Apoptosis versus Necrosis

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Introduction

This article examines the different characteristics between apoptosis and necrosis, two morphologically distinct manifestations of cell death. Necrosis is non-genetic and triggered by external forces, such as trauma or infection; whereas is apoptosis is a genetically programmed type of cell death. Understanding this difference is not straightforward, yet interpreting the difference is essential for medics in order to deliver the optimal treatment regime. Apoptosis rarely requires medical intervention; however, necrosis always requires medical treatment. Untreated necrosis is dangerous and can lead to death, and it is therefore of considerable medical concern.

Comparing Apoptosis and Necrosis

Necrosis describes the process of cell death, a phenomenon that occurs in a certain locale within the living organism. Necrosis can occur accidentally with the outcome being disorganized and destructive, affecting one or more cells. The process occurs due to various external factors like infection, toxins, or trauma. Biologically these are manifest in a haphazard way [1]. From this perspective, changes that could induce necrosis in a given territory at the level of a living organism are primarily connected with the occurrence of injuries. Severe cell damage can occur suddenly; such as sometimes being caused by ischemia or hyperthermia following a physical and chemical trauma. In this context necrosis can be considered as a type of cellular metabolic collapse, something that occurs when cells can no longer maintain ion homeostasis (the asymmetric concentrations of the major inorganic cations and anions is a major function of cellular membranes) [2].

Necrosis takes place following several stages that occur in succession. In the first stage, pre-necrosis, this is characterized dystrophic changes by reversible cell damage. In the next stage, termed necrobiosis, this is characterized by dystrophic to irreversible cell damage; here the cells are "dying" during which catabolic processes prevail compared with the anabolic. The last and final stage, called necrosis itself, is characterized by disruption of vital cell as a biological system [3].

Stage IV is referred post-necrosis, and this is characterized by the disintegration of the autolysis and cell processes occurring by the action of lysosomal enzymes and the generation of its own inflammatory response. In terms of biomolecular alterations, necrosis characteristically occurs by inflating the cells and organelles, including expansion of early changes in conformation mitochondria and also in their functions. In this context necrosis usually occurs by cell plasmolysis. This occurs due to excessive water penetration into the cell, leading to plasma membrane lysis. Necrosis begins with changes in the cytoplasm and mitochondria swelling and ends with lysis of cells together with total disintegration of organelles [4].

Studies have shown that cellular changes occur as the adenosine triphosphate (ATP) levels are depleted and transmembrane ion gradient dissipates [5]. The cell membrane can become a major site of disruption, with membranes losing their ability to control osmotic pressure; as a result of these processes, the cell can swell and crack.
The damage to internal membranes can allow for the release of lysosomal enzymes, which, in turn, release the cell contents into the extracellular space. This causes a nonspecific inflammatory response. Necrosis is also characterized by random digestion of DNA with DNA fragmentation after lysis.

During necrosis, cell nuclei undergo changes termed karyopyknosis, this means nuclei become pyknotic (the irreversible condensation of chromatin in the nucleus of a cell) and become fragmented into blocks. This is followed by changes termed karyolysis, which is the complete dissolution of the chromatin of a dying cell due to the enzymatic degradation by endonucleases.

Hence it can be concluded that necrosis is defined as an unplanned process of cell death that is triggered by factors not under the control of the body. Contrary to necrosis, which is programmed cell death and genetically independent, apoptosis is a genetically programmed cell death where certain biochemical events lead to characteristic cell morphology changes and death. Such programmed cell death process can be activated by intracellular genetically defined development program and through the extracellular endogenous proteins or cytokines; or, alternatively, hormones with xenobiotic components, radiation, hypoxia, or oxidative stress.

The most important elements of apoptosis are the activities of caspases (the family of protease enzymes that play an essential role in programmed cell death); here apoptosis morphological expression is represented by apoptotic bodies. Apoptosis occurs in two circumstances, namely in normal tissues where cells responsible for deletion and certain pathologies. In contrast pathological necrosis, apoptosis is always the consequence of a major cellular damage [1]. Early in the process there is a sustained increase in cytosolic ionized calcium levels in many cell types [2].

Cross-linking occurs in the cytoplasm protein, a process that takes place by the action transglutaminases. In this process, cytoskeletal filament aggregation also occurs in parallel formations. Moreover, the endoplasmic reticulum expands and merges with the plasma membrane, creating fusion craters at sacciform (‘bag’ or ‘sac’) shape [6]. Further with apoptosis, the cell membrane specific modifications that occur consist of swelling, to a greater extent compared to the types of changes that occur with necrosis [4].

Hence apoptosis refers to morphological changes that occur during the process that defines cell death, including specific changes, other than those appearing in necrosis. In this sense, apoptosis occurs in scattered individual cells and groups of cells that are not adjacent, unlike what typically occurs happens with necrosis [7].

