Cardiovascular disease remains the most significant cause of morbidity and mortality in the United States. In 1998 approximately 1.3 million Americans experienced a myocardial infarction (MI) and 700,000 of them died. It is estimated that 12.4 million Americans are alive today with a history of MI, angina, or both. The financial impact of this disease is enormous. The cost estimate for cardiovascular disease in 1998 was over $110 billion. It is important for all primary care providers to implement screening and preventive care programs to reduce the burden of cardiovascular disease. Because of the high morbidity and mortality it is also important to recognize the early manifestations of this disease.

Unfortunately, in up to 20% of patients the first manifestation of ischemic heart disease (IHD) is sudden cardiac arrest. Most deaths from IHD occur outside the hospital and within 2 hours of the onset of symptoms. Since the 1960s a great deal of effort has been directed toward the practice of cardiopulmonary resuscitation and emergency cardiac care. These efforts have been directed toward minimizing the number of cardiac deaths. Recently revised evidence-based guidelines present a summary of the collaborative effort of the American Heart Association and the International Liaison Committee on Resuscitation. Furthermore, there has been a substantial undertaking to identify and treat individuals with significant cardiovascular risk factors with the goal of lowering morbidity and mortality. This effort has been successful as noted by the decline in death rates from myo-
cardial ischemia and its complications. This chapter discusses three
issues, relevant to the family physician, regarding IHD: the evalua-
tion of patients with chest pain, the diagnosis and management of
angina pectoris, and the diagnosis and management of MI.

Chest Pain

Chest pain is one of the common reasons for patients visiting pri-
mary care physicians. The major diagnostic considerations for chest
pain are listed in Table 2.1. Of the diagnostic considerations, which
are the most commonly seen by family physicians? A Family Prac-
tice Research Network investigated this issue. Over 1 year the Michi-
gan Research Network (MIRNET) prospectively collected informa-
tion on 399 patients with episodes of chest pain. The most common
diagnostic findings were (1) musculoskeletal pain (20.4%); (2) reflux
esophagitis (13.4%); (3) costochondritis (13.1%); and (4) angina pec-
toris (10.3%). The highest priority is generally given to distin-
guishing cardiac from noncardiac chest pain. Of the many diseases
listed, the most common differential diagnostic considerations are of
esophageal and psychiatric etiologies.

Table 2.1. Common Causes of Chronic and Recurrent Chest Pain

<table>
<thead>
<tr>
<th>Cardiac causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
</tr>
<tr>
<td>Pericarditis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chest wall problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costochondritis</td>
</tr>
<tr>
<td>Myofascial syndrome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gastrointestinal causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal motility disorders</td>
</tr>
<tr>
<td>Gastroesophageal reflux</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neurologic causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiculopathy</td>
</tr>
<tr>
<td>Zoster (postherpetic neuralgia)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychiatric causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
</tr>
<tr>
<td>Depression</td>
</tr>
<tr>
<td>Hyperventilation</td>
</tr>
<tr>
<td>Panic disorder</td>
</tr>
</tbody>
</table>
Noncardiac Chest Pain

Noncardiac chest pain remains a complex diagnosis and management problem. Studies have demonstrated that 10% to 30% of patients with chest pain who undergo coronary arteriography have no arterial abnormalities. Follow-up studies of these patients have shown that the risk of subsequent myocardial infarction is low. Fifty to seventy-five percent of these patients have persistent complaints of chest pain and disability. The most common noncardiac problems in the differential are esophageal disorders, hyperventilation, panic attacks, and anxiety disorders.

Esophageal Chest Pain

Of the patients who have undergone coronary arteriography and have been found to have normal coronary arteries, as many as 50% have demonstrable esophageal abnormalities. Richter et al critically reviewed 117 articles on recurring chest pain of esophageal origin to clarify issues related to this disease. They paid specific attention to the following controversial issues: potential mechanisms of esophageal pain, differentiation of cardiac and esophageal causes, evaluation of esophageal motility disorders, use of esophageal tests for evaluating noncardiac chest pain, usefulness of techniques for prolonged monitoring of intraesophageal pressure and pH, and the relation of psychological abnormalities to esophageal motility disorders. They concluded that (1) specific mechanisms that produce chest pain are not well understood; (2) esophageal chest pain has usually been attributed to the stimulation of chemoreceptors (acid and bile) or mechanoreceptors (spasm and distention); and (3) studies done to confirm direct associations between these factors and pain have not been consistent in their findings.

It appears that the triggers for esophageal chest pain are multifactorial and often idiosyncratic to the individual. Differentiating cardiac from esophageal disease can be frustrating. As many as 50% of patients with coronary disease have esophageal disease. There are many esophageal disorders that produce pain mimicking myocardial ischemia. Areskog et al have shown that esophageal abnormalities are common in patients who are admitted to a coronary care unit and are later found to have no evidence of cardiac disease. The clinical history frequently does not differentiate between cardiac and esophageal chest pain, although features may be helpful in this process. Features suggesting esophageal origin include pain that continues for hours, pain that interrupts sleep or is meal-related, pain relieved by antacids, or the presence of other esophageal symptoms.
(heartburn, dysphagia, regurgitation). Conversely, it is well documented that gastroesophageal reflux may be triggered by heavy exercise and may produce exertional chest pain mimicking angina even during treadmill testing.

Tests that can be done to determine the presence of esophageal disease include esophageal motility testing, continuous ambulatory esophageal pH monitoring, and provocative testing (e.g., acid perfusion and balloon distension). Although findings from these tests have produced a better understanding of the pathologic conditions leading to the development of chest pain with esophageal disorders, there is no consensus as to the usefulness of these tests for the specific patient with chest pain. As noted by Pope, “What is needed is a simple and safe provocative esophageal maneuver to turn on chest pain that possesses a high degree of sensitivity.”

There is clearly an interaction between psychological abnormalities and esophageal disorders. Patients with esophageal disorders have been shown to have significantly higher levels of anxiety, somatization, and depression. It is not clear if there is a cause-and-effect relation. Given the aforementioned difficulties in the diagnosis of esophageal chest pain, the differentiation of this pain from cardiac disease, and the close relation between cardiac, esophageal, and psychiatric disease, it is wise to maintain a consistent approach to the evaluation of these patients. Richter et al. developed a stepwise approach for patients with recurring chest pain. They recommended exclusion of cardiac disease, with the subsequent evaluation to rule out structural abnormalities of the upper gastrointestinal (GI) tract (barium swallow, upper GI series, and endoscopy). Also recommended is a trial of antireflux therapy for 1 to 2 months. In those patients who fail to respond, specialized testing may then be appropriate (esophageal motility, 24-hour pH monitoring, provocative testing, and psychological evaluation).

