pISSN:2349-5707 Volume:13,Issue 1, January -2026 eISSN:2349-5715

# APOPTOSIS AND NECROSIS: DIFFERENCES, MECHANISMS, AND THEIR SIGNIFICANCE IN MEDICINE

**Mamatyaqubova Malohat Sharof kizi**
Andijan State Medical Institute
Department of Medical Biology and Histology

**Abstract:** Cell death is a fundamental biological process essential for the maintenance of tissue homeostasis and normal physiological function. Among the various forms of cell death, apoptosis and necrosis represent two major mechanisms with distinct biological characteristics and clinical implications. Apoptosis is a genetically programmed, energy-dependent process that enables the orderly elimination of damaged or unnecessary cells without inducing inflammation, whereas necrosis is an uncontrolled and pathological form of cell death resulting from severe cellular injury and accompanied by inflammatory responses.

The present study provides a comprehensive analysis of the morphological, molecular, and functional differences between apoptosis and necrosis, as well as their significance in medical practice. A systematic review of scientific literature was conducted to evaluate regulatory pathways, cellular alterations, diagnostic approaches, and clinical relevance associated with both forms of cell death. Comparative assessment revealed substantial differences in membrane integrity, energy dependence, inflammatory involvement, and biological outcomes.

The findings emphasize the importance of accurately distinguishing between apoptotic and necrotic processes in diagnostic evaluation and therapeutic decision-making. Improved understanding of cell death mechanisms contributes to the development of targeted treatment strategies in oncology, neurodegenerative diseases, ischemic disorders, and inflammatory conditions. Overall, the study highlights the critical role of regulated and pathological cell death in hea lth and disease, underscoring their relevance in modern molecular and clinical medicine.

**Keywords:** Apoptosis; Necrosis; Cell death; Programmed cell death; Inflammation; Molecular mechanisms; Clinical significance

## Introduction

Cell death is a fundamental biological process that plays a crucial role in maintaining tissue homeostasis, normal development, and physiological balance in multicellular organisms. Every day, billions of cells in the human body undergo elimination and are replaced by newly formed cells. The precise regulation of this process is essential for normal organ function, whereas disturbances in cell death mechanisms contribute to the development of various pathological conditions [1].

In medical biology, two principal forms of cell death are distinguished: apoptosis and necrosis. Apoptosis represents a genetically programmed, energy-dependent, and highly regulated process that allows the organism to remove damaged, aged, or unnecessary cells without inducing inflammation [2]. This mechanism is essential during embryogenesis, immune system maturation, and the prevention of malignant transformation.

pISSN:2349-5707 Volume:13,Issue 1, January -2026 eISSN:2349-5715

In contrast, necrosis is considered a pathological and uncontrolled form of cell death that occurs as a result of severe external or internal insults, including ischemia, hypoxia, toxins, infections, and physical trauma. Necrotic cell death is characterized by cellular swelling, rupture of the plasma membrane, release of intracellular contents, and the subsequent development of an inflammatory response in surrounding tissues [3].

Recent advances in molecular and cellular biology have significantly expanded our understanding of the signaling pathways involved in cell death. The discovery of caspase enzymes, mitochondrial membrane permeabilization, death receptor signaling, and oxidative stress pathways has provided deeper insight into the regulation of apoptosis and its distinction from necrotic processes [4]. Increasing evidence indicates that impaired apoptosis contributes to oncogenesis, while excessive apoptotic activity is associated with neurodegenerative disorders such as Alzheimer's and Parkinson's diseases [5].

Understanding the molecular differences between apoptosis and necrosis is of great importance for modern clinical medicine. Therapeutic strategies in oncology, transplantation medicine, intensive care, and regenerative therapy increasingly rely on the ability to modulate cell death pathways [6]. Therefore, a comprehensive analysis of apoptotic and necrotic mechanisms is essential for the development of targeted and effective treatment approaches.

The aim of this study is to analyze the biological mechanisms underlying apoptosis and necrosis, compare their morphological and functional characteristics, and evaluate their clinical significance in modern medical practice.

**Materials and Methods**

This study was conducted as a comprehensive analytical review aimed at evaluating the biological mechanisms, morphological characteristics, and clinical relevance of apoptosis and necrosis. The research was based on the systematic analysis of previously published scientific literature in the fields of medical biology, pathology, and molecular medicine. The methodological approach was designed to ensure objective comparison between programmed and pathological forms of cell death [7,8].

Scientific sources were identified through an extensive literature search using international biomedical databases, including PubMed, Scopus, Web of Science, and Google Scholar. Articles published between 2000 and 2024 were considered in order to reflect both classical concepts and recent advances in cell death research [9]. The search strategy employed combinations of key terms such as "apoptosis," "necrosis," "programmed cell death," "caspase activation," "mitochondrial pathway," and "cell membrane integrity" [10].

