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THE PATHOPHYSIOLOGICAL MECHANISMS OF OXIDATIVE STRESS IN HUMAN DISEASES

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Abstract: Oxidative stress represents a critical imbalance between the generation of reactive oxygen species (ROS) and the capacity of antioxidant defenses, leading to cellular and tissue damage. This phenomenon has been implicated in the pathogenesis of various diseases, including cardiovascular disorders, neurodegeneration, cancer, and chronic inflammation. This study provides an overview of the molecular and pathophysiological mechanisms underlying oxidative stress and evaluates its role in disease progression. By reviewing experimental and clinical findings, the article highlights potential therapeutic strategies aimed at modulating oxidative pathways to prevent or mitigate disease outcomes.

Keywords: oxidative stress, pathophysiology, free radicals, antioxidant defense, chronic disease

Introduction

Pathological physiology, as an integrative discipline, seeks to understand the functional disturbances that underlie disease processes. Among these disturbances, oxidative stress is one of the most extensively studied yet complex phenomena. It occurs when the excessive production of reactive oxygen species (ROS) overwhelms the cellular antioxidant defense system. ROS are natural by-products of cellular metabolism, particularly within mitochondria, but when uncontrolled, they cause damage to lipids, proteins, and DNA.

Over the past decades, oxidative stress has emerged as a unifying mechanism contributing to diverse pathological conditions. Cardiovascular diseases such as atherosclerosis, ischemia-reperfusion injury, and hypertension are closely associated with ROS-mediated endothelial dysfunction. In the nervous system, excessive oxidative damage contributes to the pathogenesis of Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. Furthermore, chronic inflammation, cancer initiation, and metabolic disorders such as diabetes mellitus are profoundly influenced by oxidative imbalance. Understanding the pathophysiological basis of oxidative stress is crucial for the development of novel diagnostic and therapeutic strategies.

Oxidative stress is defined as a state of imbalance between the excessive generation of reactive oxygen species (ROS) and the ability of the body's antioxidant defense systems to neutralize them. ROS include free radicals such as superoxide anion (O_2^-), hydroxyl radical (•OH), and non-radical species like hydrogen peroxide (H_2O_2). While small amounts of ROS are essential for physiological signaling processes including immune defense and cell signaling, their uncontrolled accumulation leads to lipid peroxidation, protein denaturation, and DNA damage.

The origins of oxidative stress are multifactorial. Endogenous sources include mitochondrial oxidative phosphorylation, peroxisomal metabolism, and enzymatic reactions involving xanthine oxidase or NADPH oxidases. Exogenous contributors include ultraviolet radiation, air pollution,

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smoking, alcohol consumption, and exposure to toxins. These internal and external factors together create conditions that promote oxidative imbalance, especially in individuals with compromised antioxidant defense systems.

Over the past decades, oxidative stress has been implicated in a wide range of human pathologies. In cardiovascular medicine, ROS-induced endothelial dysfunction is considered a hallmark of atherosclerosis and hypertension. In neurology, oxidative stress is linked to neurodegenerative disorders such as Alzheimer's and Parkinson's disease, where it contributes to neuronal death and impaired synaptic transmission. In oncology, oxidative DNA damage acts as a mutagenic factor that drives carcinogenesis. Additionally, metabolic diseases such as diabetes mellitus exhibit chronic oxidative stress that exacerbates vascular and organ complications.

Importantly, oxidative stress is not only a consequence but also a driver of disease progression. For example, inflammation generates ROS via activated neutrophils and macrophages, while ROS in turn activate transcription factors such as NF-κB, perpetuating inflammatory responses. This vicious cycle demonstrates how oxidative stress is interwoven into the pathophysiological fabric of many chronic diseases.

The relevance of studying oxidative stress in pathological physiology lies in its potential for therapeutic targeting. Antioxidant therapy, redox-sensitive drug development, and identification of oxidative biomarkers are promising strategies for early diagnosis, prevention, and treatment. However, despite decades of research, clinical translation of antioxidant-based therapies remains inconsistent, highlighting the complexity of redox biology.

Thus, the purpose of this paper is to provide a detailed overview of the pathophysiological mechanisms of oxidative stress and to critically evaluate its role in the development and progression of human diseases. By synthesizing experimental and clinical evidence, this study aims to highlight both the opportunities and limitations of targeting oxidative stress in modern medicine.

Methods

The research is based on a systematic review of experimental and clinical studies published between 2010 and 2024 in PubMed, Scopus, and Web of Science databases. Keywords used for data collection included "oxidative stress," "pathophysiology," "ROS," and "antioxidant therapy." Inclusion criteria focused on studies that examined molecular mechanisms of oxidative stress and its direct involvement in disease models. Exclusion criteria involved papers without experimental or clinical data. The selected articles were analyzed to identify common mechanisms, disease associations, and therapeutic interventions.

Results

Analysis of the literature indicates several consistent findings. First, oxidative stress is a major driver of endothelial dysfunction in cardiovascular diseases. ROS impair nitric oxide bioavailability, leading to vasoconstriction and hypertension. In ischemia-reperfusion injury, the sudden burst of ROS upon reoxygenation results in massive cellular necrosis and apoptosis.

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Second, in neurodegenerative diseases, oxidative stress disrupts neuronal homeostasis by damaging mitochondria and impairing synaptic plasticity. Accumulation of misfolded proteins, such as beta-amyloid in Alzheimer's disease, further amplifies oxidative injury.

Third, chronic oxidative stress promotes mutagenesis and genomic instability, which contribute to carcinogenesis. ROS-mediated activation of signaling pathways such as NF-κB and MAPK also drives inflammation and tumor progression.

Finally, antioxidant defense systems, including superoxide dismutase, catalase, and glutathione peroxidase, are frequently impaired in pathological states. This impairment exacerbates disease severity and accelerates progression.

Discussion

The reviewed evidence strongly supports the notion that oxidative stress is not merely a by-product of cellular metabolism but a central pathophysiological mechanism in many diseases. Its multifactorial role explains why diverse pathological conditions share common molecular features, such as mitochondrial dysfunction, chronic inflammation, and apoptosis.

From a therapeutic perspective, antioxidant supplementation has been widely explored. However, clinical trials with vitamins C and E, as well as other antioxidants, have produced inconsistent results. This suggests that targeting oxidative stress requires more specific strategies, such as mitochondrial-targeted antioxidants, enzyme mimetics, or modulation of redox-sensitive signaling pathways. Moreover, early detection of oxidative biomarkers could serve as predictive tools in clinical practice.

Conclusion

Oxidative stress is a fundamental pathophysiological mechanism contributing to the development and progression of numerous human diseases. By impairing cellular integrity and disrupting physiological signaling pathways, it exacerbates cardiovascular, neurological, oncological, and metabolic disorders. Future research should focus on precision medicine approaches to modulate redox balance, as well as the identification of reliable biomarkers for early intervention. Pathological physiology, by elucidating the underlying functional disturbances, provides the necessary framework to translate these findings into clinical innovations.

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