**Psychiatric Illness**

There has long been a connection between psychiatric disorders and noncardiac chest pain. Katon et al. reported the results of an evaluation of 74 patients with chest pain and no history of organic heart disease. Each patient underwent a structured psychiatric interview immediately after coronary arteriography. Patients with chest pain and negative coronary arteriograms were significantly younger, more likely to be female, more apt to have a higher number of autonomic symptoms (tachycardia, dyspnea, dizziness, paresthesias) associated with chest pain, and more likely to describe atypical chest pain. These patients also had significantly higher scores on indices of anxiety and
depression that met *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edition (DSM-III) criteria for panic disorder, major depression, and phobias.

The strong association between anxiety and depression disorders in patients with noncardiac chest pain has been observed in many other studies. Specific medical therapy directed at anxiety and depression may help some of these patients. Cannon et al\textsuperscript{19} reported a study on a group of patients with chest pain despite normal coronary angiograms. Imipramine was shown to improve their symptoms. Patients who were given 50 mg nightly had a statistically significant reduction (52\%) in episodes of chest pain.

**Cardiac Chest Pain: Angina Pectoris**

Angina is not simply one type of pain; it is a constellation of symptoms related to cardiac ischemia. The description of angina may fit several patterns:

1. **Classic angina.** Classic angina presents as an ill-defined pressure, heaviness (feeling like a weight), or squeezing sensation brought on by exertion and relieved by rest. The pain is most often substernal and left-sided. It may radiate to the jaw, interscapular area, or down the arm. Angina usually begins gradually and lasts only a few minutes.

2. **Atypical angina.** Similar symptoms are experienced but with the absence of one or more of the criteria for classic angina. For example, the pain may not be consistently related to exertion or relieved by rest. Conversely, the pain may have an atypical character (sharp, stabbing), but the precipitating factors are clearly anginal.

3. **Anginal equivalent.** The sensation of dyspnea is the sole or major manifestation.

4. **Variant (Prinzmetal’s) angina.** This angina occurs at rest and may manifest in stereotyped patterns, such as nocturnal symptoms or symptoms that appear only after exercise. It is thought to be caused by coronary artery spasm. Its symptoms often occur periodically, with characteristic pain-free intervals, and are associated with typical electrocardiographic (ECG) changes, most commonly ST segment elevation.

5. **Syndrome X (microvascular angina).** Some patients with the clinical diagnosis of coronary artery disease have no evidence of obstructive atherosclerosis. Several reports investigating this population have found a subset with metabolic evidence for ischemia
(myocardial lactate during induced myocardial stress as evidence for ischemia). The term syndrome X has been proposed. It has been suggested that some of these patients have microvascular angina.

It is important for clinicians to recognize the factors that may confound the clinical diagnosis of angina pectoris: (1) The severity of pain is not necessarily proportional to the seriousness of the underlying illness. (2) The physical examination is not generally helpful for differentiating cardiac from noncardiac disease. A normal examination cannot be counted on to rule out significant cardiac disease. (3) The ECG is normal in more than 50% of patients with IHD. A normal ECG cannot be used to rule out significant cardiac disease. (4) Denial is a significant component in the presentation of chest pain caused by MI. (5) Some of the diseases common in the differential diagnosis of chest pain may present concurrently. Major depressive disorder and panic disorder are known to be prevalent in patients with esophageal disorders. Colgan et al reported that of 63 patients with chest pain and normal angiograms 32 (51%) had evidence of an esophageal disorder, and 19 of the 32 (59%) had a current psychiatric disorder (anxiety or depression). Patients with concurrent disorders are particularly challenging to the clinician sorting out the cause of the chest pain.

**Clinical Tools Used to Distinguish Cardiac from Noncardiac Chest Pain**

Despite the difficulties noted above, there are important clinical tools that can be used to distinguish cardiac from noncardiac chest pain.

**History**

Despite the cited difficulties, the history is key to distinguishing cardiac from noncardiac etiologies of chest pain. Noncardiac chest pain is often fleeting, brief, sharp, or stabbing. The pain may be reproduced by palpating the chest wall. The duration of pain is also important. Symptoms that last many hours or days are not likely to be anginal. A great deal of work has been done to assess the probability of IHD in a given patient based on the clinical presentation. In 1979 Diamond and Forrester presented such an approach. Using data from the clinical presentation correlated with autopsy and angiographic information, they presented a pretest likelihood of coronary artery disease in symptomatic patients according to age, sex, and type of chest pain (nonanginal, atypical angina, or typical angina).
Several observations can be made from this chart (Table 2.2): Men have a substantially greater risk than women for any given type of chest pain and at any given age. A middle-aged man with atypical chest pain is at high risk for having significant coronary artery disease. Young women (ages 30–40 years) with classic angina have a relatively low risk of having significant coronary artery disease.

### Table 2.2. Pretest Likelihood of Significant Ischemic Heart Disease (IHD) Based on Symptoms

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Nonanginal</th>
<th>Atypical angina</th>
<th>Typical angina</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–39</td>
<td>5.0/0.8</td>
<td>22/4</td>
<td>69/26</td>
</tr>
<tr>
<td>40–49</td>
<td>14/3</td>
<td>46/13</td>
<td>87/55</td>
</tr>
<tr>
<td>50–59</td>
<td>21/8</td>
<td>59/32</td>
<td>92/79</td>
</tr>
<tr>
<td>60–69</td>
<td>28/18</td>
<td>67/54</td>
<td>94/90</td>
</tr>
</tbody>
</table>

*Source: Diamond and Forrester* \(^{22}\) Copyright © 1979 Massachusetts Medical Society. Reprinted with permission. All rights reserved.

Several observations can be made from this chart (Table 2.2): Men have a substantially greater risk than women for any given type of chest pain and at any given age. A middle-aged man with atypical chest pain is at high risk for having significant coronary artery disease. Young women (ages 30–40 years) with classic angina have a relatively low risk of having significant coronary artery disease.

