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Huntington's Disease: Pathophysiology, Clinical Features, and Emerging Therapeutic Approaches

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Abstract: *Huntington's disease (HD) is an inherited neurodegenerative disorder that gradually affects movement, thinking, and emotional well-being. It is caused by an abnormal expansion of CAG repeats in the huntingtin (Htt) gene, producing a mutant form of the protein (mHtt) that misfolds and interferes with normal cellular functions. These misfolded proteins, along with other abnormal sequences like polyalanine and polyserine, contribute to the progressive loss of neurons in key brain regions. Diagnosis of HD combines clinical evaluation, neurological examination, and imaging, but genetic testing, including analysis of CAG repeats, provides a definitive confirmation. Prenatal testing is also available for at-risk individuals. Clinically, patients show a mix of involuntary movements (chorea), slowed thinking, memory problems, and psychiatric symptoms such as anxiety, depression, and irritability. Recent advances in therapy include drug-based symptom management, non-drug interventions, and promising approaches like stem cell therapy aimed at replacing damaged neurons and supporting brain repair. Nanoparticle-based treatments are being explored, although challenges like toxicity and immune reactions remain. Additionally, natural herbs such as Bacopa monnieri (BM) and Curcuma longa (CL) offer antioxidant and neuroprotective benefits. Overall, a combined approach of medications, therapies, natural compounds, and multidisciplinary care is essential to improve quality of life and slow disease progression in HD.*

Keywords: Pathogenesis, Polyglutamine, Nanoparticles, mHtt protein, Neuroinflammation

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