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Parkinson's Disease: Is Victory in Sight?

by Hans R. Larsen, MSc ChE

If research into Parkinson's disease continues at its present pace this dreaded disease may well be fully understood and largely preventable early in the 21st Century. Parkinson's disease (*paralysis agitans*, shaking palsy) was first described in 1817. L-dopa, the mainstay of current drug therapy was introduced in 1970 and since then hundreds of research papers have been published on the disease. It is now increasingly clear not only what causes Parkinson's, but also how it can be prevented and its relentless progress slowed down.

Incidence and Symptoms
Idiopathic (of no known cause) Parkinson's disease affects about one percent of the population over the age of 60 years in the United States. It is more common among men than among women and also seems to be more widespread in northern countries. The incidence of the disease increases with age although aging itself is not believed to be a causative factor. Parkinson's disease is rarely inherited and less than one per cent of all cases are thought to have a genetic component. At this time there is no medical cure for the condition, but drugs that alleviate the symptoms and slow the progress of the disease are available(1-5).

The main symptom of Parkinson's disease is a pronounced tremor affecting the extremities notably the hands, chin or lips. The tremor is most evident at rest and disappears with movement. Other characteristic symptoms of Parkinson's disease are stiffness or slowness of movement, a shuffling walk, stooped posture, and difficulties in performing simple tasks. Memory impairment and cognitive dysfunction are rarely encountered in early stage Parkinson's disease. Depression is, however, a common feature and about 30 per cent of Parkinson's disease victims eventually develop Alzheimer's disease or other forms of dementia(1-3,6-8).

Environmental and Dietary Factors
Parkinson-like symptoms can also occur as a result of head injuries, carbon monoxide poisoning or poisoning by pharmaceutical or other drugs. Certain diuretics (reserpine), antipsychotics (chlorpromazine), and heart drugs (verapamil) have all been implicated in causing or worsening Parkinson's disease symptoms as has the "designer drug" MPTP (methylphenyl-tetrahydropyridine). In some cases, drug-induced Parkinson's disease may be halted or reversed if the drug is promptly withdrawn. Naproxen and other NSAIDs (non-steroidal anti-inflammatory drugs) may also exacerbate Parkinson's disease(1,2,8-10).

Recent research carried out in Iceland, which has a very high incidence of Parkinson's disease, has shown that children born during or after a whooping cough (*pertussis*) epidemic are particularly vulnerable to Parkinson's disease in later life(11). This finding supports the idea that Parkinson's disease may develop later in life as a result of a neurotoxic event that occurred at an early age(8).

The main pathological feature of Parkinson's disease is the progressive destruction of dopamine- producing cells in the *substantia nigra* region of the brain stem. The loss of dopamine production affects the balance between dopamine and acetylcholine in the brain with the result that messages to the muscles become garbled. It is estimated that the characteristic Parkinson's disease symptoms develop once 70 per cent of the dopaminergic neurons in the *substantia nigra* have been destroyed(1,2,5,8).

The question as to what causes the destruction of the dopamine-producing cells has puzzled researchers for years but a consensus is now emerging that Parkinson's disease is caused by oxidative stress and metal toxicity(1,2,5,8). The idea that oxidative stress, i.e. an excess of free radicals in the body, can cause disease was first brought forward in 1983(12). In 1994 Professors Halliwell and Jenner of King's College, London proposed that neurodegenerative diseases and Parkinson's disease in particular were the result of oxidative stress(13,14). Numerous studies have shown that Parkinson's disease victims have low levels of natural antioxidants (glutathione and superoxide dismutase) and high levels of iron in the *substantia nigra* areas of their brains. It is believed that iron helps catalyze the free radical reactions that destroy the dopamine-producing cells(2,8,15-21). Other metals, notably manganese, cadmium, copper, and mercury (from dental amalgams) have also been implicated as causative factors in the development of Parkinson's disease(2,8,22-27).

People who live in areas where the aluminum content of the drinking water is high have an excessive risk of developing Parkinson's disease(4,28-32). Recent research has linked high aluminum levels in drinking water to acid rain that leaches the aluminum out of the soil and transfers it to the ground water(4,28,29). Occupational exposure to pesticides and herbicides has also been linked to a significantly higher risk of developing Parkinson's disease(33-36).

Diet is another important factor in Parkinson's disease. Researchers at the University of Magdeburg in Germany recently reported that people with a high intake of sugar (mono- and disaccharides) increase their risk of developing Parkinson's disease by a factor of three as compared to people with a more moderate intake. The same study also showed that diets high in vitamin C and beta-carotene provide significant protection(37). American researchers have concluded that a high intake of animal fats is associated with a five-fold increase in the risk of developing Parkinson's disease(20).

Antioxidants: The Key to Prevention and Control
Researchers at the University of Hawaii recently reported that people with a high blood level of the natural antioxidant uric acid have a lower risk of developing Parkinson's disease than do people with lower levels. Unfortunately, high levels of uric acid may cause heart disease and gout, and as a matter of fact, the overall mortality rate in the high uric acid group was about 30 per cent higher than in the low uric acid group. Nevertheless, the uric acid study does provide evidence that high levels of antioxidants may help prevent Parkinson's disease(21,38).

