and making it prone to rupture. T lymphocytes tends to accumulate at the border of plaque, which is the frequent site of plaque rupture.

As the fibrous cap thins through collagen degradation and eventually ruptures, blood is exposed to the thrombogenic triggers of collagen and lipid. In this setting, platelets are activated and begin to aggregate at the site of rupture. Platelets release vasoconstrictor substances thromboxane and serotonin, but more importantly, they serve as the trigger for thrombin formation, which leads to local thrombosis. Thrombin accumulation along with ongoing platelet activation can lead to rapid accumulation of thrombus in the vessel lumen. The combination of platelet-mediated thrombus accumulation and vasoconstriction can significantly limit blood flow, leading to myocardial ischemia. The degree of ischemia and its duration can culminate in MI. Complete vessel occlusion by thrombus leads to the greatest degree of myocardial ischemia and infarction, typically resulting in an ST elevation myocardial infarction (STEMI). Incomplete vessel occlusion limits blood flow enough to cause symptomatic myocardial ischemia and lesser degrees of MI, resulting in the syndromes of unstable angina or non–ST elevation myocardial infarction (NSTEMI).

MI is the most profound consequence of atherosclerotic plaque pathology, but significant disability can also develop when atherosclerotic plaques expand in size, leading to obstruction of blood flow and resultant myocardial ischemia. Plaque growth, driven by smooth muscle cell proliferation, initially causes the vessel to expand toward the adventitia (Glagov remodeling). Once a limit of lateral expansion is reached, the enlarging plaque encroaches on the vessel lumen. Typically, when the diameter of the lumen is decreased by at least 70%, myocardial ischemia and symptoms of angina can develop under conditions of increasing demand for blood flow. In the case of exercise, increases in heart rate and blood pressure lead to increasing myocardial oxygen demand; when flow-limiting atherosclerotic lesions are present, oxygen demand may not be met by supply and myocardial ischemia ensues. The greater the degree of vessel obstruction, the more likely it is that myocardial ischemia and angina will occur at low workloads, even to the point of angina at rest (Fig. 8-1). Other forms of stress, such as emotional stress or cold exposure, can also cause symptoms of angina in patients with significant obstructive plaque through mechanisms such has hypertension (increased myocardial oxygen demand) or sympathetically mediated vasonstriction.

CLINICAL PRESENTATIONS OF CORONARY ARTERY DISEASE

The clinical syndromes that patients experience due to the presence of CAD principally relate to the occurrence of myocardial ischemia. Myocardial ischemia develops when there is a mismatch of oxygen delivery and oxygen demand. Given that extraction of oxygen by the myocardium is very high, any increase in oxygen demand must be met with an increase in coronary blood flow. Oxygen demand is directly related to increases in heart rate, myocardial contractility, and wall stress (which are related to blood pressure and cardiac dimensions). There is a reflex increase in myocardial oxygen demand driven by these factors as the heart is required to deliver more systemic blood flow in the face of various stresses, the most common of which is increased exertion. Coronary blood flow also depends on the vascular tone of arterioles that are under the control of vasodilators derived from normal functioning endothelium and autonomic tone.

Coronary blood flow increases to meet an increase in myocardial oxygen demand through endothelium-mediated vasodilation. In the face of atherosclerosis, endothelial dysfunction may develop, resulting in reduced endothelium-mediated vasodilation. Endothelial dysfunction coupled with a flow-limiting stenosis sets the stage for the development of myocardial ischemia. The coronary vessel distal to a flow-limiting stenosis tends to be maximally dilated. As myocardial oxygen demand increases, the

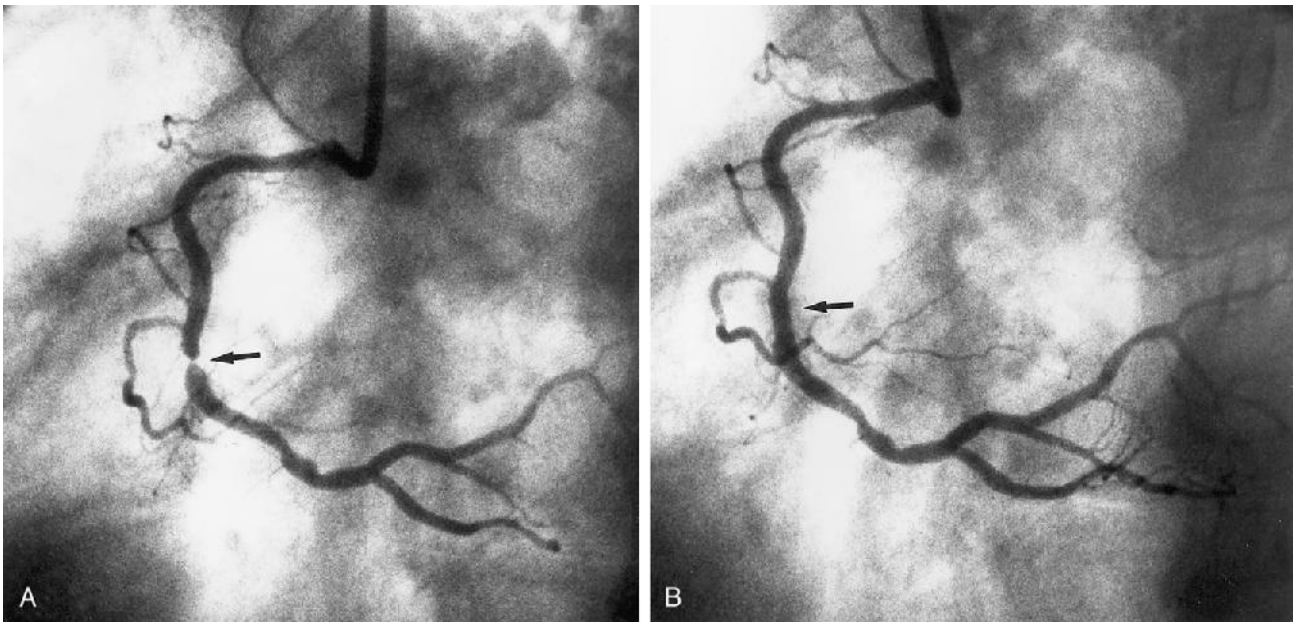

FIGURE 8-1 Angiograms of the right coronary artery. **A,** Discrete stenosis is observed in the middle segment of the artery *(arrow)*. **B,** The same artery is shown after successful balloon angioplasty of the stenosis and placement of an intracoronary stent *(arrow)*.