Drug Trial for Parkinson's

Twenty-eight medical centers in the United States and Canada are to join in what will be the most ambitious prospective clinical trial ever in the fight against Parkinson's disease. The 5-year trial, which has just been funded by a $10-million grant from the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), will determine whether two drugs—Deprenyl and tocopherol—can slow or even arrest progression of this neurodegenerative disease.

More than 1 million people suffer from Parkinson's disease in this country, most of whom are over the age of 60. And each year nearly 61,000 younger people with the disease become unemployed as a result of progressive disability. As John Penny of the University of Michigan points out, "the overall cost savings to society would exceed $10 million annually if Deprenyl and/or tocopherol prove effective in maintaining work capacity in the early Parkinson patient for *just an additional week*." For this and other reasons, the 800 participants in the clinical trial will be persons in the early stages of the disease.

The impetus for the Deprenyl/tocopherol trial comes from the remarkable revolution that has swept Parkinson's disease research in recent years. In 1983 it was discovered that a chemical by the shorthand name of MPTP, which is a contaminant of a certain "synthetic heroin," rapidly and selectively destroys the same group of brain cells that slowly degenerate in natural Parkinson's disease. The explosion of research on MPTP-induced parkinsonism gave birth to the idea that natural Parkinson's disease may be caused by prolonged exposure to low levels of an environmental toxin, perhaps MPTP or something akin to it.

In fact, it turned out that MPTP itself does not kill brain cells, but a metabolic derivative of it that goes by the name MPP+. The key discovery that led eventually to the planned clinical trial was that the conversion of MPTP to MPP+ could be prevented by the drug Deprenyl, which blocks the activity of monoamine oxidase. If natural Parkinson's disease is caused by an environmental chemical like MPTP, then Deprenyl might prevent the production of the toxic agent and therefore protect the susceptible brain cells.

In addition, some researchers believe that the brain cell degeneration seen in Parkinson's disease may be inflicted by certain chemicals generated by the activity of monoamine oxidase on the neurotransmitter dopamine, which is normally produced by the degenerating cells. The administration of Deprenyl might therefore be protective in this way too, as would tocopherol, a derivative of vitamin E, which mops up harmful oxidative chemicals of the sort that might be a culprit here.

Treatment of parkinsonian patients in North America currently focuses on symptoms, not prevention. Patients are given L-dopa, which makes up some of the deficit of dopamine that results from brain cell degeneration, and thereby eliminates the muscle stiffness and tremors that characterize the disease. Meanwhile, the loss of brain cells continues, and symptoms become more and more difficult to alleviate. Eventually L-dopa therapy has to be stopped, because the side effects become worse than the disease, sometimes including horrible hallucinations. Prevention of brain cell degeneration, even by a modest amount, could therefore extend the useful life of L-dopa, once it became necessary.

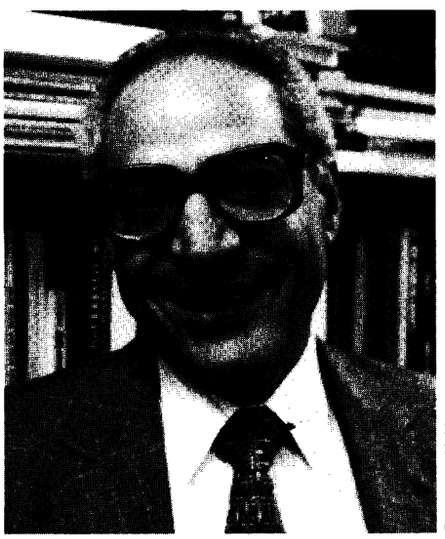
Deprenyl has been part of the treatment of Parkinson's disease for some years in many European countries, often in combination with L-dopa. Although this experience shows that Deprenyl is no miracle cure, so far there is insufficient information to determine what, if any, effect the drug has in slowing down the disease. One retrospective study, published in 1983, seemed to indicate significant beneficial effects, including prolongation of life. But in Europe, no prospective trial has been conducted that would give the necessary degree of control over drug dosage, drug combination, and careful monitoring of symptoms and so on that would unequivocally determine the true efficacy of the treatment.

The idea for the North American prospective study of Deprenyl and tocopherol was conceived in 1985, with the formation of the Parkinson Study Group, a coalition of researchers and clinicians involved with the disease (*Science*, 1 November 1985, p. 527). Ira Shoulson of the University of Rochester and Stanley Fahn of Columbia University were instrumental in setting up the group and are principal investigators for the NINCDS-funded project. ■ ROGER LEWIN

ticles will be sent to the Netherlands for analysis by a world expert on the microstructure of wood.

Next, the contents will be photographed with a compact television camera designed for looking into nuclear power plants. Heat-free light will be supplied by a fiberoptic light source which will also contain no infrared or ultraviolet. Still pictures, some in stereo, will be taken by a $32,000 camera designed by Emory Kristof of the National Geographic, who designed the photography for the Titanic expedition. The BU center will use these to make a map of the contents.

Finally, sensors will be inserted into the chamber to measure humidity, temperature, and air pressure at different levels. The chamber will then be resealed with epoxy resin. An environmental sensor may be left to ascertain whether there are changes as a result of the probe. There are no plans at present to retrieve the second boat.



Constance Holden

Farouk El-Baz. *The project director says if anyone has a better idea about how to proceed with the probe into the boat pit, he wants to hear about it.*

El-Baz calls the expedition "a pioneering effort in applying new remote sensing technology to the science of archeology." He says the techniques could be used, for example, for probing the cavities in Mayan structures in Guatemala, and exploring tombs in China that the Chinese do not want to excavate because they lack the museum space to properly preserve the contents.

El-Baz wants other scientists to know about the Giza project before the site work begins—"If anybody out there has a better idea about doing any of these steps please let us know so we can modify the plan. We can do this only once." ■

CONSTANCE HOLDEN