Acute Renal Failure

**FIGURE 14-37**
Potential causes of apoptosis in acute renal failure (ARF). The same cytotoxic stimuli that induce necrosis cause apoptosis. The mechanism of cell death induced by a specific injury depends in large part on the severity of the injury. Because most cells require constant external signals, called survival signals, to remain viable, the loss of these survival signals can trigger apoptosis. In ARF, a deficiency of growth factors and loss of cell-substrate adhesion are potential causes of apoptosis. The death pathways induced by engagement of tumour necrosis factor (TNF) with the TNF receptor or Fas with its receptor (Fas ligand) are well known causes of apoptosis in immune cells. TNF and Fas can also induce apoptosis in epithelial cells and may contribute to cell death in ARF.

**FIGURE 14-38**
Apoptosis is mediated by a highly coordinated and genetically programmed pathway. The response to an apoptotic stimulus can be divided into a commitment and execution phases. During the commitment phase the balance between a number of proapoptotic and antiapoptotic mechanisms determine whether the cell survives or dies by apoptosis. The BCL-2 family of proteins consists of at least 12 isoforms, which play important roles in this commitment phase. Some of the BCL-2 family of proteins (eg, BCL-2 and BCL-XL) protect cells from apoptosis whereas other members of the same family (eg, BAD and Bax) serve proapoptotic functions. Apoptosis is executed by a final common pathway mediated by a class of cysteine proteases-caspases. Caspases are proteolytic enzymes present in cells in an inactive form. Once cells are committed to undergo apoptosis, these caspases are activated. Some caspases activate other caspases in a hierarchical fashion resulting in a cascade of caspase activation. Eventually, caspases that target specific substrates within the cell are activated. Some substrates for caspases that have been identified include nuclear membrane components (such as lamin), cytoskeletal elements (such as actin and fodrin) and DNA repair enzymes and transcription elements. The proteolysis of this diverse array of substrates in the cell occurs in a predestined fashion and is responsible for the characteristic morphologic features of apoptosis.
Pathophysiology of Ischemic Acute Renal Failure


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