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Review Article

The First Step Into Death: Postulation on Identifying the Initial Irreversible Event That Ends Life

Md Ikbal Husain and Biplab De*

Regional Institute of Pharmaceutical Science and Technology, Abhoynagar, Agartala, Tripura-799005, India

***Corresponding Author:** Biplab De, Regional Institute of Pharmaceutical Science and Technology, Abhoynagar, Agartala, Tripura-799005, India.

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Abstract

Life and death are not sudden events; rather, they are a series of irreversible chemical changes for normal event. There are many unexplained issues related to DNA-RNA, Neuroscience, Soul, life after death etc. knocking almost everyone, then also both the event of life and death have been continuing and continuing under the control of nature. For centuries, both philosophers and scientists have been interested in figuring out the initial stage of this process of death in normal cases. According to recent research, mitochondrial dysfunction more precisely, the opening of the mitochondrial permeability transition pore (mPTP) is the first irreversible event in cellular death. This review explores the biochemical, physiological and philosophical implications of defining the starting point of death. It highlights the cellular conditions necessary for life, the mitochondrial processes that cause permanent harm and how these scientific understandings relate to philosophical viewpoints regarding the nature of life's end. In addition to defining mortality, an understanding of the initial irreversible event of death gives therapeutic opportunities for reducing pathological cell death in serious disorders.

Keywords: Death; mPTP; Biochemical Regulation; Cellular Dysfunction

Introduction

Death, which was often thought to be the end of life, is now more widely acknowledged as a biological process with a defined starting point. Recovery is not possible due to a combination of molecular failures rather than just a lack of function [1]. So, one can describe that life is a fully automated programmed living tool originated from chromosome and is ended after gaining a defined and characterized shape i.e. death ultimately is held with a body.

From a cellular perspective, structural integrity, ionic equilibrium and energy maintenance are essential for life; if any of these foundational systems collapse irreversibly, death ensues. The study of these events, especially the first irreversible change provides essential insights into cellular resilience, therapeutic intervention and the broader philosophy of existence [2].

The requirement to determine the cellular moment of no return is highlighted by the distinction between biological death, the permanent loss of cellular function and clinical death, which is the end of cardiac and respiratory activity. Recent developments in the study of calcium signalling and mitochondrial physiology have shown that mitochondria may act as the "gatekeepers of death," deciding whether a cell survives or dies [3,4].

Death reflection on Brain, Heart and other parts of body

Death is a series of malfunctions in interconnected biological systems rather than being limited to a single organ.

The first major organ to stop working when the oxygen and glucose supply is cut off is the brain, which is frequently referred to as the seat of consciousness. Neural depolarization and calcium overload occur within 4-6 minutes of cardiac arrest, causing irreversible synapse failure and cytotoxic edema. Brain death is frequently diagnosed by electroencephalogram quiet or "flatline" [5].

On the other hand, electrical or mechanical stimulation might bring the heart back to life after a brief arrest; however, contractility permanently stops once the mitochondrial membrane potential falls and ATP synthesis stops [6].

The metabolic activity of other organs, such the liver and kidneys, persists for minutes to hours, suggesting that organismal death occurs asynchronously. Death is better seen as a slow systemic disintegration rather than an immediate event, as indicated by the temporal separation between organ failures [7].

Explanation of death in different religions

- Death is a concept that connects biology and metaphysics in all civilizations.
- Hindu philosophy views death as a metamorphosis rather than a cessation, representing the Atman (soul) moving from one body to another. The body, according to the Bhagavad Gita, is a clothing that the soul throws away when it is no longer appropriate [8].
- According to Islamic religion, death (Maut) is a divine decision and a gateway to an afterlife where spiritual consciousness will continue [9].
- In Christianity, death signifies the division of the soul from the body, which is followed by judgment and either eternal life or damnation [10].
- Buddhism believes rebirth as conditioned by karma after death, which is the breakdown of the aggregates (skandhas) [11].
- One fundamental feature unites all points of view: death is continuance in a different realm rather than destroyed. There are fascinating similarities between these traditional concepts and the modern investigation of awareness at the moment of brain death.
- It is made clear that, the present composition is not discussing or supporting any issues narrated in different religions.

Death is not just an outcome – It has a starting point

In traditional medical practice, a person is generally considered dead when their measurable physiological parameters stop [12]. But biological death starts long before these systemic failures are noticeable [13]. Irreversible molecular abnormalities set off a chain reaction that cannot be stopped by biological repair at the cellular level. The integrity of the mitochondria is essential to this process. The organelles control calcium homeostasis and apoptosis in addition to producing adenosine triphosphate (ATP). The cell can no longer sustain ionic gradients when mitochondrial function is compromised, which causes swelling, rupture and demise [3].

According to this theory, death is not a final event but rather a cumulative loss of order, a shift from reversible dysfunction to irreversible failure. Death is not a single event in this sense, but rather a process with a defined beginning [14].

Cellular life requirement

Three interrelated principles define cellular life: biochemical regulation, membrane stability, and energy production. The majority of cellular ATP is produced by mitochondria via oxidative phosphorylation, while cell membranes preserve the ion gradients necessary for equilibrium. One of the most important processes in metabolism and apoptosis, calcium signalling is coordinated by the endoplasmic reticulum and mitochondria [15].