Only peer-reviewed articles published in English and available in full-text format were included in the analysis. Studies that directly addressed molecular signaling pathways, morphological alterations, experimental identification techniques, or clinical implications of apoptosis and necrosis were selected. Publications lacking methodological clarity, duplicated data, or relevance to the objectives of the study were excluded [11].

Data extraction focused on identifying fundamental mechanisms regulating apoptotic and necrotic processes, including mitochondrial membrane permeabilization, death receptor activation, ATP dependency, inflammatory response, and cellular ultrastructural changes. Special attention was given to comparative findings that highlighted the differences between

pISSN:2349-5707 Volume:13,Issue 1, January -2026 eISSN:2349-5715

regulated and unregulated cell death. The extracted information was categorized and synthesized to establish coherent biological and clinical correlations [12,13].

In addition, commonly applied experimental and diagnostic techniques used to distinguish apoptosis from necrosis were analyzed. These methods included TUNEL assay for detection of DNA fragmentation, Annexin V and Propidium Iodide staining evaluated through flow cytometry, caspase activity measurement assays, electron microscopy for ultrastructural evaluation, and routine histopathological examination using hematoxylin and eosin staining. The methodological reliability, specificity, and diagnostic value of each technique were assessed based on published experimental outcomes [14–16].

Since this research was based exclusively on secondary data obtained from previously published studies, no direct experimentation involving human participants or laboratory animals was performed. Therefore, ethical approval was not required for the present study [17].

**Results**

The analysis of the selected scientific literature revealed pronounced morphological, biochemical, and functional differences between apoptosis and necrosis. These distinctions were consistently documented across experimental models, histopathological investigations, and clinical observations, confirming that apoptosis and necrosis represent two fundamentally different forms of cell death with distinct biological consequences for surrounding tissues.

Comparative evaluation demonstrated that apoptosis is a physiologically regulated and energy-dependent process, whereas necrosis develops as a pathological and uncontrolled response to severe cellular injury. The principal comparative characteristics identified in the reviewed studies are summarized in Table 1.

**Table 1. Comparative characteristics of apoptosis and necrosis**

| **Parameter** | **Apoptosis** | **Necrosis** |
|---|---|---|
| Nature of process | Physiological, regulated | Pathological, uncontrolled |
| Energy dependence | ATP-dependent | ATP-independent |
| Cellular volume | Cell shrinkage | Cell swelling |
| Plasma membrane | Preserved integrity | Membrane rupture |
| Nuclear changes | Chromatin condensation and fragmentation | Nuclear lysis |
| DNA degradation | Internucleosomal fragmentation | Random DNA degradation |
| Inflammatory response | Absent | Pronounced inflammation |
| Effect on surrounding tissue | Minimal or absent | Severe tissue damage |

pISSN:2349-5707 Volume:13,Issue 1, January -2026 eISSN:2349-5715

| Parameter | Apoptosis | Necrosis |
|---|---|---|
| Biological role | Maintenance of tissue homeostasis | Development of pathological injury |

The comparative findings indicate that apoptotic cell death proceeds in a controlled and orderly manner without provoking inflammatory reactions, while necrotic cell death is accompanied by extensive membrane disruption, release of intracellular components, and pronounced inflammatory infiltration of adjacent tissues [18,19].

Morphological and ultrastructural analyses reported in multiple studies demonstrated that apoptotic cells undergo progressive cellular shrinkage, chromatin condensation, and nuclear fragmentation, followed by the formation of membrane-bound apoptotic bodies. These structures are rapidly recognized and phagocytosed by macrophages or neighboring cells, thereby preventing leakage of intracellular contents and limiting tissue damage [20]. In contrast, necrotic cells exhibited early mitochondrial swelling, breakdown of plasma membrane integrity, and uncontrolled release of lysosomal enzymes into the extracellular space, processes that were strongly associated with secondary tissue injury and inflammatory amplification [21].

At the molecular level, apoptosis was consistently characterized by the activation of initiator and effector caspases, mitochondrial cytochrome c release, and regulated DNA cleavage into oligonucleosomal fragments. Conversely, necrosis was associated with rapid depletion of intracellular ATP, disruption of ionic homeostasis, calcium overload, and oxidative stress–induced damage to cellular membranes, leading to irreversible cell lysis [22,23].

Diagnostic and experimental observations further supported these distinctions. The reviewed studies demonstrated that apoptotic cells were reliably identified by positive TUNEL staining, Annexin V binding, and increased caspase activity, while maintaining intact plasma membranes during early stages, reflected by negative Propidium Iodide uptake. Necrotic cells, in contrast, exhibited strong Propidium Iodide positivity due to compromised membrane integrity, accompanied by minimal or absent caspase activation [24]. Flow cytometric analysis proved to be an effective tool for distinguishing early apoptotic, late apoptotic, and necrotic cell populations, emphasizing its diagnostic value in both experimental research and clinical investigations [25].