### Diagnostic Testing

After establishing a pretest probability of IHD, there are a variety of tests available to help establish an accurate diagnosis. Although many tests are now firmly established in clinical practice, none is particularly suited to wide-scale, cost-effective application because each has limitations concerning sensitivity and specificity.

### Exercise Tolerance Testing

In 1997 the American College of Cardiology and the American Heart Association Task Force on Assessment of Cardiovascular Procedures set guidelines for exercise treadmill testing (ETT). \(^{23}\) For patients with symptoms suggestive of coronary artery disease there are five basic indications for undertaking exercise stress testing: (1) as a diagnostic test for patients with suspected IHD, (2) to assist in identifying those patients with documented IHD who are potentially at high risk due to advanced coronary disease or left ventricular dysfunction, (3) to evaluate patients after coronary artery bypass surgery, (4) to quantify a patient’s functional capacity or response to therapy, and (5) to follow the natural course of the disease at appropriate intervals. The purpose of ETT for the patient with chest pain is to help establish whether the pain is indeed due to IHD.

Although there are many exercise protocols available, the protocols proposed by Bruce in 1956 remain appropriate. A review of the
ETT for family physicians has been published. In the standard ETT (Bruce protocol) the patient is asked to exercise for 3-minute intervals on a motorized treadmill device while being monitored for the following: heart rate and blood pressure response to exercise, symptoms during the test, ECG response (specifically ST segment displacement), dysrhythmias, and exercise capacity. Contraindications to ETT include unstable angina, MI, rapid atrial or ventricular dysrhythmias, poorly controlled congestive heart failure (CHF), severe aortic stenosis, myocarditis, recent significant illness, and an uncooperative patient. A significant (positive) test includes an ST segment depression of 1.0 mm below the baseline. Many factors influence the results of an ETT and can lead to false-positive or false-negative findings. Factors leading to false-positive results include (1) the use of medications such as digoxin, estrogens, and diuretics; and (2) conditions such as mitral valve prolapse, cardiomyopathy, and hyperventilation. Factors leading to false-negative results include (1) the use of medications such as nitrates, beta-blockers, calcium channel blockers; and (2) conditions such as a prior MI or a submaximal effort. The sensitivity of the ETT has been estimated to range from 56% to 81% and the specificity from 72% to 96%. The key point is that given the vagaries of the ETT for diagnosing IHD (generally low sensitivity and specificity) a patient with a high pretest likelihood of IHD (e.g., a 50-year-old man with typical angina) still has a high probability of having significant disease even in the face of a normal (negative) test. Furthermore, a patient with a low probability of IHD (e.g., a 40-year-old woman with atypical chest pain) still has a low chance of significant disease even if the test is positive. The optimal use of diagnostic testing is for those patients with moderate pretest probabilities (e.g., a 40- to 50-year-old man with atypical pain).

In addition to the diagnostic implications of an ETT, there are prognostic implications. The following are considered to be parameters associated with poor prognosis or increased disease severity: failure to complete stage 2 of a Bruce protocol, failure to achieve a heart rate over 120 bpm (off beta-blockers), onset of ST segment depression at a heart rate of less than 120 bpm, ST segment depression over 2.0 mm, ST segment depression lasting more than 6 minutes into recovery, ST segment depression in multiple leads, poor systolic blood pressure response to exercise, ST segment elevation, angina with exercise, and exercise-induced ventricular tachycardia.

Radionuclide Perfusion Imaging. There are patients in whom the standard ETT is not a useful diagnostic tool and in whom a ra-
dionuclide procedure would be more appropriate. Patients with baseline ECG abnormalities due to digitalis or left ventricular hypertrophy with strain or those with bundle branch block (especially left bundle branch block) cannot have proper evaluation of the ST segment for characteristic ischemic changes. In these patients a radionuclide stress test is appropriate. The principle behind radionuclide testing is as follows: Myocardial thallium 201 chloride uptake is proportional to the coronary blood flow. A myocardial segment supplied by a stenotic coronary artery receives less flow relative to normal tissue, causing a thallium perfusion defect. Thallium washout is also slower in stenotic areas. With perfusion imaging, both stress and rest images are compared for perfusion. As a general rule, a defect is visible on thallium imaging if there is 50% or greater stenosis in a coronary artery. In the standard exercise thallium test, repeat imaging is performed 3 to 4 hours after completion of the ETT. Some investigators advocate 24-hour imaging in patients with perfusion defects to look for delayed reversibility.

For patients unable to exercise, thallium imaging can be performed using dipyridamole (Persantine) as a coronary vasodilator. Adenosine may also be used. Its advantages over dipyridamole include an ultrashort half-life (less than 10 seconds) and better coronary vasodilation. Two technetium radiopharmaceuticals [technetium sestamibi (Cardiolyte) and technetium teboroxime (Cardiotec)] have been approved for myocardial perfusion imaging. These agents may eventually replace thallium because of more favorable imaging characteristics.27

Compared to the standard ETT, the thallium 201 ETT has the advantage of increased sensitivity (80–87%) and specificity (85–90%).27 Dipyridamole, adenosine, and technetium perfusion testing has a sensitivity ranging from 70% to 95% and specificity from 60% to 100%. Unfortunately, the cost of these procedures is more than five times as great as a standard ETT ($1000–$1400 versus $175–$250).25

**Stress Echocardiography.** Ischemic heart disease can be detected with stress echocardiography. During stress-induced myocardial ischemia, the affected ventricular walls become hypokinetic. Studies suggest that physical exercise and dobutamine may be the preferable means of provoking ischemia in patients undergoing stress echocardiography.28,29 Preliminary data suggest a higher sensitivity and specificity than for the standard ETT and increased usefulness for predicting subsequent myocardial events; however, the primary utility of this test appears to be for detection of ischemia in patients who
are unable to exercise adequately. Similar values for sensitivity and specificity between stress echocardiography and perfusion imaging have been reported. Stress echocardiography may be particularly valuable in patients who have a questionable defect on perfusion imaging.

