

LE Magazine September 1996

LEF CONTROVERSY

Evidence For The Efficacy Of Low-Dose Deprenyl

The experiments of Tatton, et al. the University of Toronto¹³⁻¹⁵ provide significant evidence that deprenyl's ability to protect and rescue dying neurons may take place at well below that required for MAO-B inhibition though an entirely different mechanism of action, which Toronto scientists believe involves "trophic-like" activity in surrounding reactive astrocytes. In a recent paper, they concluded that:

*"Neuronal rescue by selegiline could contribute to the reported slowing the progression of Alzheimer's disease and Parkinson's disease and should be possible at markedly lower doses than those required to provide neuroprotection through MAO-B inhibition"*¹⁵

Further evidence for the desirability of lower doses of deprenyl in Parkinson's patients comes from Saskatchewan study,³⁰ in which l-deprenyl and its metabolite l-amphetamine produced enhancing benefits in muddled rats. The investigators concluded that since l-amphetamine was able to produce the same cognitive benefits as deprenyl *without* MAO-B activity then *"MAO-B inhibition is not necessary for the cognitive enhancement or the protection against the aging related decline in cognitive function such as that seen after chronic L-deprenyl."*

CURRENT RECOMMENDATIONS

The Foundation now recommends a lower dose of deprenyl for Parkinson's patients and for antiaging purposes based upon the evidence presented in this article. We recommend that healthy, aging persons take no more than 10 mg of deprenyl per week, and that untreated, early-stage Parkinson's patients take the lowest dose of deprenyl that produces symptomatic relief (1.5 mg-to-10 mg a day), with the dose of deprenyl reduced or eliminated as the patient moves into the latter stages of the disease. We believe the same strategy should be probably be used in Alzheimer's patients, but await the results of Alzheimer's trials now in progress, which will provide further evidence on the use of deprenyl in such patients. *Parkinson's and Alzheimer's patients must be under the care of a doctor, preferably a specialist in treating these diseases.*

PARKINSONISM: AN ENERGY DEFICIENCY DISEASE

One of the characteristics of exposure to neurotoxins is depletion of energy-generating capacity in the mitochondria (the power plants of the cell), especially in Complex I, the largest of the energy chain components, which uses NADH (Nicotinamide Adenine Dinucleotide) in the initial phase of energy production⁴⁵ NADH is absolutely critical for the production of energy within our cells. For every molecule of NADH that enters the energy chain, 3 molecules of ATPe (energy currency) are produced: There is now solid evidence of seriously impaired energy function in NADH-dependent Complex I due to mitochondrial abnormalities in Parkinson's patients. In one study, there was a 37% decline in Complex I energy function in 17 patients with Parkinson's disease compared to 22 age-matched controls.⁴⁷

NADH THERAPY FOR PARKINSON'S DISEASE

There are studies showing that NADH levels are diminished significantly in Parkinson's patients and that NADH supplementation can stimulate the synthesis of dopamine. Clinical studies in Europe have demonstrated in more than 2,000 early-stage Parkinson's patients that NADH therapy can produce clearcut clinical benefits in up 78.2% of the patients.⁴⁸ The amount of NADH used varied according to the severity of the disease. Positive results were also obtained with NADH therapy in Alzheimer's patients.⁴⁹ (For an in-depth article on NADH, see the June 1996 issue of *LIFE EXTENSION* Magazine).

NEUROTROPHIC FACTORS IN PARKINSON'S DISEASE

Recent evidence that deprenyl may be able to protect neurons via "trophic-like" effects is indicative of a new approach to the treatment of Parkinson's (and other neurodegenerative diseases)-the use of neurotrophic (growth) factors to stimulate the activity,

regeneration, and revitalization of existing neurons in the brain.

Until recently, the only such factor that was considered to be important for the health and vigor of brain neurons is Nerve Growth Factor (NGF), but there are now several other factors that are under investigation as neurotrophic factors. These include Brain-Derived Neurotrophic Factor (BDNF), Ciliary Neurotrophic Factor (CNTF), and Mitogenic Growth Factors (MGF). There are many studies showing that these growth factors promote the survival and differentiation of nigral dopaminergic neurons and that they protect these neurons from neurotoxic damage.⁵⁰

CLINICAL TRIALS AND PRACTICE

The research with neurotrophic growth factors has reached the point where clinical trials are being initiated in both Parkinson's disease and ALS (Lou Gehrig's disease) by companies such as Regeneron Pharmaceuticals, Synergen, Cephalon, and Amgen.⁵⁰ One of the Mitogenic Growth Factors being studied as a therapy to regenerate dopaminergic neurons are the insulin growth factors (IGF-1 and IGF-2). Of interest is the fact that IGF-1 is the major metabolite of growth hormone, which is now being used clinically (with other hormones) in attempts to restore lost youth and vigor in healthy, aging persons.

Hormone replacement therapy is being investigated for rejuvenation purposes in the U.S., England, Sweden and Denmark. There also is a clinic in the midwest that has reported remarkable results with hormone replacement therapy in Parkinson's, Alzheimer's and Stroke patients. We will be carrying in-depth reports about the latest developments in hormone replacement therapy-- both for neurodegenerative diseases and for aging--in future issues of *LIFE EXTENSION MAGAZINE*.

THE NEED FOR NEW BRAIN CELLS

The major limitation of today's therapies is the fact that they only affect the functioning neurons that remain in the brain of Parkinson's patients. Since 70-80% of the dopaminergic neurons in the substantia nigra of Parkinson's patients have been destroyed by the time the disease is diagnosed, even a therapy that prevents further loss of neurons would not cure the disease.

The long-term answer to Parkinson's disease and other neurodegenerative disease's will be the provision of new cells to replace the ones that have been lost. For the past 15 years, there have been promising animal studies using fetal brain grafts to attempt to replace critical neurons. There has also been limited experimentation in humans using this technique, but the result of their research have not been good enough to warrant its routine use in clinical practice. We will reporting on the latest advances in this field in a future issue of the magazine.

Our conclusion about deprenyl is that on balance, it is still a useful drug for Parkinson's disease and for antiaging purposes, but that it should be used at lower doses than previously recommended under the close supervision of a doctor. We will continue bringing you updates on deprenyl and other anti-Parkinson's therapies as the research picture unfolds.

References

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