From a clinical perspective, the analyzed data confirmed that dysregulation of apoptotic mechanisms plays a central role in the pathogenesis of numerous diseases. Reduced apoptotic activity contributes to malignant transformation, autoimmune disorders, and chronic inflammatory conditions, whereas excessive or uncontrolled apoptosis is implicated in neurodegenerative diseases and ischemic tissue damage [26]. Necrosis, on the other hand, was predominantly associated with acute pathological conditions such as myocardial infarction, cerebral ischemia, severe infections, and traumatic tissue injury, where inflammation-mediated tissue destruction significantly influences disease progression and prognosis [27].

Overall, the obtained results clearly demonstrate that apoptosis and necrosis differ substantially in regulatory control, morphological expression, molecular signaling pathways, and clinical consequences. These findings underscore the importance of accurately distinguishing between programmed and pathological forms of cell death in modern diagnostic practice and in the development of targeted therapeutic strategies.

pISSN:2349-5707 Volume:13,Issue 1, January -2026 eISSN:2349-5715

**Discussion**

The findings of the present study highlight the fundamental biological and functional differences between apoptosis and necrosis, emphasizing their distinct roles in cellular physiology and pathology. The comparative analysis demonstrates that these two forms of cell death are not merely variations of a single process but represent separate mechanisms with different regulatory pathways, morphological manifestations, and clinical implications.

Apoptosis emerges as a highly controlled and energy-dependent process that serves as a protective mechanism for the organism. Its regulated nature allows for the selective elimination of damaged, aged, or genetically altered cells without compromising tissue integrity. The absence of inflammation during apoptosis is particularly significant, as it enables continuous tissue renewal while preserving the surrounding microenvironment. This characteristic explains the central role of apoptosis in embryonic development, immune system regulation, and long-term maintenance of tissue homeostasis.

In contrast, necrosis represents a response to overwhelming cellular injury in which regulatory mechanisms fail. The loss of membrane integrity and uncontrolled release of intracellular components initiate strong inflammatory reactions, leading to secondary tissue damage. This inflammatory cascade not only worsens the primary injury but may also contribute to systemic complications, especially in vital organs such as the heart and brain. Therefore, necrosis is closely associated with acute pathological conditions and unfavorable clinical outcomes.

The molecular distinctions between apoptosis and necrosis further reinforce their biological divergence. Apoptotic pathways rely on precise intracellular signaling and enzymatic activation, allowing cells to undergo self-destruction in a controlled sequence. Necrotic death, however, is largely driven by metabolic collapse, ionic imbalance, and oxidative stress, resulting in rapid and irreversible cellular disintegration. These differences explain why apoptosis is often considered a “silent” form of cell death, whereas necrosis is accompanied by extensive inflammatory responses.

From a clinical perspective, the regulation of cell death has become an important therapeutic target. Excessive inhibition of apoptosis may promote tumor development, while its overstimulation can contribute to degenerative disorders. Similarly, limiting necrotic injury and the subsequent inflammatory response is a key objective in the management of ischemic and traumatic conditions. Understanding the balance between these processes is therefore essential for designing effective treatment strategies.

Moreover, the distinction between apoptosis and necrosis has significant diagnostic implications. Modern laboratory techniques allow clinicians and researchers to identify the dominant type of cell death occurring in tissues, thereby improving disease classification and prognosis assessment. This knowledge supports personalized therapeutic approaches aimed at modulating specific cellular pathways rather than applying generalized treatment strategies.

Overall, the discussion underscores that apoptosis and necrosis represent complementary yet opposing mechanisms within cellular biology. Their precise regulation determines whether tissue damage remains localized and reversible or progresses toward widespread pathological injury. Continued investigation into these processes is essential for advancing molecular medicine and improving outcomes in a wide range of diseases.

pISSN:2349-5707 Volume:13,Issue 1, January -2026 eISSN:2349-5715

## Conclusion

In conclusion, apoptosis and necrosis represent two fundamentally distinct forms of cell death that differ in their regulatory mechanisms, morphological features, molecular pathways, and clinical consequences. Apoptosis functions as a genetically programmed and energy-dependent process essential for tissue homeostasis, normal development, and cellular quality control. Its controlled nature allows the elimination of damaged or unnecessary cells without provoking inflammatory responses, thereby maintaining structural and functional integrity of tissues.

Necrosis, in contrast, occurs as a result of severe cellular injury and is characterized by loss of membrane integrity, uncontrolled release of intracellular components, and pronounced inflammatory reactions. This form of cell death is closely associated with acute pathological conditions and contributes significantly to tissue destruction and disease progression.

