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Pathophysiology of Conversion to Symptomatic Leber Hereditary Optic Neuropathy and Therapeutic Implications: a Review.

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PURPOSE: Leber's hereditary optic neuropathy (LHON) is a genetic disease of the mitochondrial genome that mainly affects the retinal ganglion cells (RGC) of the inner retina resulting in central vision loss. New understandings in mitochondrial genetics are helping to elucidate the nuances of conversion and allow for new therapeutic options.
RECENT FINDINGS: Appreciation of the mitochondrial fission-fusion balance has allowed for increased understanding of the cascade of events that leads to clinical conversion in LOHN. Mathematical and computational models have helped to interpret the role of ROS in conversion, both as oxidative agents and as signaling molecules for cell death. The conversion from the LHON carrier to the affected patient has been clinically characterized, but the pathophysiology is just beginning to be understood. External stressors alter the mitochondrial dynamics of RGCs, leading to ROS buildup, energy shortages, decreased biogenesis and increased mitophagy, and ultimately axon degeneration and ganglion cell death. New therapeutic alternatives targeting these newly understood pathophysiological changes in the mitochondria and directly addressing the genetic mutations involved in LHON are being developed.

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