The advantages and disadvantages of each of these diagnostic tests for IHD, as well as gender-specific issues, are presented in a summary by Redberg.\textsuperscript{30}

Response to Nitroglycerin. Another approach employs clinical information to determine the probability of coronary artery disease based on response to treatment. One such study involved the use of sublingual nitroglycerin to determine the likelihood of disease. Horwitz et al\textsuperscript{31} evaluated the usefulness of nitroglycerin as a diagnostic aid for IHD. They found a sensitivity of 76\% and a specificity of 80\% in 70 patients with chest pain of anginal type. It was concluded that 90\% of patients with recurrent, angina-like chest pain who exhibit a prompt response to nitroglycerin (within 3 minutes) have IHD; however, a delayed or absent response paradoxically indicates either an absence of IHD or unusually severe disease. Therefore failure to respond to nitroglycerin should not be used to exclude the diagnosis of IHD.

Angina Pectoris

Once the diagnosis of angina is established, there are several important management considerations for this disease. The first is related to disease prognosis, the second to drug therapy, and the third to further investigative tests and invasive therapeutic interventions. Comprehensive management guidelines were prepared in 1999 by the American College of Cardiology and American Heart Association Task Force.\textsuperscript{32}

Prognosis

Three major factors determine the prognosis of patients with angina pectoris: the amount of viable but jeopardized left ventricular myocardium, the percentage of irreversibly scarred myocardium, and the severity of underlying coronary atherosclerosis. A number of studies were reported before invasive therapies were available that assess the prognosis of patients with stable angina. Most of them appeared between 1952 and 1973 and reported an annual mortality of 4\%. Since
cardiac catheterization has come into general use, the prognosis has been modified and is based on the number of diseased vessels. Currently, the annual mortality rates for patients with one-vessel disease, two-vessel disease, three-vessel disease, and left main coronary artery disease (CAD) are 1.5%, 3.5%, 6.0%, and 8.0% to 10.0%, respectively.33

Exercise tolerance testing has been used to establish the prognosis in patients with symptomatic IHD. The exercise test parameters associated with a poor outcome have been described above.26

When does angina signal severe coronary disease? Pryor et al34 developed a nomogram based on a point scoring system to help answer this question. They based the nomogram on the following factors: type of chest pain (typical, atypical, nonanginal), sex, selective cardiovascular risk factors (hypertension, smoking, hyperlipidemia, diabetes mellitus), anginal duration (months), and the presence of carotid bruits. By applying the nomogram for the individual patient one can determine the probability of severe disease (i.e., 75% narrowing of the left main coronary artery or three-vessel disease).

Drug Therapy

In patients with stable exertional angina who do not have severe disease, the goal of therapy is to abolish or reduce anginal attacks and myocardial ischemia and to promote a normal lifestyle. For the relief of angina, the treatment strategy is to lower myocardial oxygen demand and increase coronary blood flow to the ischemic regions.

Patients are screened for the presence of significant cardiovascular risk factors and are advised to modify any that are present. Three classes of antianginal drugs are commonly used: nitrates, beta-blockers, and calcium channel blockers. Each reduces myocardial oxygen demand and may improve blood flow to the ischemic regions. The mechanisms by which these agents reduce myocardial oxygen demand or increase coronary blood flow to ischemic areas differ from one class of drug to another. No greater efficacy in relieving chest pain or decreasing exercise-induced ischemia has been shown for one or another group of drugs.

Nitrates

Nitrates are potent venous and arterial dilators. At low doses venous dilation predominates, and at higher doses arterial dilation occurs as well. Nitrates decrease myocardial oxygen demand in the following ways: Decreased venous return reduces left ventricular end-diastolic volume and ventricular wall stress. Increased arterial compliance and
cardiac output lowers systolic blood pressure and decreases peripheral resistance (afterload). It also enhances myocardial oxygen supply by preventing closure of stenotic coronary arteries during exercise, dilating epicardial coronary arteries, and decreasing left ventricular end-diastolic pressure, thereby enhancing subendocardial blood flow and inhibiting coronary artery spasm. Nitrates are inexpensive and have a well documented safety record. Both short- and long-acting nitrates are available. Short-acting preparations are used for relief of an established attack, whereas long-acting nitrates are used for prevention. The most significant concern about the long-acting nitrates is tolerance. Most studies have shown that tolerance develops rapidly when long-acting nitrates are given for anginal prophylaxis.\(^{34}\)

With nitroglycerin patches tolerance can develop within 24 hours, and further therapy can lead to complete loss of the antianginal effect.\(^{35}\) Various dosing strategies with oral and transdermal formulations have been used to overcome the development of nitroglycerin tolerance. Patch-free intervals of 10 to 12 hours are commonly used to retain the antianginal effectiveness. For oral administration, nitroglycerin isosorbide dinitrate three times daily at 7 A.M., noon, and 5 P.M. appears to prevent the development of tolerance. Because of the concern for intervals during which patients remain unprotected, it is common to add another antianginal agent to the nitroglycerin regimen. Other problems with nitroglycerin include the fact that 10% of patients do not respond and 10% have associated intolerable headaches that may necessitate discontinuation.\(^{35}\)

**Beta-Blockers**

The antianginal effect of beta-blockers is well established.\(^{36}\) These agents improve exercise tolerance and reduce myocardial ischemia. The effect produces a reduction in myocardial oxygen demand through a reduction in heart rate and contractility. Many beta-blockers are available. They may be divided into those that are nonselective (\(\beta_1\) and \(\beta_2\)) (i.e., propranolol, timolol, nadolol), those that are \(\beta_1\) selective (i.e., atenolol, metoprolol, acebutolol), and those that are nonselective and produce vasodilatory effects through the ability to block \(\alpha_1\)-receptors and dilate blood vessels directly (i.e., labetalol). All beta-blockers, irrespective of their selective properties, are equally effective in patients with angina.\(^{36}\)

Some 20% of patients do not respond to beta-blockers. Those who do not respond are more likely to have severe IHD. Furthermore, some patients do not tolerate the adverse side effects, such as fatigue, depression, dyspnea, and cold extremities. Other concerns include a
small but significant aggravation of hyperlipidemia and precipitation of CHF and bronchospasm in susceptible individuals. Generally, beta-blockers are dose-adjusted to achieve a heart rate of 50 to 60 bpm. Patients should be cautioned to not stop beta-blockers abruptly, thereby avoiding a rebound phenomenon.