Although calcium is essential for cell signalling, it can also be harmful if left unchecked. The opening of the mitochondrial permeability transition pore (mPTP), which distributes the mitochondrial membrane potential ($\Delta\psi m$) and interferes with ATP generation, is caused by excessive mitochondrial calcium uptake. This occurrence stands for the biochemical threshold that prevents recovery [16].

A further factor that speeds up this breakdown is the presence of reactive oxygen species (ROS). Oxidative stress causes damage to proteins, lipids and nucleic acids, increasing the permeability of the mitochondria and starting the processes that lead to cell death [17].

The most probable first event of death

The opening of the mitochondrial permeability transition pore (mPTP) is thought to be the most likely initial irreversible event among the numerous molecular processes linked to cell death. A non-selective channel called the mPTP develops across the inner mitochondrial membrane in response to pathological circumstances such ATP depletion, oxidative stress, and calcium overload [18,19].

Persistent hole opening causes Δψm to collapse, mitochondria to enlarge, the outer membrane to tear, and pro-apoptotic substances such cytochrome C to be released. Both necrotic and apoptotic pathways are triggered by this sequence, depending on the cell's energy state [16].

The mPTP's identity and control have been thoroughly described by Bernardi and associates, who propose that the line separating irreversible cell death and reversible malfunction is marked by its protracted opening. Similar to this, Gunter and Pfeiffer's fundamental research showed how mitochondrial calcium stress serves as a prelude to irreversible metabolic failure and permeability shift.

Additionally, oxidative damage, energy depletion, and calcium deregulation are all linked by the mPTP mechanism to a single irreversible event that marks the beginning of death. Thus, the activity of the pore serves as a "biological clock" for the death of cells [20].

Chromosomal status in explaining of death

The distinction between life and death is reflected at the cellular level by the integrity of the chromosomes. The ultimate storehouse of biological identity is chromosomal DNA; once it is severely fragmented, it cannot be recovered [21].

Endonucleases split DNA into the nucleosomal fragments during apoptosis, creating the distinctive "DNA ladder". However, chromosomes randomly degrade during necrosis, which is a reflection of chaotic energy collapse [22].

Certain genes, especially those related to stress response and development are sometimes referred to as the "thanatotranscriptome", continue to be transcriptionally active for hours after clinical death, according to postmortem investigations. The chromosomal state serves as the molecular timestamp that signals the change from reversible to irreversible loss of function, and this residual transcription emphasizes that death is a process rather than an instant [23].

Other death events are secondary

DNA fragmentation, membrane blabbing and lysosomalrupture are examples of secondary manifestations of the initial mitochondrial failure that occur when the mPTP opens. Although these occurrences can be seen under a microscope, they take place after the point of irreversibility [19].

Depending on the cellular energy state and surrounding conditions, this death cascade can manifest itself in several ways, including necrosis, autophagy and apoptosis. Apoptosis is a regulated, energy-dependent process, whereas necrosis is the unchecked devastation brought on by a catastrophic energy failure. Nonetheless, both have a mitochondrial origin [24].

Further supporting the idea that mitochondrial permeability is the primary cause of death is research demonstrating that treatments that target mPTP opening, such as cyclosporine A and novel antioxidants, can postpone or stop these secondary events [16].

Philosophical Parallels

The discovery of a "first step" toward death poses significant philosophical queries on the nature of consciousness and life. The shift from reversible dysfunction to irreversible failure reflects existential concepts of the frailty of existence and how minor imbalances can lead to the loss of order and identity [25].

The question of whether death is a continuous process or a unique event has long been disputed by philosophers. The latter is supported by the scientific point of view, which frames death as an evolving disorder. Thus, the moment of existential dissolution, when the system loses its defining self-organization can be understood as the first irreversible molecular alteration [26].

In this context, mitochondrial malfunction represents more than just biological failure; it represents the metaphysical transition from unity to entropy, from vitality to cessation. The "first step into death" is a representation of life's inherent vulnerability rather than just a molecular reality [27,28].

Life after death

Life after death is a question that cuts across scientific boundaries. In his book Life Beyond Death, Swami Abhedananda says that consciousness is unbreakable and lives in a more subtle form outside of the body. Like replacing an old dress, he describes death as the soul's escape from its physical body. Indirect resonances with this perspective can be found in contemporary neuroscience and quantum explanations of consciousness, which imply that information may be altered rather than destroyed after it is created. Accordingly, the initial stage of death might not represent a conclusion but rather a reorganization of life outside the realm of the material senses [29,30]. The evidences in this aspect, i.e. life after death are not supported widely and proves are not well accepted; and thus discussion in this part are not extended. Ultimately, no one comes back into the life as alive after death; and due to these reasons, even the knowledge for the event of death is still controversial.

Conclusion

Death is fundamentally a sequence that is started by a single irreversible molecular event rather than a sudden end. The idea that the main cause of cellular death is the continuous opening of the mitochondrial permeability transition pore (mPTP) is strongly supported by evidence from mitochondrial physiology.

All subsequent morphological and biochemical symptoms of death are preceded and determined by this occurrence. It represents the permanent loss of structural integrity, ionic balance, and energy metabolism. Researchers might better understand disease causes and create focused efforts to maintain cellular viability under stress by acknowledging the mPTP opening as the "first step into death".

From a philosophical perspective, determining the point of death transforms mortality as a slow disintegration of life's order rather than as an end. Both existentially and biologically, death starts when the first irreversible barrier of recovery is crossed rather than when systems fail.

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