renal failure, leading to heart failure in 60%.
Rheumatoid arthritis (RA)	Fibrinous pericarditis occurs in 30% with RA. Usually clinically silent, but constriction is possible. Effusions can be large. Rheumatoid nodules can affect myocardium, valve or conduction system.
Ankylosing spondylitis	10% have aortic root inflammation, then sclerosis, then aortic regurgitation (usually with chronic disease). Conduction abnormalities possibilities.
Scleroderma (systemic sclerosis)	Raynaud's phenomenon is an early symptom (coronary spasm is possible). Fibrosis possible in heart, lungs and kidney. CHF, ventricular arrhythmia, or conduction disease occurs in one third of patients. Fibrosis can lead to pulmonary hypertension and cor pulmonale, or there may be primary pulmonary hypertension (vasospasm without lung fibrosis).
Polymyositis and Dermatomyositis	40% have cardiac involvement: conduction abnormalities, tachyarrhythmias, pericarditis with effusion, or dilated cardiomyopathy. Coronary arteritis is possible but rare.
Giant cell (temporal) arteritis	Aortitis may lead to chest pain, myocardial ischemia, aortic aneurysm, stroke, aortic regurgitation, or limb claudication.
Ehlers-Danlos syndrome	Multiple genotypes with variable cardiac involvement. MVP and aortic disease (rupture or dissection) the major problems.

*(Continued)*

<b>Table 8.6 (Continued)</b>	
<b>Condition</b>	<b>Cardiovascular Effects/Comment</b>
<b>Connective Tissue Disease</b>	
Marfan's syndrome	Aortic root dilatation and dissection (beta blockade slows progression); mitral valve prolapse is common (Chapter 7).
Osteogenesis imperfecta	Fragile bones, blue sclera. AR and MR possible, plus large artery fragility.
<b>Neoplastic Disease</b>	
Metastatic tumors	30 × more common than primary tumors of the heart. Lung, breast, lymphoma, leukemia and melanoma most common. Most clinical disease is pericardial, with myocardial or intracavitary disease less common.
Atrial myxoma	Can mimic mitral valve disease. Thromboembolism (stroke) is common. Most have constitutional symptoms (fever, weight loss, fatigue) with an elevated sedimentation rate.
Rhabdomyoma	Benign tumor of myocardium in young children, often accompanies tuberous sclerosis. Surgically resectible. Rare.
Other benign myocardial tumors	Lipoma, papillary fibroelastoma, fibroma, hemangioma, mesothelioma involving mitral or tricuspid valves. Rare.
Angiosarcoma	Malignant, usually in the RA or pericardium. Right heart failure or pericardial pain. Death within a year. Rare.
Rhabdomyosarcoma	Malignant, in any cardiac chamber, and may alter valve function. Rare.
Complications of radiation	Pericarditis is the most common and may lead to constriction. Accelerated coronary atherosclerosis is possible. Radiation or surgery to the neck can cause carotid sinus syncope
Adriamycin	Cardiomyopathy may occur when the cumulative dose is >450 mg/m <sup>2</sup>
5-Fluorouracil	Coronary artery spasm and angina.
Cyclophosphamide	At high doses (pre-bone marrow transplant), hemorrhagic myopericarditis is possible.
<b>Neuromuscular and Neurologic Disease</b>	
Duchenne muscular dystrophy	Cardiac involvement common: cardiomyopathy, conduction disorders, MVP (from papillary muscle disease), narrow and deep Q waves.
Myotonic dystrophy	80% have cardiac involvement, usually conduction disorders and other arrhythmias. Myocardial disease rare.
Friedreich's ataxia	Dilated cardiomyopathy (CHF is the most common cause of death). Degree of LV dysfunction does not parallel severity of the neuromuscular disorder.* There is an hypertrophic variant as well.

(Continued)