**Calcium Channel Blockers**

Calcium channel blockers are a diverse group of compounds, all of which impede calcium ion influx into the myocardium and smooth muscle cells. These agents relieve myocardial ischemia by reducing myocardial oxygen demand secondary to decreased afterload and myocardial contractility. In addition, they dilate coronary arteries. There are three classes of calcium channel blockers: papaverine derivatives (verapamil), dihydropyridines (nifedipine, nicardipine), and benzothiazepines (diltiazem). Each of the drugs in the three classes has different effects on the atrioventricular (AV) node, heart rate, coronary vasodilation, diastolic relaxation, cardiac contractility, systemic blood pressure, and afterload. All three classes are effective for the management of patients with stable angina. Most studies have shown them to have effects equal to those of beta-blockers. Calcium channel blockers may be preferred in patients with obstructive airway disease, hypertension, peripheral vascular disease, or supraventricular tachycardia. In general, they are well tolerated. The most troublesome side effects include constipation, edema, headache, and aggravation of congestive heart failure.

Concern has developed that short-acting calcium channel blockers may be associated with an increased risk of MI. There has been evidence of a 58% to 70% increase in risk of MI compared to that in patients on beta-blockers or diuretics. The phenomenon has been noted to be dose-related. At present the National Heart, Lung, and Blood Institute has issued a statement recommending caution with the use of short-acting calcium channel blockers.

**Combination Therapy**

It is important to maximize therapy with any one class of antianginal drug before considering it a failed trial. If monotherapy fails, it is appropriate to add another agent. Generally beta-blockers and nitrates or calcium channel blockers and nitrates complement each other. Calcium channel blockers and beta-blockers can be used together. Combination therapy may be more effective than either agent alone. It is important to be cautious, as some combinations produce deleterious effects. For example, verapamil and beta-blockers may produce extreme bradycardia or heart block.
Aspirin
Aspirin is effective for primary and secondary prevention of MI, presumably by inhibiting thrombosis. Although there is controversy as to the ideal therapeutic dose, low-dose therapy (81–325 mg) is generally recommended. Alternative antiplatelet regimens to aspirin include ticlopidine and clopidogrel. A 1994 review found no evidence that any antiplatelet regimen was more effective than medium-dose aspirin alone in the prevention of vascular events. Another review of randomized trials comparing either ticlopidine or clopidogrel with aspirin found several trials showing a small additional benefit of these two drugs over aspirin in reducing the odds of a vascular event.

Invasive Testing
Cardiac catheterization is not routinely recommended for initial management of patients with stable angina. Patients who warrant such an evaluation are those who exhibit evidence of severe myocardial ischemia on noninvasive testing or who have symptoms refractory to antianginal medications. In patients who undergo catheterization, the most important determinant of survival is left ventricular function followed by the number of diseased vessels. Patients with left main artery disease or three-vessel disease with diminished left ventricular function are candidates for a coronary artery bypass graft procedure. Others (those with one- or two-vessel disease) are managed medically or considered for percutaneous transluminal coronary angioplasty (PTCA).

Unstable Angina Pectoris
Unstable angina manifests clinically either as an abrupt onset of ischemic symptoms at rest or as an intensification or change in the pattern of ischemic symptoms in a patient with a history of IHD. This intensification may be manifested by an increase in the frequency, severity, and duration of symptoms as well as an increasing ease of provocation (symptoms at rest or with minimal effort). Recurrence of ischemic symptoms soon after an MI (usually within 4 weeks) is also considered a sign of unstable angina. Unstable angina is generally diagnosed on clinical grounds alone. Because of the episodic nature of ischemia in unstable angina, however, transient ECG abnormalities (ST segment depression or elevation or T wave abnormalities, i.e., inversion, flattening, or peaking) may not be documented in 50% to 70% of patients with the clinical diagnosis of
unstable angina. In studies in which prolonged Holter monitoring was used during the in-hospital phase of unstable angina, transient ischemic ST segment deviations have been described in 60% to 70% of cases, more than 70% of them being clinically unsuspected or silent.\(^{42}\)

**Prognosis**

The prognosis of patients with unstable angina is not as good as those with chronic stable angina. Mortality is increased in those who fail to respond to initial therapy, who have severe left ventricular dysfunction, and who have multivessel CAD (particularly left main artery disease).

**Management Strategy**

An important development in the management of unstable angina was the 1994 report of the Agency for Health Care Policy and Research.\(^{43}\) This report includes clinical practice guidelines that are based on a consensus panel of experts. The guidelines allow physicians to consider outpatient management for a select subgroup of patients with unstable angina, specifically those who are thought to be at low risk for MI. According to the report, in the initial management physicians should use the information in Table 2.3 to determine whether a particular patient has high, intermediate, or low likelihood of having significant CAD. For example, the patient with low likelihood might be nondiabetic, have atypical chest pain, be younger (<60 years for men, <70 years for women), and have a normal ECG. The next step is to determine the level of risk for MI. The information in Table 2.4 allows a similar stratification of risk. For example, a low-risk patient is one with a history of angina that is now provoked at a lower threshold but not at rest, and the ECG is normal or unchanged. Low-risk patients may be treated with aspirin, nitroglycerin, beta-blockers, or a combination. Follow-up should be no later than 72 hours. High- or moderate-risk patients should be admitted for intensive medical management. Intensive medical management includes consideration of aspirin, heparin, nitrates, beta-blockers, calcium channel blockers (if the patient is already on adequate doses of nitrates and beta-blockers or unable to tolerate them), and morphine sulfate.

Once patients are stable, they should be considered for noninvasive exercise testing to further define the prognosis and direct the treatment plan. Low-risk patients can be managed medically. Those at intermediate risk should be considered for additional testing (either a cardiac catheterization, radionuclide stress test, or echocardiography).
### Table 2.3. Likelihood of Significant Coronary Artery Disease (CAD) in Patients with Symptoms Suggesting Unstable Angina

<table>
<thead>
<tr>
<th>High likelihood (any of the listed features)</th>
<th>Intermediate likelihood (absence of high-likelihood features and any of the listed features)</th>
<th>Low likelihood (absence of high- or intermediate-likelihood features but may have the listed features)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known history of CAD</td>
<td>Definite angina: men &lt;60, women &lt;70</td>
<td>Chest pain, probably not angina</td>
</tr>
<tr>
<td>Definite angina: men ≥60 women ≥70</td>
<td>Probable angina: men &gt;60 or women &gt;70</td>
<td>One risk factor but not diabetes</td>
</tr>
<tr>
<td>Hemodynamic changes or ECG changes with pain</td>
<td>Probably not angina in diabetics or in nondiabetics with ≥two other risk factors(^a)</td>
<td>T wave flat or inverted &lt;1 mm in leads with dominant R waves</td>
</tr>
<tr>
<td>Variant angina</td>
<td>Extracardiac vascular disease</td>
<td>Normal ECG</td>
</tr>
<tr>
<td>ST increase or decrease ≥1 mm</td>
<td>ST depression 0.05 to 1.00 mm</td>
<td></td>
</tr>
<tr>
<td>Marked symmetric T wave inversion in multiple precordial leads</td>
<td>T wave inversion ≥1 mm in leads with dominant R waves</td>
<td></td>
</tr>
</tbody>
</table>

