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Oxidative Stress and the Pathogenesis of Neurodegenerative Disorders

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Microglia-derived inflammatory neurotoxins play a principal role in the pathogenesis of neurodegenerative disorders including Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and HIV-associated dementia; chief among these is reactive oxygen species. The detrimental effects of oxidative stress in the brain and nervous system are primarily a result of the diminished capacity of the central nervous system to prevent ongoing oxidative damage. A spectrum of environmental cues, mitochondrial dysfunction, accumulation of aberrant misfolded proteins, inflammation, and defects in protein clearance are known to evolve and form as a result of disease progression. These factors likely affect glial function serving to accelerate the tempo of disease. Understanding the relationships between disease progression, free radical formation, neuroinflammation, and neurotoxicity is critical to elucidating disease mechanisms and the development of therapeutic modalities to combat disease processes. In an era where populations continue to age, the prevalence and incidence of age-related neurodegenerative diseases are on the rise; therefore, the need for novel therapeutic strategies that attenuate neuroinflammation and protect neurons against oxidative stress is ever more immediate.