<b>Table 8.6 (Continued)</b>	
<b>Condition</b>	<b>Cardiovascular Effects/Comment</b>
<b>Neuromuscular and Neurologic Disease</b>	
Stroke	Deep and symmetrical T wave inversion with troponin elevation (subendocardial myolysis); atrial and ventricular arrhythmias; hypertension in the initial stages, especially with hemorrhagic stroke (usually back to baseline in 10 days); noncardiac pulmonary edema (ARDS) is possible
<b>End-stage Renal Disease (ESRD)</b>	
Hypertension	HBP develops in most patients, regardless of the etiology of renal failure (see text)
Heart failure	Multiple complications of ESRD contribute: hypertension, hypervolemia, anemia, lipid abnormalities, disordered calcium metabolism, dialysis shunts, thiamine and other vitamin deficiencies.
Uremic pericarditis	Incidence is 20% with chronic hemodialysis. Tamponade is possible. More frequent dialysis is the treatment.
ASCVD	The process is accelerated, and MI is a common cause of death.
<b>Nutritional Disorders</b>	
Obesity	The metabolic syndrome, LVH plus dilatation (elevated preload and afterload, see Chapter 2), cardiomyopathy, obstructive sleep apnea, premature CAD, SCD.
Alcohol	HBP resistant to therapy, AF (holiday heart), cardiomyopathy (incidence in alcoholics is 10%–40%), favorable effect on CAD.
Thiamine deficiency (beriberi)	Vasodilatation, biventricular failure, edema. Common in alcoholics. It can be aggravated by diuretic therapy (increased excretion of thiamine parallels increased excretion of K and Mg). CHF may improve with replacement. (Consider this in a frail patient with CHF who is not eating well.)
Protein calorie malnutrition	A decrease in body weight is accompanied by smaller heart size, slower heart rate and QT interval prolongation. LVEF is normal. SCD possible with electrolyte disturbances.
Elevated homocysteine	Early ASCVD, increased risk of venous and arterial thrombosis (possibly through endothelial effects). Correct with folate and pyridoxine (see Chapter 3).
Selenium deficiency (Keshan's disease)	Cardiomyopathy (described in China)

BP, blood pressure; HBP, high BP; LV, left ventricle; LVEF, LV ejection fraction; CHF, congestive heart failure; CAD, coronary artery disease; AR, aortic regurgitation; MR, mitral regurgitation; ARDS, adult respiratory distress syndrome; SCD, sudden cardiac death (usually ventricular fibrillation); ASCVD, atherosclerotic cardiovascular disease

\*This is true of most neuromuscular diseases that affect the myocardium.

## References

1. Vasan RS, Beiser A, Seshadri S, et al. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *JAMA* 2002;287:1003–1010.
2. Chobanian AV, Bakris GL, Cushman WC, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003;289:2560–2572.
3. Flack JM, Peters R, Mehra VC, Nasser SA. Hypertension in special populations. *Cardiol Clin* 2002;20:303–319.
4. Onusko E. Diagnosing secondary hypertension. *Am Fam Physician* 2003;67:67–74.
5. Aronow WS, Ahn C. Incidence of new coronary events in older persons with prior myocardial infarction and systemic hypertension treated with beta blockers, angiotensin-converting enzyme inhibitors, diuretics, calcium antagonists, and alpha blockers. *Am J Cardiol* 2002;89:1207–1209.
6. Ram CV, Fenves A. Clinical pharmacology of antihypertensive drugs. *Cardiol Clin* 2002;20:265–280.
7. Pearce WH. What's new in vascular surgery. *J Am Coll Surg* 2003;196:253–266.
8. Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;346:1437–1444.
9. United Kingdom Small Aneurysm Trial Participants. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;346:1445–1452.
10. Khan IA, Nair CK. Clinical, diagnostic, and management perspectives of aortic dissection. *Chest* 2002;122:311–328. Also note, Januzzi JL, Isselbacher EM, Fattori R, et al. Characterization of the young patient with aortic dissection: results from the International Registry of Aortic Dissection (IRAD). *J Am Coll Cardiol* 2004;43:665–669.
11. McLaughlin VV, Rich S. Severe pulmonary hypertension: critical care clinics. *Crit Care Clin* 2001;17:453–467.
12. Crockett AJ, Cranston JM, Moss JR, Alpers JH. A review of long-term oxygen therapy for chronic obstructive pulmonary disease. *Respir Med* 2001;95:437–443.
13. Lehrman S, Romano P, Frishman W, et al. Primary pulmonary hypertension and cor pulmonale. *Cardiol Rev* 2002;10:265–278.
14. Sastry BKS, Narasimhan DM, Reddy NK, Raju BS. Clinical efficacy of sildenafil in primary pulmonary hypertension: a randomized, placebo-controlled, double-blind, crossover study. *J Am Coll Cardiol* 2004;43:1149–1153.

## Additional Reading

Medalion B, Katz MG, Cohen AJ, et al. Long-term beneficial effect of coronary artery bypass grafting in patients with COPD. *Chest* 2004;125:56–62. (*While not discussed in this chapter, many of our patients with heart disease also have chronic lung disease—without cor pulmonale. This study found that the 9-year survival after CABS was 62% for those with COPD vs. 95% for a control group without lung disease. Nevertheless, the authors claim a survival benefit for CABS when compared to medical therapy.*)