Source: Braunwald et al.\(^{43}\)

\(^a\)CAD risk factors include diabetes, smoking, hypertension, and elevated cholesterol.
**Table 2.4. Short-Term Risk of Death or Nonfatal Myocardial Infarction in Patients with Symptoms Suggesting Unstable Angina**

<table>
<thead>
<tr>
<th>High risk (at least one of the listed features must be present)</th>
<th>Intermediate risk (no high-risk feature but must have any of the listed features)</th>
<th>Low risk (no high- or intermediate-risk feature but may have any of the listed features)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged ongoing (&gt;20 min) rest angina</td>
<td>Rest angina now resolved but not low likelihood of CAD</td>
<td>Increased angina frequency, severity, or duration</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>Rest angina (&gt;20 min or relieved with rest or nitroglycerin)</td>
<td>Angina provoked at a lower threshold</td>
</tr>
<tr>
<td>Angina with new or worsening mitral regurgitation murmurs</td>
<td>Angina with dynamic T wave changes</td>
<td>New-onset angina within 2 weeks to 2 months</td>
</tr>
<tr>
<td>Rest angina with dynamic ST changes ≥1 mm</td>
<td>Normal or unchanged ECG</td>
<td>Nocturnal angina</td>
</tr>
<tr>
<td>Angina with S₃ or rales</td>
<td>New onset of CCSC III or IV angina during past 2 weeks but not low likelihood of CAD</td>
<td></td>
</tr>
<tr>
<td>Angina with hypotension</td>
<td>Q waves or ST depression ≥1 mm in multiple leads</td>
<td></td>
</tr>
<tr>
<td>Age &gt;65 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Source: Braunwald et al.⁴³*

CCSC = Canadian Cardiovascular Study Class.
graphic stress test). Those at high risk should be referred for cardiac catheterization.43

Since the publication of the 1994 report, efforts have been directed at the use of markers of cardiac injury, i.e., cardiac troponins (troponin T and troponin I). Their detection, even at low levels, is highly sensitive and specific for injury. Troponin elevation in patients otherwise considered to have unstable angina identifies a subset of patients requiring more aggressive intervention. Hamm and Braunwald44 have proposed a risk-stratification algorithm that incorporates troponin testing.

**Antiplatelet Therapy**

Antiplatelet therapy is an important addition for patients with unstable angina. A number of studies have demonstrated that a common cause of crescendo angina is platelet aggregation and thrombus formation on the surface of an ulcerated plaque. In the Veterans Administration Cooperative Study, men with unstable angina who received aspirin (325 mg/day) had a 50% reduction in subsequent death from MI.45 As noted previously, ticlopidine and clopidogrel are alternative antiplatelet regimens to aspirin.

**Percutaneous Transluminal Coronary Angioplasty**

There has been a marked increase in the use of angioplasty over the past 20 years. The American College of Cardiology and the American Heart Association Task Force have published guidelines for the selection of patients for coronary angioplasty.46 Among patients with unstable angina, PTCA is recommended for those who do not show an adequate response to medical treatment (continued chest pain or evidence of ongoing ischemia during ECG monitoring) or who are intolerant of medical therapy because of uncontrollable side effects.

The long-term outcome after successful angioplasty has been reported to be excellent even when compared with patients undergoing bypass surgery.47 Further research is important in the areas of long-term outcome for multiple lesions, extensive disease, and avoidance of complications. Technologies such as stents, laser angioplasty, and atherectomy await further evaluation.

**Coronary Artery Bypass Graft**

Large randomized trials have shown that surgical revascularization is more effective than medical therapy for relieving angina and improving exercise tolerance for at least several years. Development of atherosclerosis in the coronary artery bypass graft resulting in angina generally occurs within 5 to 10 years. However, patients with inter-
nal mammary artery grafts have substantially fewer problems with graft occlusion (90% patency rate at 10 years). Improved survival with surgical versus medical therapy is seen only in the subset of patients with severe CAD or left ventricular dysfunction.48

Silent Ischemia

Many investigations have established that most ischemic episodes in patients with stable angina are not accompanied by chest pain (silent ischemia). What remains unclear is the precise nature of events that accompany ischemic events that do or do not produce pain. Patients with predominantly silent ischemia may be hyposensitive to pain in general; denial may play a role, or they may experience pain but attribute the symptoms to a less significant event. It is well documented that personality-related, emotional, and social factors can modulate the perception of pain. It is not surprising that the symptoms among cardiac patients with the same degree of disease vary greatly. Personality inventory studies have shown that patients with reproducible angina have higher scores on indices of nervousness and excitability than do those who are free of symptoms. Many studies have shown that stress of various types can influence the frequency and duration of ischemic episodes in patients with angina.49

Silent ischemia is prevalent. Seventy percent of ischemic episodes in patients with IHD are estimated to be asymptomatic. Among patients with stable angina who undergo 24-hour Holter monitoring, 40% to 72% of the episodes are painless. Among patients with unstable angina, more than half manifest painless ST segment depression.

In 1988 Cohn50 proposed classifying silent ischemia into three clinical types to help clarify the prevalence, detection, prognosis, and management of this syndrome. Type 1 includes persons with ischemia who are asymptomatic, never having had any signs or symptoms of cardiovascular disease. Type 2 includes persons who are asymptomatic after an MI but still show painless ischemia. Type 3 includes patients with both angina and silent ischemia. From Cohn’s data 2.5% to 10.0% of middle-aged men have type 1 silent ischemia. Among middle-aged men known to have CAD, 18% have type 2 and 40% have type 3.

