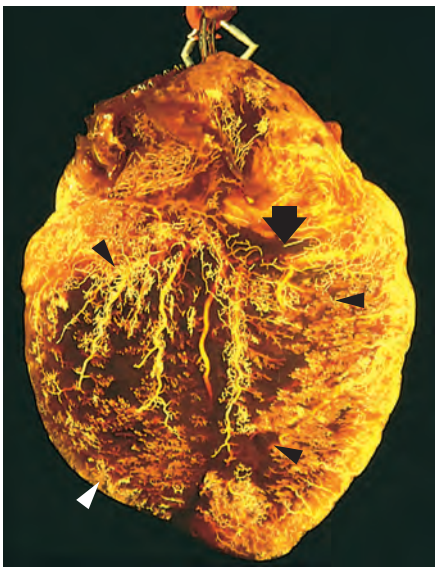

**Figure 12-9** Postmortem angiogram showing the posterior aspect of the heart of a patient who died during the evolution of acute myocardial infarction, demonstrating total occlusion of the distal right coronary artery by an acute thrombus *(arrow)* and a large zone of myocardial hypoperfusion involving the posterior left and right ventricles, as indicated by *arrowheads*, and having almost absent filling of capillaries. The heart has been fixed by coronary arterial perfusion with glutaraldehyde and cleared with methyl salicylate, followed by intracoronary injection of silicone polymer (yellow). (Photograph courtesy Lewis L. Lainey. Reproduced with permission from Schoen FJ: Interventional and Surgical Cardiovascular Pathology: Clinical Correlations and Basic Principles. Philadelphia, WB Saunders, 1989, p. 60.)

permanent myocardial injury provides the rationale for rapid diagnosis in acute MI—to permit early coronary intervention to establish reperfusion and salvage as much "at risk" myocardium as possible.

The earliest detectable feature of myocyte necrosis is the disruption of the integrity of the sarcolemmal membrane, allowing intracellular macromolecules to leak out of necrotic cells into the cardiac interstitium and ultimately into the microvasculature and lymphatics. This escape of intracellular myocardial proteins into the circulation forms the basis for blood tests that can sensitively detect irreversible myocyte damage, and are important for managing MI (see later). With prolonged severe ischemia, injury to the microvasculature follows injury to the cardiac myocytes. The temporal progression of these events is summarized in Table 12-4.

**Table 12-4** Approximate Time of Onset of Key Events in Ischemic Cardiac Myocytes

| Feature | Time |
|---|---|
| Onset of ATP depletion | Seconds |
| Loss of contractility | <2 min |
| ATP reduced | |
| to 50% of normal | 10 min |
| to 10% of normal | 40 min |
| Irreversible cell injury | 20-40 min |
| Microvascular injury | >1 hr |

ATP, Adenosine triphosphate.

The progression of ischemic necrosis in the myocardium is summarized in Figure 12-11. Due to the myocardial perfusion pattern from epicardium to endocardium, ischemia is most pronounced in the subendocardium; thus, irreversible injury of ischemic myocytes occurs first in the subendocardial zone. With more extended ischemia, a *wavefront* of cell death moves through the myocardium to encompass progressively more of the transmural thickness and breadth of the ischemic zone. The precise location, size, and specific morphologic features of an acute MI depend on:

- The location, severity, and rate of development of coronary obstructions due to atherosclerosis and thromboses
- The size of the vascular bed perfused by the obstructed vessels
- The duration of the occlusion
- The metabolic and oxygen needs of the myocardium at risk

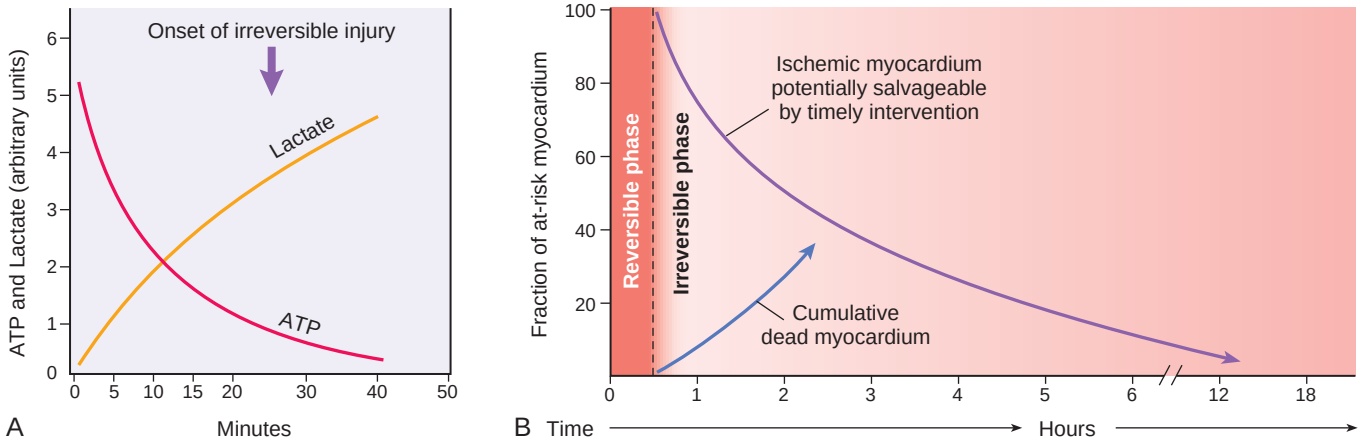


**Figure 12-10** Temporal sequence of early biochemical findings and progression of necrosis after onset of severe myocardial ischemia. **A,** Early changes include loss of adenosine triphosphate (ATP) and accumulation of lactate. **B,** For approximately 30 minutes after the onset of even the most severe ischemia, myocardial injury is potentially reversible. Thereafter, progressive loss of viability occurs that is complete by 6 to 12 hours. The benefits of reperfusion are greatest when it is achieved early, and are progressively lost when reperfusion is delayed. (Modified with permission from Antman E: Acute myocardial infarction. In Braunwald E, et al [eds]: Heart Disease: A Textbook of Cardiovascular Medicine, 6th ed. Philadelphia, WB Saunders, 2001, pp 1114-1231.)