There are several possible mechanisms for the recognition of apoptotic cells by phagocytes, with cells displayed as apoptotic target statuses. Although apoptosis is a process that differs to necrosis, representing the physiological pathway of cell death, apoptosis can also be caused by pathological stimuli where apoptosis is develops the necessary energy in the form of ATP [8]. Unlike with necrosis, apoptosis cannot communicate with the series of metabolic events that invariably occur during the development of the process. The ATP issue is of importance, since classic apoptotic triggers can be changed from apoptosis to necrosis, when cells are pre-empted of ATP.

With apoptosis, from the biochemical point of view, in the cell the reduction of the synthesis of RNA and protein is followed by degradation [5]. Initially it was thought that the transition from normal to apoptotic is a fast process. However, contraction that cannot be observed in an intermediate state using flow cytometry and cell sorting can lead to observations on the order discerning apoptotic events. Further, intimacy events of apoptosis have been studied using the technique PFGE (pulsed field gradient gel electrophoresis) [3].

From another perspective, a considerable number of mutations affecting specific stages of the process of apoptosis have been identified. Further, corresponding genes have been identified for specific mutations, and these are ordered in a genetic map. On this basis, the events of apoptosis have been extensively studied. Research results have shown that the genes that make up the map of apoptosis specific mutations are involved in the decision to enter the programmed cell death pathway. The results of these studies reveal that genes ced-3 and ced-4 are required for all forms of apoptosis and they are involved in the apoptotic pathways that encode end-effectors [9].

The cell death abnormality gene 9 (Ced-9) is useful for suppressing (or inhibiting) apoptosis in cells programmed to survive; from this point of view the gene is considered as a key regulatory gene. It seems that the genes mentioned, either in whole or in part, are involved in encoding a protein homologous to Bel-2 family of human system. Hence it is believed that the expression of Bel-2 may be involved in inhibiting apoptosis in certain species of primate, or even where a partial loss of function could be substituted by Ced-9. This would indicate that at least some components of the apoptotic pathway are conserved
in evolution.

Other research results suggest that mutations occur in six genes affecting apoptotic bodies by embedding non-professional neighboring cells. Here it has been observed that intracellular proteins Ced-2, Ced-5 and Ced-10 signal in a manner comparable to their counterparts in mammalian Crkll, DOCK 180, and cancer, are involved in mediating in the reorganization and in included cell of cytoskeleton extension. Ced-7, homologous ABC-1 activates both cell and in the dying included cell, possibly in the transmembrane transport of lipids. Data also suggests the presence of Ced-1 analog scavenger receptors in the mammalian system; with these, Ced-7 and Ced-1 promote, and probably embed, interacting protein Ced-6 signaling adapters.

Examples of Necrosis and Apoptosis

Medical doctors need to understand the difference between necrosis and apoptosis because of the different medical responses required. When cells die by apoptosis, inflammation does not occur; with necrosis, the cell membrane is ruptured and the released cell content causes a significant inflammatory response.

Hence understanding the differences between necrosis and apoptosis can assist the medic in assessing different medical conditions. Medical researchers also need to understand the differences, since this contributes to research that seeks to ensure human body cells do not trigger cell death too soon or too late. Such research can contribute to our understanding of controlling diseases.

Conditions relating to necrosis can be divided into external and internal factors. Some external cases include mechanical trauma, such as physical damage to the body that triggers cell breakdown. One example is from the bites of certain spiders. A second external factor arises from damage to blood vessels (affecting blood supply to tissues); and ischemia [10]. In addition, variations with heat, such as extremely high or low temperature, can cause thermal disruption, which can also trigger necrosis. An example is with the result of frostbite. Internal factors leading to necrosis include trophoneurotic disorders or injury and paralysis of nerve cells.

With apoptosis, as discussed earlier, this is a highly regulated and controlled process. Normal apoptosis is a part of life; cells that die typically do so neatly, without any adverse impact on neighboring cells. Classic example of apoptosis is during embryogenesis, when skin cells forming a web between fingers are destroyed. This process contrasts with acute injury, where cells typically swell and burst, spilling their contents and causing a damaging inflammatory response, as with cell necrosis.

However, apoptosis can sometimes be advanced in the body for multiple reasons. One example is with cancer. Here the typical functioning of cellular pathways becomes disrupted to the degree this impairs the ability of a cell to undergo normal apoptosis. Hence the cell continues beyond its typical life and it can thus replicate and pass on its faulty machinery to its progeny [11]. This enhances the possibility of cells becoming cancerous. A second example arises from viral infections, such as the Human Immunodeficiency Virus or other viruses, such as canine distemper virus or the oropouche virus.

Summary

This article has considered the differences between necrosis and apoptosis, for the purposes of increasing medical understanding. Necrosis occurs when cells are exposed to a variance away from ideal physiological conditions, leading to damage to the cell plasma membrane. As the membrane is damaged, cytoplasmic contents, like lysosomal enzymes, can be released into the extracellular fluid. In contrast, apoptosis is a mode of cell death that happens under normal physiological conditions, being part of normal cell turnover.

In drawing out these cell-death differences in this paper, more recent research has been highlighted. Assessing these two phenomena is of importance given that virtually all cell deaths can be classified dichotomously as either apoptosis or necrosis. This aids the medical doctor in making the correct decision in relation to a patient.

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References


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