

**Public Lecture by Richard H. Haas M.B., B. Chir
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**Energy Metabolism in Parkinson's Disease – A New Treatment Perspective
Wednesday, October 20, 2004 at 6:00 p.m. in the Garren Auditorium, Basic Science Building
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Parkinson's disease results from deficiency of dopamine, a brain neurotransmitter. Nerve cells in an area of the brain stem, the substantia nigra, progressively malfunction and eventually die. Treatment with L-DOPA has dramatically improved the quality of life for millions of Parkinson disease sufferers but does not prevent progression of the underlying disease with its loss of dopaminergic cells. The National Parkinson Foundation estimates that 60,000 new cases are diagnosed each year in the US with as many as 1.5 million affected. An intense research effort has been directed at understanding the cause of nerve cell degeneration with the hope of preventing or arresting progression of this devastating disease.

In 1983 a clue to at least one cause of neuronal degeneration in Parkinson's disease came from the streets of San Francisco. Langston and Ballard found that a street drug contaminated with the toxin MPTP was responsible for an outbreak of irreversible Parkinson's disease in young people. Further research identified MPP+, a metabolite of MPTP as the neurotoxic agent. Its action is to inhibit mitochondrial function at complex I.

Mitochondria are present in all metabolically active cells and they perform a wide range of essential functions perhaps the most important of which is the production of energy – particularly important for energy hungry brain cells. Complex I is the first step in the electron transport chain, the energy production pathway, and coenzyme Q₁₀ is the second step in the pathway.

There is now good evidence from our group and others that mitochondrial failure plays a part in the early symptoms of Parkinson's disease. We found complex I and II/III deficiency in early untreated Parkinson disease platelet mitochondria and with this in mind set out to find a possible treatment. We discovered that coenzyme Q₁₀ the antioxidant and mitochondrial electron transport chain component was reduced in Parkinson's disease and correlated to complex I deficiency.

My colleague Dr. Clifford Shults working with the Parkinson Study Group and with funding from the National Institute of Neurological Disorders and Stroke directed a national multicenter trial of coenzyme Q₁₀ treatment in Parkinson's disease. This was completed in 2002 with positive results suggesting that further trials are warranted. A higher dose study is being carried out by the NIH. Future approaches to Parkinson's disease treatment and prevention with a focus on the mitochondrial component should be fruitful and might include gene therapy approaches to supplement complex I deficiency. The new field of Mitochondrial Medicine is in its infancy but we are hopeful that improved understanding in this area will benefit not only children afflicted with life threatening diseases but also adults with common age related disorders such as cardiac failure, diabetes, Alzheimer's disease and Parkinson's disease.