Methods of Detection

Certain tests can be used to assess the presence of silent ischemia: ETT, ambulatory ECG for ST segment changes (Holter monitor), ra-
dionuclide tests including thallium scintigraphy and gated pooled [multiple gated acquisition (MUGA)] scan, and stress echocardiography. Of these tests, the most commonly considered are ETT and Holter monitoring.

For Holter monitoring, when ST segment changes that meet strict criteria are seen in a patient with known IHD, it is generally accepted that they represent episodes of myocardial ischemia. Ischemic criteria include at least 1.0 mm of horizontal or down-sloping ST segment depression that lasts for at least 1 minute and is separated from other discrete episodes by at least 1 minute of a normal baseline. The methodology has limitations, including difficulty reading ST segment changes in patients with an abnormal baseline (left ventricular hypertrophy with strain) or in those with a left bundle branch block.

It is not thought at this time that any of the methods to detect silent ischemia are useful for screening for the presence of IHD in apparently healthy populations. Although this subject remains controversial, it may be wise to screen those patients at high risk (i.e., diabetics or patients with two or more cardiac risk factors).

Prognostic Implications

The presence of frequent, prolonged ischemic episodes despite medical therapy in patients with stable and unstable angina has been associated with a poor prognosis. Using Cohn’s classification system, those patients with type 2 silent ischemia have the worst prognosis, especially those with left ventricular dysfunction and three-vessel disease. Exercise tests done 2 to 3 weeks after an MI have shown an adverse 1-year prognosis associated with silent ischemia. It is unclear whether those with type 3 have a worse prognosis.

Management

Antiischemic medical and revascularization therapies have been shown to reduce asymptomatic ischemia. It is prudent to consider patients with persistent asymptomatic ischemia to be at higher risk for subsequent events and therefore to warrant more aggressive therapy. Patients with type 1 are advised to modify risk factors and avoid activities known to produce ischemia. Those with strongly positive tests can be considered for angiography. For patients with types 2 or 3, treatment with beta-blockers for a cardioprotective effect should be considered. It remains unresolved whether asymptomatic ischemia has a causal relation with subsequent MI and cardiac death or is merely a marker of high risk.
Myocardial Infarction

Clinical Presentation

The classic initial manifestations of an acute MI include prolonged substernal chest pain with dyspnea, diaphoresis, and nausea. The pain may be described as a crushing, pressing, constricting, vise-like, or heavy sensation. There may be radiation of the pain to one or both shoulders and arms or to the neck, jaw, or interscapular area. Only a few patients have this classic overall picture. Although 80% of patients with an acute MI have chest pain at the time of initial examination, only 20% describe it as crushing, constricting, or vise-like. The pain may also be described atypically, such as sharp or stabbing, or it can involve atypical areas such as the epigastrium or the back of the neck. “Atypical” presentations are common in the elderly. Pathy found that the initial manifestations of an acute MI were more likely to include symptoms such as sudden dyspnea, acute confusion, cerebrovascular events (e.g., stroke or syncope), acute CHF, vomiting, and palpitations. There is strong evidence that a substantial proportion of MIs are asymptomatic. In an update of the Framingham Study, Kannel and Abbott reported that 28% of infarcts were discovered only through the appearance of new ECG changes (Q waves or loss of R waves) observed on a routine biennial study. These infarctions had been previously unrecognized by both patient and physician.

Physical Examination

For the patient with an “uncomplicated MI” there are few physical examination findings. The main purpose of the examination is to assess the patient for evidence of complications from the MI and to establish a baseline for future comparisons. Signs of severe left ventricular dysfunction include hypotension, peripheral vasoconstriction, tachycardia, pulmonary rales, an S3, and elevated jugular venous pressure (see Chapter 5). Preexisting murmurs should be verified. A new systolic murmur can result from a number of causes: papillary muscle dysfunction, mitral regurgitation as a result of ventricular dilatation, ventricular septal rupture, and acute severe mitral regurgitation due to papillary muscle rupture.

Electrocardiography

The classic ECG changes of acute ischemia are peaked, hyperacute T waves, T wave flattening or inversion with or without ST segment
depression, horizontal ST segment depression, and ST segment elevation. Changes associated with an infarction are (1) the fresh appearance of Q waves or the increased prominence of preexisting ones; (2) ST segment elevations; and (3) T wave inversions. It is important to recognize that with acute MI the ECG may be entirely normal or contain only “soft” ECG evidence of infarction.

In the past infarcts were classified as transmural or subendocardial, depending of the presence of Q waves. This terminology has now been replaced by the terms Q-wave and non–Q-wave MI. This distinction has more clinical relevance, as several studies have indicated differences in etiology and outcome. The key differences between these two groups are as follows: (1) Q-wave infarctions account for 60% to 70% of all infarcts and non–Q-wave infarctions for 30% to 40%. (2) ST segment elevation is present in 80% of Q-wave infarctions and 40% of non–Q-wave infarctions. (3) The peak creatine kinase tends to be higher in Q-wave infarctions. (4) Postinfarction ischemia and early reinfarction are more common with non–Q-wave infarctions. (5) In-hospital mortality is greater with Q-wave infarctions (20% versus 8% for non–Q-wave infarctions). In general, it is thought that the non–Q-wave infarction is a more unstable condition because of the higher risk of reinfarction and ischemia.

**Laboratory Findings**

Elevation of the creatine kinase muscle and brain subunits (CK-MB) isoenzyme is essential for the diagnosis of acute MI. In general, acute elevations of this enzyme are accounted for by myocardial necrosis. Detectable CK-MB from noncardiac causes is rare except during trauma or surgery. The peak level appearance of CK-MB is expected within 12 to 24 hours after the onset of symptoms; normalization is expected in 2 to 3 days. Therefore patients should have a CK-MB level determined on admission and every 8 to 12 hours thereafter (repeated twice). Reliance on a single CK assay in an emergency room setting to rule out MI is not sensitive and should be discouraged. Cardiac troponins (T and I) are newer markers for cardiac injury. The troponins first become detectable after the first few hours following the onset of myocardial necrosis, and they peak after 12 to 24 hours. Normalization of troponin T levels requires 5 to 14 days; troponin I levels requires 5 to 10 days.55

**Management Guidelines**

Comprehensive management guidelines were prepared in 1999 by the American College of Cardiology and American Heart Associa-
The main priority for patients with an acute MI is relief of pain. The frequent clinical observation of rapid, complete relief of pain after early reperfusion with thrombolytic therapy has made it clear that the pain of an acute MI is due to continuing ischemia of living jeopardized myocardium rather than to the effects of completed myocardial necrosis.