That antioxidants also slow down the progression of existing Parkinson's disease was demonstrated in 1991 in a pilot study carried out by Dr. Stanley Fahn of Columbia University. Dr. Fahn found that Parkinson's disease patients given large doses of oral vitamin-C and synthetic vitamin-E supplements (3000 mg and 3200 IU daily respectively) delayed the progression of their disease to the point where they needed l-dopa 2.5 years later than a group of patients who were not taking supplements(39,40). Later research has shown that synthetic vitamin E in itself does not retard the

progression of Parkinson's disease(2,41). Thus it is likely that it was vitamin C by itself or its combination with vitamin E that was the active component in Dr. Fahn's experiment. This fits with a later finding that vitamin E, a fat-soluble vitamin, does not readily cross the blood-brain barrier nor does it accumulate in the cerebrospinal fluid that bathes the brain(5,42). Vitamin C, on the other hand, while not crossing the blood-brain barrier does enter the cerebrospinal fluid and can be found there in concentrations proportional to dietary intake(43- 45). Inasmuch as vitamin C is a highly effective antioxidant and is particularly adept in quenching hydroxyl radicals (the main culprits in the dopamine-cell destruction), it is becoming increasingly clear that this vitamin may be an excellent protector against Parkinson's disease and can materially help in slowing down the progression of the disease(46).

Flavonoids, and in particular the proanthocyanidins (grape seed and pine bark extracts) which are water- soluble, stronger antioxidants than vitamin C, and readily cross into the brain fluid should also be excellent candidates as Parkinson's disease preventers and retarders. Clinical trials are, however, still required to support this hypothesis(47).

Another promising candidate in Parkinson's disease prevention is coenzyme Q10 (ubiquinone) that also is absorbed in brain fluids and is a very powerful antioxidant. Recent research has shown that the coenzyme Q10 content of the mitochondria (energy-producing cell components) in the brain declines rapidly when Parkinson's disease is induced in monkeys; this reduction in coenzyme Q10 level leads to a detrimental increase in free radical destructive reactions(48).

The overall conclusion of this recent research is that one can lower one's risk of developing Parkinson's disease by reducing one's intake of animal fats and sugar, avoiding excessive exposure to metals such as aluminum, iron, manganese, mercury, cadmium and copper, and by ensuring an adequate intake of antioxidants.

Conventional Treatment
Meanwhile, what can be done for people who already have the disease? Conventional medical treatment relies heavily on l-dopa (levo-dihydroxy-phenylalanine) a dopamine-precursor that can cross the blood- brain barrier and is converted to dopamine in the brain. L-dopa is now rarely used by itself, but rather in combination with carbidopa (Sinemet) or benserazide (Madopar) that protects it from breaking down before it reaches the brain tissue. As l-dopa must compete with other amino acids in crossing both from the gut to the blood stream and from the blood stream to the brain it is usually recommended that it be taken between meals rather than with meals(1,2,8,49).

Although l-dopa medications can bring significant relief from Parkinson's disease symptoms they become less effective with time. After four or five years of increasing dosages their effect becomes sporadic and unpredictable (the "on-off syndrome") and patients become increasingly helpless and depressed. There is also evidence that the use of l-dopa medications may lead to a deficiency of B vitamins, especially niacin and vitamin B-6. Most Parkinson's disease experts now recommend that l-dopa therapy be started as late as possible after diagnosis of Parkinson's disease so as to postpone the day when it no longer works and to limit its many serious adverse effects(1,2,5,7,8,50).

Selegiline (Deprenyl, Eldepryl) is another drug used in Parkinson's disease therapy. It works by blocking the breakdown of dopamine in the brain. Recent trials have shown that starting Parkinson's disease patients off on selegiline can extend the time period before they need l-dopa by about nine months(2,5,8,51). Combinations of l-dopa medications and selegiline have also been tried in early stage Parkinson's disease patients, but were found to have no advantage. As a matter of fact, a recent study concluded that the combination therapy increased mortality by about 50 per cent when compared to Parkinson's disease patients treated with l-dopa medications alone(7,52).

Anticholinergenic drugs work by reducing the amount of acetylcholine produced in the brain and thereby redresses the imbalance between dopamine and acetylcholine. They are no longer recommended for older patients as they have serious neuropsychiatric side-effects(7,8).

Alternative Treatment
Until recently there were few alternative treatments available for Parkinson's disease patients. This is now changing. Supplementation with vitamin C and E markedly slows the progression of the disease in its early stages. Other antioxidants such as coenzyme Q10 and proanthocyanidins may be equally or more effective - however, this remains to be proven in clinical trials. Supplementation with vitamin B complex may also be necessary, especially for patients who take l-dopa medications. The timing of protein intake can markedly increase the effectiveness of l-dopa and thereby lead to reduced dosage requirements. Researchers now recommend that protein intake be kept as low as possible and that protein be included primarily in the evening meal(47,49).

Australian researchers have found that broad beans (*Vicia faba*) is an extremely good source of l- dopa and can, in some cases, actually replace l-dopa. A 100 g serving of broad beans (including the pods) provides about 250 mg of l-dopa and in addition, a significant amount of proanthocyanidins. The broad beans remain effective even if canned or frozen, but should always be consumed whole as the pod has been found to have the highest concentration of l-dopa. Medication dosage may have to be adjusted if broad beans are consumed on a regular basis(49,53).

Stress aggravates Parkinson's disease and relaxation therapy has been found useful in the treatment of the disease. A well thought-out program of rest, exercise, and physiotherapy can also significantly ameliorate the symptoms of Parkinson's disease(1,8,54).

The finding that Parkinson's disease is almost certainly caused by oxidative stress aggravated by metal toxicity is a major step forward in understanding and eventually conquering the disease. At present the best preventive strategy is to limit the intake of animal fats and sugar, eat a diet rich in fruits and vegetables, avoid toxic metals and an excessive iron intake, and insure an adequate intake of antioxidants. These preventive measures may also be useful in slowing down the progression of the disease. As research intensifies new avenues will no doubt open up and in a few years Parkinson's disease will hopefully be both preventable and controllable.

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