Table 2-1 Cellular Responses to Injury

Nature of Injurious Stimulus	Cellular Response
Altered physiologic stimuli; some nonlethal injurious stimuli	Cellular adaptations
Increased demand, increased stimulation (e.g., by growth factors, hormones)	Hyperplasia, hypertrophy
Decreased nutrients, decreased stimulation	Atrophy
Chronic irritation (physical or chemical)	Metaplasia
Reduced oxygen supply; chemical injury; microbial infection	Cell injury
Acute and transient	Acute reversible injury Cellular swelling fatty change
Progressive and severe (including DNA damage)	Irreversible injury → cell death Necrosis Apoptosis
Metabolic alterations, genetic or acquired; chronic injury	Intracellular accumulations; calcification
Cumulative sublethal injury over long life span	Cellular aging

in physiologic states (e.g., pregnancy) and some pathologic stimuli, during which new but altered steady states are achieved, allowing the cell to survive and continue to function (Fig. 2-1 and Table 2-1). The adaptive response may consist of an increase in the size of cells (hypertrophy) and functional activity, an increase in their number (hyperplasia), a decrease in the size and metabolic activity of cells (atrophy), or a change in the phenotype of cells (metaplasia). When the stress is eliminated the cell can recover to its original state without having suffered any harmful consequences.

If the limits of adaptive responses are exceeded or if cells are exposed to injurious agents or stress, deprived of essential nutrients, or become compromised by mutations that affect essential cellular constituents, a sequence of events follows that is termed cell injury (Fig. 2-1). Cell injury is *reversible* up to a certain point, but if the stimulus persists or is severe enough from the beginning, the cell suffers *irreversible injury* and ultimately undergoes *cell death*. *Adaptation, reversible injury*, and *cell death* may be stages of progressive impairment following different types of insults. For instance, in response to increased hemodynamic loads, the heart muscle becomes enlarged, a form of adaptation, and can then become injured. If the blood supply to the myocardium is compromised or inadequate, the muscle first suffers reversible injury, manifested by certain cytoplasmic changes (described later). Eventually, the cells suffer irreversible injury and die (Fig. 2-2).

Cell death, the end result of progressive cell injury, is one of the most crucial events in the evolution of disease in any tissue or organ. It results from diverse causes, including ischemia (reduced blood flow), infection, and toxins. Cell death is also a normal and essential process in embryogenesis, the development of organs, and the maintenance of

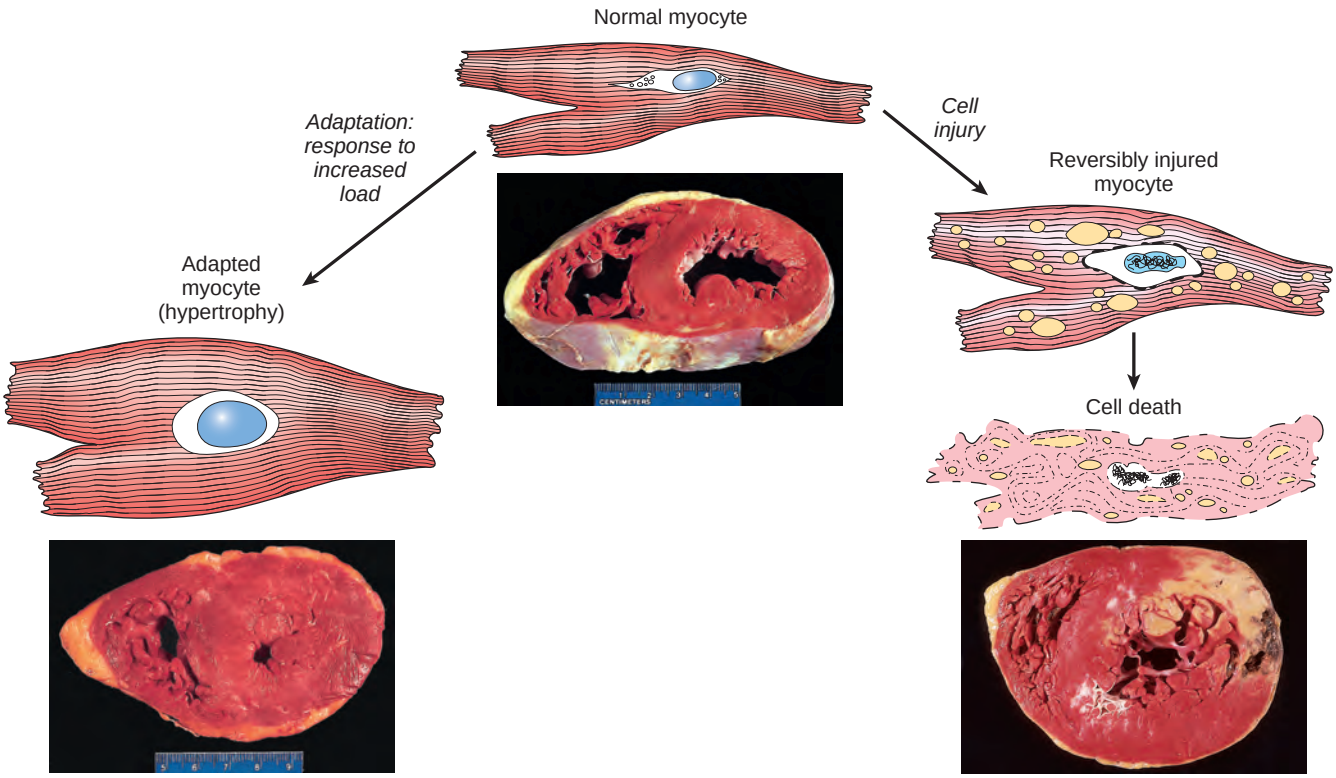

Figure 2-2 The relationship between normal, adapted, reversibly injured, and dead myocardial cells. All three transverse sections of the heart have been stained with triphenyltetrazolium chloride, an enzyme substrate that colors viable myocardium magenta. The cellular adaptation shown here is myocardial hypertrophy *(lower left)*, caused by increased blood pressure requiring greater mechanical effort by myocardial cells. This adaptation leads to thickening of the left ventricular wall (compare with the normal heart). In reversibly injured myocardium (illustrated schematically, *right*), there are functional alterations, usually without any gross or microscopic changes but sometimes with cytoplasmic changes such as cellular swelling and fat accumulation. In the specimen showing necrosis, a form of cell death *(lower right)*, the light area in the posterolateral left ventricle represents an acute myocardial infarction caused by reduced blood flow (ischemia).