Effective analgesia should be administered at the time of diagnosis. Analgesia can be achieved by the use of sublingual nitroglycerin or intravenous morphine (or both). Sublingual nitroglycerin is given immediately unless the systolic blood pressure is less than 90 mm Hg. If the systolic blood pressure is under 90 mm Hg, nitroglycerin may be used after intravenous access has been obtained. Long-acting oral nitrate preparations are avoided for management of early acute MI. Sublingual or transdermal nitroglycerin can be used, but intravenous infusion of nitroglycerin allows more precise control. The intravenous dose can be titrated by frequently measuring blood pressure and heart rate. Morphine sulfate is also highly effective for the relief of pain associated with an acute MI. In addition to its analgesic properties, morphine exerts favorable hemodynamic effects by increasing venous capacitance and reducing systemic vascular resistance. The result is to decrease myocardial oxygen demand. As with nitroglycerin, hypotension may occur. The hypotension may be treated with intravenous fluids or leg elevation.

**Oxygen**

Supplemental oxygen is given to all patients with an acute MI. Hypoxemia in a patient with an uncomplicated infarction is usually caused by ventilation-perfusion abnormalities. When oxygen is used it is administered by nasal cannula or mask at a rate of 4 to 10 L/min. In patients with chronic obstructive pulmonary disease it may be wise to use lower flow rates.

**Thrombolytic Therapy**

In addition to relieving pain and managing ischemia, thrombolytic therapy must be considered. Thrombosis has a major role in the development of an acute MI. Approximately 66% of patients with MIs have ST segment elevation, making it likely that the process is caused by an occlusive clot. The goal of thrombolytic therapy is reperfusion with a minimum of side effects. The most commonly used thrombolytic agents are streptokinase, anisoylated plasminogen streptokinase activator complex (APSAC), recombinant tissue-type plasminogen activator (rt-PA), urokinase, and pro-urokinase.
Early administration of thrombolytic therapy, within 6 to 12 hours from the onset of symptoms, has been associated with a reduction in mortality. Indications for thrombolytic therapy include typical chest pain >30 minutes but <12 hours that is unrelieved by nitroglycerin, and ST segment elevation in more than two contiguous leads (>1 mm in limb leads or >2 mm in chest leads) or ST segment depression in only V1 and V2 or a new left bundle branch block. Relative contraindications for thrombolytic therapy include history of stroke, active bleeding, blood pressure >180 mm Hg systolic, major surgery/trauma in the last 3 to 6 months, recent noncompressible vascular puncture, and possible intracranial event/unclear mental status. Wright and colleagues present a summary of the major thrombolytic trials. Advances in this therapeutic modality during the past 5 years include new third-generation fibrinolytic agents and various strategies to enhance administration and efficacy of these agents. A number of ongoing trials are attempting to determine whether the combination of fibrinolytic therapy with low molecular weight heparin enhances coronary reperfusion and reduces mortality and late reocclusion. Also presented is a dose and cost summary of the available fibrinolytic agents.

Complications (Mechanical)
The most common complications of an acute MI are mechanical and electrical. Mechanical complications include those that are quickly reversible and those that are clearly life-threatening. Reversible causes of hypotension include hypovolemia, vasovagal reaction, overzealous therapy with antianginal or antiarrhythmic drugs, and brady- and tachyarrhythmias. Other, more serious etiologies include primary left ventricular failure, cardiac tamponade, rupture of the ventricular septum, acute papillary muscle dysfunction, and mitral regurgitation (see Chapter 9).

Killip and Kimball developed a classification of patients with acute MI.

Class 1: Patients with uncomplicated infarction without evidence of heart failure as judged by the absence of rales and an S3.
Class 2: Patients with mild to moderate heart failure as evidenced by pulmonary rales in the lower half of the lung fields and an S3.
Class 3: Patients with severe left ventricular failure and pulmonary edema.
Class 4: Patients with cardiogenic shock, defined as systolic blood pressure less than 90 mm Hg with oliguria and other evidence of poor peripheral perfusion.
Cardiogenic shock has emerged as the most common cause of in-hospital mortality of patients with an acute MI. Despite advances in medical therapy, cardiogenic shock has a dismal prognosis (80–90% mortality). The management of patients with cardiogenic shock includes adequate oxygenation, reduction in myocardial oxygen demands, protection of ischemic myocardium, and circulatory support (see Chapter 9). The potential for myocardial salvage with emergency reperfusion should be considered in all cases.

**Complications (Electrical)**

The past 30 years has seen major developments in the recognition and treatment of arrhythmias (see Chapter 4). The most common include the brady- and tachyarrhythmias, AV conduction disturbances, and ventricular arrhythmias. Organized treatment protocols have been developed for each of these dysrhythmias.\(^{58}\)

**Post-MI Evaluation**

Recommendations for pre- and postdischarge evaluations of patients with an acute MI have been outlined by the American College of Cardiologists, the American Heart Association, and the American College of Physicians.\(^{46}\) They include recommendations for testing exercise tolerance and strategies to determine those who would benefit from medical or surgical intervention. These recommendations include a submaximal ETT at 6 to 10 days and at 3 weeks to determine functional capacity.

**Rehabilitation**

The goal of cardiac rehabilitation includes maintenance of a desirable level of physical, social, and psychological functioning after the onset of cardiovascular illness.\(^ {59}\) Specific goals of rehabilitation include risk stratification, limitation of adverse psychological and emotional consequences of cardiovascular disease, modification of risk factors, alleviation of symptoms, and improved function. Risk stratification is accomplished by exercise tolerance testing. Additionally, high-risk patients include those with CHF, silent ischemia, and ventricular dysrhythmias. All patients should undergo an evaluation to reduce risk factors (smoking, hyperlipidemia, and hypertension). Risk modification of these factors has been associated with significant reduction in subsequent cardiac events. Enrollment in a cardiac rehabilitation program with particular emphasis on exercise has been shown to reduce cardiovascular mortality.\(^ {60}\)
References

19. Cannon RO, Quyyumi AA, Mincemoyer R, Stine AM, Gracely RH,
37. Opie LH. Calcium channel antagonists. Part II. Use and comparative properties of prototypical calcium antagonists in ischemic heart disease,


