

Apoptosis – is it good or bad?

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The most widely used classification of mammalian cell death recognizes two types: apoptosis and necrosis. Autophagy, which has been proposed as a third mode of cell death allows a starving cell, or in situations when cell is deprived of growth factors, to survive. Apoptosis, autophagy and necrosis, a particular mode of cell death may predominate, depending of the injury and the type of cell. [1] One very important characteristic of all multicellular organisms is apoptosis, the controlled death of cells. In necrosis, early loss of integrity of the plasma membrane resultant with swelling of the cell and its organelles. A key morphologic feature of apoptosis is collapses of cell and its subcellular components.[2] The distinction between apoptosis and necrosis is due in part to differences in how the plasma membrane participates in these processes. In apoptosis, plasma membrane integrity persists until late in the process. In necrosis, early loss of integrity of the plasma membrane allows an influx of extracellular ions and fluid, with resultant swelling of the cell and its organelles. During that time, on the inside of cell there occurs the cleavage of cytoskeletal proteins by aspartate specific proteases, which thereby collapses subcellular components. Other characteristic features are chromatin condensation, nuclear fragmentation and the formation of plasma membrane blebs. The type and intensity of noxious signals, ATP concentration, cell type, and other factors determine how cell death occurs. Acute myocardial ischemia induces necrosis (because the ischemia precipitates rapid and profound decreases of ATP), whereas chronic congestive heart failure induces apoptosis (with more modest and chronic decreases of ATP). The blockade of a particular pathway of cell death may not prevent the destruction of the cell but may instead recruit an alternative path: antiapoptotic caspase inhibitors cause hyperacute necrosis of hepatocytes and kidney tubular cells induced by TNF- α . The over expression of antiapoptotic proteins may allow injured cells to survive, and autophagy may assist by providing critical metabolites. Apoptotic cells induce anergy or an immunosuppressive phenotype, whereas necrotic cells augment inflammation, in part by binding the receptor C-type lectin domain family 9 on dendritic cells.

Clinical implications of apoptosis are consist in more than 50% of neoplasm's that have defects in the apoptotic machinery mutations in the tumor-suppressor gene *TP53*, that is called the "guardian of the genome," initiates apoptosis in response to DNA damage induced by radiation, chemical agents, oxidative stress, and other agents.[3] Abnormalities in apoptosis can increase susceptibility to autoimmune diseases.[4] There is growing evidence that neuronal apoptosis plays a key role in neonatal brain disorders.[5] Hepatocytes are particularly prone to apoptosis in response to various types of stress, including infections.[6] Necrosis predominates in ischemic injury, but often there are apoptotic cells in the hypoxic penumbra in myocardial infarction and stroke and in globally hypoxic zones after reperfusion injury. Sepsis is perhaps the most remarkable clinical setting in which apoptosis occurs. Massive apoptosis of immune effectors' cells and gastrointestinal epithelial cells develops in patients with sepsis.[7] The profound loss of immune effectors' cells in sepsis inhibits the ability of the immune system to eradicate the primary infection and renders the patient susceptible to nosocomial infections. Finally, why apoptosis is good? Because without apoptosis, 2 tons of bone marrow and lymph nodes and a 16-km intestine would probably accumulate in a human by the age of 80.[8]

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