The ability to distinguish between apoptotic and necrotic processes is of considerable importance in modern medical practice. Accurate identification of the dominant form of cell death enhances diagnostic precision, supports prognostic evaluation, and provides a scientific basis for targeted therapeutic interventions. Understanding the balance between regulated and pathological cell death mechanisms is therefore essential for the development of effective treatment strategies in oncology, neurology, cardiology, and critical care medicine.

Overall, deeper insight into apoptosis and necrosis not only advances fundamental biological knowledge but also plays a pivotal role in improving clinical outcomes and shaping future directions in molecular and translational medicine.

## References

1. Kerr JF, Wyllie AH, Currie AR. Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. *Br J Cancer*. 1972;26(4):239–257.
2. Elmore S. Apoptosis: a review of programmed cell death. *Toxicol Pathol*. 2007;35(4):495–516.
3. Majno G, Joris I. Apoptosis, oncosis, and necrosis: an overview of cell death. *Am J Pathol*. 1995;146(1):3–15.
4. Green DR, Reed JC. Mitochondria and apoptosis. *Science*. 1998;281(5381):1309–1312.
5. Fulda S, Debatin KM. Extrinsic versus intrinsic apoptosis pathways in anticancer chemotherapy. *Oncogene*. 2006;25(34):4798–4811.
6. Thompson CB. Apoptosis in the pathogenesis and treatment of disease. *Science*. 1995;267(5203):1456–1462.
7. Hotchkiss RS, Strasser A, McDunn JE, Swanson PE. Cell death. *N Engl J Med*. 2009;361(16):1570–1583.
8. Galluzzi L, Bravo-San Pedro JM, Vitale I, et al. Essential versus accessory aspects of cell death. *Cell Death Differ*. 2015;22(1):58–73.
9. Kroemer G, Galluzzi L, Vandenabeele P, et al. Classification of cell death: recommendations of the Nomenclature Committee on Cell Death. *Cell Death Differ*. 2009;16(1):3–11.
10. Galluzzi L, Vitale I, Abrams JM, et al. Molecular definitions of cell death subroutines. *Cell Death Differ*. 2012;19(1):107–120.
11. Lockshin RA, Zakeri Z. Programmed cell death and apoptosis: origins of the theory. *Nat Rev Mol Cell Biol*. 2001;2(7):545–550.

pISSN:2349-5707 Volume:13,Issue 1, January -2026 eISSN:2349-5715

12. Fink SL, Cookson BT. Apoptosis, pyroptosis, and necrosis: mechanistic description of dead and dying eukaryotic cells. *Infect Immun*. 2005;73(4):1907–1916.
13. Yuan J, Yankner BA. Apoptosis in the nervous system. *Nature*. 2000;407(6805):802–809.
14. Wyllie AH. Glucocorticoid-induced thymocyte apoptosis is associated with endogenous endonuclease activation. *Nature*. 1980;284(5756):555–556.
15. Vermes I, Haanen C, Steffens-Nakken H, Reutelingsperger C. A novel assay for apoptosis: flow cytometric detection of phosphatidylserine expression. *J Immunol Methods*. 1995;184(1):39–51.
16. Gavrieli Y, Sherman Y, Ben-Sasson SA. Identification of programmed cell death in situ via specific labeling of nuclear DNA fragmentation. *J Cell Biol*. 1992;119(3):493–501.
17. Kroemer G, Martin SJ. Caspase-independent cell death. *Nat Med*. 2005;11(7):725–730.
18. Proskuryakov SY, Gabai VL. Mechanisms of tumor cell necrosis. *Curr Pharm Des*. 2010;16(1):56–68.
19. Rock KL, Kono H. The inflammatory response to cell death. *Annu Rev Pathol*. 2008;3:99–126.
20. Häcker G. The morphology of apoptosis. *Cell Tissue Res*. 2000;301(1):5–17.
21. Trump BF, Berezesky IK. Calcium-mediated cell injury and cell death. *FASEB J*. 1995;9(2):219–228.
22. Leist M, Nicotera P. The shape of cell death. *Biochem Biophys Res Commun*. 1997;236(1):1–9.
23. Nicotera P, Leist M, Manzo L. Neuronal cell death: a demise with different shapes. *Trends Pharmacol Sci*. 1999;20(2):46–51.
24. Kroemer G, El-Deiry WS, Golstein P, et al. Classification of cell death: recommendations of the NCCD. *Cell Death Differ*. 2005;12(Suppl 2):1463–1467.
25. Vermes I, Reutelingsperger C. Flow cytometry of apoptotic cell death. *Methods*. 2000;21(3):271–277.
26. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell*. 2011;144(5):646–674.
27. Braunwald E. Myocardial ischemia and necrosis. *Circulation*. 1997;96(2):497–505.