THE ROLE OF OXIDATIVE STRESS IN THE PATHOGENESIS OF HUMAN DISEASES

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Abstract: *Oxidative stress (OS) is defined as an imbalance between the production of reactive oxygen and nitrogen species and the capacity of antioxidant defense systems to neutralize them. This imbalance causes cellular and tissue damage that plays a crucial role in the development of numerous diseases, including cardiovascular disorders, diabetes mellitus, neurodegenerative syndromes, and cancer. In recent decades, oxidative stress has attracted significant attention as a unifying mechanism of disease pathogenesis. This article reviews the sources of oxidative stress, its biological effects, the involvement in major human diseases, and potential therapeutic approaches.*

Keywords: *oxidative stress, reactive oxygen species, antioxidants, pathogenesis, chronic diseases*

Introduction: In the modern era of medicine, understanding the molecular basis of diseases has become one of the most important directions of research. Among various pathological processes, oxidative stress has emerged as a key concept that bridges basic cellular biochemistry with clinical manifestations of disease.

Under normal conditions, reactive oxygen species (ROS) and reactive nitrogen species (RNS) are produced as natural by-products of cellular metabolism. They are necessary for signaling pathways, immune defense, and regulation of homeostasis. However, when their production exceeds the capacity of antioxidant systems, oxidative stress occurs. The resulting damage affects lipids, proteins, and nucleic acids, leading to structural and functional impairment of cells and organs.

Mechanisms of Oxidative Stress

• Sources of ROS and RNS:

Mitochondria are the primary sites of ROS generation. Other sources include NADPH oxidases, xanthine oxidase, and inflammatory cells such as neutrophils. Environmental factors such as smoking, radiation, pollution, and unhealthy diet also contribute.

• Biological effects:

1. Lipid peroxidation – damages cell membranes, increases permeability.
2. Protein oxidation – alters enzyme activity and structural proteins.
3. DNA damage – causes mutations, genomic instability, and may initiate carcinogenesis.

• Antioxidant defenses:Endogenous antioxidants include enzymatic systems (superoxide dismutase, catalase, glutathione peroxidase) and non-enzymatic molecules (glutathione, vitamins C and E, carotenoids). When these defenses fail, oxidative stress dominates.

Role in Human Diseases

1. Cardiovascular diseases

Oxidative stress contributes to endothelial dysfunction, atherosclerosis, hypertension, and ischemic heart disease. Oxidized LDL is a major factor in plaque formation and progression. Reperfusion after ischemia also generates massive ROS, worsening tissue injury.

2. Diabetes mellitus

Hyperglycemia enhances mitochondrial ROS production. Oxidative stress impairs insulin signaling, damages pancreatic beta-cells, and accelerates vascular complications such as nephropathy and retinopathy.

3. Neurodegenerative diseases

In conditions like Alzheimer's and Parkinson's disease, oxidative damage to neurons leads to cell death. The brain is highly susceptible because of its high oxygen consumption and lipid-rich membranes. Accumulation of oxidized proteins and lipids is a hallmark of these disorders.

4. Cancer

ROS-induced DNA mutations, activation of oncogenes, and suppression of tumor suppressor genes create a favorable environment for malignant transformation. At the same time, tumor cells often adapt by upregulating antioxidant pathways, which makes treatment challenging.

5. Aging and chronic inflammation

Oxidative stress is considered a central mechanism of aging. Chronic low-grade inflammation further amplifies ROS generation, creating a vicious cycle that underlies many age-related diseases.

Therapeutic Perspectives• Lifestyle modification: A diet rich in fruits and vegetables, regular exercise, and avoidance of smoking and toxins reduce oxidative burden.

• Pharmacological antioxidants: Molecules such as N-acetylcysteine, alpha-lipoic acid, and melatonin are being investigated. However, large clinical trials show mixed results, suggesting that targeted therapies may be more effective than generalized antioxidant supplementation.

• Future directions: Personalized medicine approaches that assess individual oxidative stress markers may allow tailored antioxidant interventions. Gene therapy and nanotechnology are also promising fields.

Conclusion: Oxidative stress represents a fundamental pathological mechanism linking molecular damage to clinical disease. Its role has been established in cardiovascular disorders, diabetes, neurodegenerative diseases, cancer, and aging. Understanding oxidative stress not only provides insight into disease mechanisms but also opens new avenues for prevention and therapy. While antioxidant treatments hold promise, more research is needed to translate these strategies into effective clinical practice.

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