endothelial swelling that occludes capillaries and may limit the reperfusion of critically injured myocardium (called *no-reflow*). Although the clinical significance of myocardial reperfusion injury is debated, it has been estimated that up to 50% (or more) of the ultimate infarct size can be attributed to its effects.

Biochemical abnormalities (and their functional consequences) may also persist for days to weeks in reperfused myocytes. Such changes are thought to underlie a phenomenon referred to as *stunned myocardium,* a state of prolonged cardiac failure induced by short-term ischemia that usually recovers after several days. Myocardium that is subjected to chronic, sublethal ischemia may also enter into a state of lowered metabolism and function called *hibernation*. Subsequent revascularization (e.g., by CABG surgery, angioplasty, or stenting) often restores normal function to such hibernating myocardium.

Clinical Features. **MI is diagnosed by clinical symptoms, laboratory tests for the presence of myocardial proteins in the plasma, and characteristic electrocardiographic changes.** Patients with MI classically present with prolonged (more than 30 minutes) chest pain described as crushing, stabbing, or squeezing, associated with a rapid, weak pulse; profuse sweating (diaphoresis), and nausea and vomiting are common, and can suggest involvement of the posterior-inferior ventricle with secondary vagal stimulation. Dyspnea due to impaired contractility of the ischemic myocardium and the resultant pulmonary congestion and edema is a frequent symptom. However, in as many as 25% of patients the onset is entirely asymptomatic (e.g., in the setting of diabetic neuropathy) and the disease is discovered only by electrocardiographic changes or laboratory tests that show evidence of myocardial damage (see later).

The laboratory evaluation of MI is based on measuring the blood levels of proteins that leak out of irreversibly damaged myocytes; the most useful of these molecules are cardiac-specific troponins T and I (cTnT and cTnI), and the MB fraction of creatine kinase (CK-MB) (Fig. 12-17). The diagnosis of myocardial injury is established when blood levels of these cardiac biomarkers are elevated. The rate of appearance of these markers in the peripheral circulation depends on several factors, including their intracellular location and molecular weight, the blood flow and lymphatic drainage in the area of the infarct, and the rate of elimination of the marker from the blood.

The most sensitive and specific biomarkers of myocardial damage are cardiac-specific proteins, particularly cTnT and cTnI (proteins that regulate calcium-mediated contraction of cardiac and skeletal muscle). *Troponins I* and *T* are not normally detectable in the circulation. Following an MI, levels of both begin to rise at 3-12 hours; cTnT levels peak somewhere between 12-48 hours while cTnI levels are maximal at 24 hours. *Creatine kinase* is an enzyme expressed in brain, myocardium, and skeletal muscle; it is a dimer composed of two isoforms designated "M" and "B." While MM homodimers are found predominantly in cardiac and skeletal muscle, and BB homodimers in brain, lung, and many other tissues, MB heterodimers are principally localized to cardiac muscle (with considerably lesser amounts found in skeletal muscle). Thus, the MB form of creatine kinase (CK-MB) is sensitive but not specific, since it can also be elevated after skeletal muscle injury. CK-MB begins to rise within 3 to 12 hours of the onset of MI, peaks at about 24 hours, and returns to normal within approximately 48 to 72 hours.

To summarize:

- Time to elevation of CKMB, cTnT and cTnI is 3 to 12 hrs
- CK-MB and cTnI peak at 24 hours
- CK-MB returns to normal in 48-72 hrs, cTnI in 5-10 days, and cTnT in 5 to 14 days

Consequences and Complications of Myocardial Infarction. Extraordinary progress has been made in the treatment of patients with acute MI. Concurrent with the decrease in the overall mortality of IHD since the 1960s,

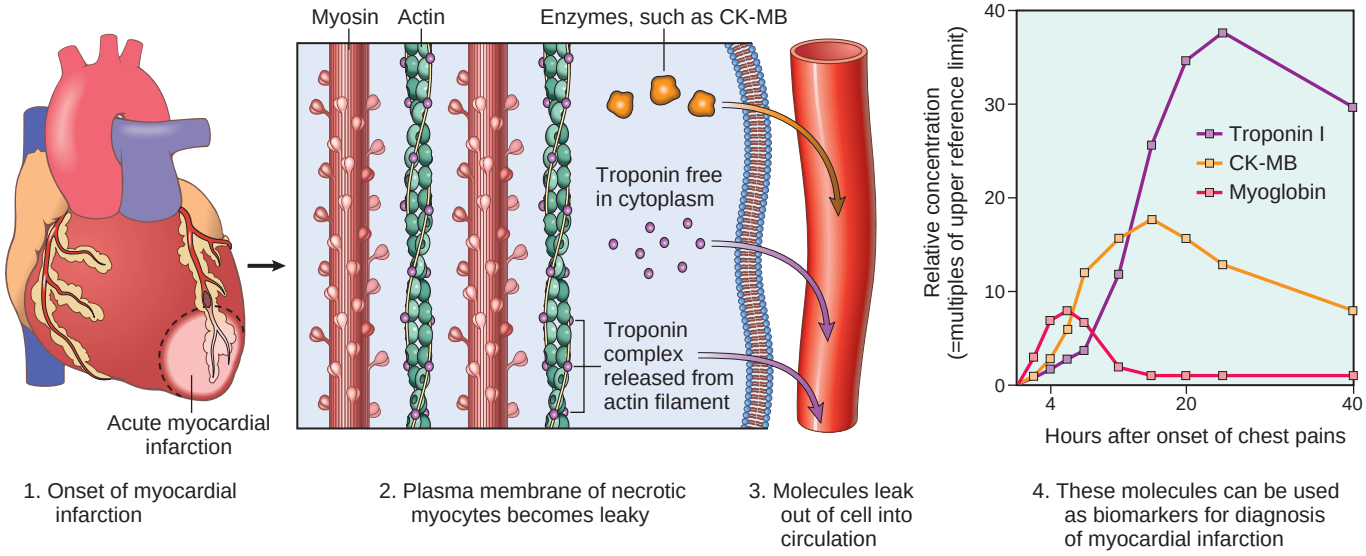

Figure 12-17 Release of myocyte proteins in myocardial infarction. Some of these proteins, for example, troponin I or troponin T, and creatine kinase, MB fraction (CK-MB) are routinely used as diagnostic biomarkers.