

1.2 Differences between necrosis and apoptosis

There are many observable morphological (Figure 1, Table 1) and biochemical differences (Table 1) between necrosis and apoptosis².

Necrosis occurs when cells are exposed to extreme variance from physiological conditions (e.g., hypothermia, hypoxia) which may result in damage to the plasma membrane. Under physiological conditions direct damage to the plasma membrane is evoked by agents like complement and lytic viruses.

Necrosis begins with an impairment of the cell's ability to maintain homeostasis, leading to an influx of water and extracellular ions. Intracellular organelles, most notably the mitochondria, and the entire cell swell and rupture (cell lysis). Due to the ultimate breakdown of the plasma membrane, the cytoplasmic contents including lysosomal enzymes are released into the extracellular fluid. Therefore, *in vivo*, necrotic cell death is often associated with extensive tissue damage resulting in an intense inflammatory response⁵.

Apoptosis, in contrast, is a mode of cell death that occurs under normal physiological conditions and the cell is an active participant in its own demise ("cellular suicide"). It is most often found during normal cell turnover and tissue homeostasis, embryogenesis, induction and maintenance of immune tolerance, development of the nervous system and endocrine-dependent tissue atrophy.

Cells undergoing apoptosis show characteristic morphological and biochemical features⁶. These features include chromatin aggregation, nuclear and cytoplasmic condensation, partition of cytoplasm and nucleus into membrane bound-vesicles (apoptotic bodies) which contain ribosomes, morphologically intact mitochondria and nuclear material. *In vivo*, these apoptotic bodies are rapidly recognized and phagocytized by either macrophages or adjacent epithelial cells⁷. Due to this efficient mechanism for the removal of apoptotic cells *in vivo* no inflammatory response is elicited. *In vitro*, the apoptotic bodies as well as the remaining cell fragments ultimately swell and finally lyse. This terminal phase of *in vitro* cell death has been termed "secondary necrosis" (Figure 1).



Necrosis	Apoptosis
<p>Morphological features</p> <ul style="list-style-type: none"> ● Loss of membrane integrity ● Begins with swelling of cytoplasm and mitochondria ● Ends with total cell lysis ● No vesicle formation, complete lysis ● Disintegration (swelling) of organelles 	<ul style="list-style-type: none"> ● Membrane blebbing, but no loss of integrity ● Aggregation of chromatin at the nuclear membrane ● Begins with shrinking of cytoplasm and condensation of nucleus ● Ends with fragmentation of cell into smaller bodies ● Formation of membrane bound vesicles (apoptotic bodies) ● Mitochondria become leaky due to pore formation involving proteins of the bcl-2 family.
<p>Biochemical features</p> <ul style="list-style-type: none"> ● Loss of regulation of ion homeostasis ● No energy requirement (passive process, also occurs at 4°C) ● Random digestion of DNA (smear of DNA after agarose gel electrophoresis) ● Postlytic DNA fragmentation (= late event of death) 	<ul style="list-style-type: none"> ● Tightly regulated process involving activation and enzymatic steps ● Energy (ATP)-dependent (active process, does not occur at 4°C) ● Non-random mono- and oligonucleosomal length fragmentation of DNA (Ladder pattern after agarose gel electrophoresis) ● Prelytic DNA fragmentation ● Release of various factors (cytochrome C, AIF) into cytoplasm by mitochondria ● Activation of caspase cascade ● Alterations in membrane asymmetry (i.e., translocation of phosphatidylserine from the cytoplasmic to the extracellular side of the membrane)
<p>Physiological significance</p> <ul style="list-style-type: none"> ● Affects groups of contiguous cells ● Evoked by non-physiological disturbances (complement attack, lytic viruses, hypothermia, hypoxia, ischemia, metabolic poisons) ● Phagocytosis by macrophages ● Significant inflammatory response 	<ul style="list-style-type: none"> ● Affects individual cells ● Induced by physiological stimuli (lack of growth factors, changes in hormonal environment) ● Phagocytosis by adjacent cells or macrophages ● No inflammatory response

▲ Table 1: Differential features and significance of necrosis and apoptosis.

