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# Natural Approaches to the Treatment of Parkinson's Disease

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**T**here are nearly 2 million Americans, mostly men, that suffer from Parkinson's disease. Since it was first described in 1817, it has been well researched, and much is now known about its etiology and the precise symptoms associated with the progression of neurologic degeneration. From a pathologic perspective, this condition results from the degeneration within the nuclear masses of the extrapyramidal system. Among the classical symptoms that are observable and that serve as measures of therapeutic success are the characteristic tremor of resting muscles, a slowing of voluntary movement and gait, altered posture, and overall muscular weakness.

Understanding the disease process, the manifestation of symptoms, and the physiology of proper neurologic activity, allows the clinician the opportunity to offer alternative therapeutic approaches that can augment standard drug therapy. Simply put, the manifestation of symptoms arises from an imbalance between dopamine and acetylcholine. As the dopamine levels become depleted, the now less-opposed acetylcholine results in parkinsonism.

Among pharmaceutical approaches that can help to mitigate the symptoms of Parkinson's disease are agents, such as diphenhydramine, that have anticholinergic activity. Such drugs block the muscarinic effects of acetylcholine. Another approach is to use certain tricyclic antidepressants, which can both prevent the reuptake of dopamine and also produce anticholinergic effects. As the disease process continues, supplementation of

dopamine activity is attempted with such drugs as levodopa (L-dopa), carbidopa, or a combination approach.

## Dietary Considerations

### *Protein*

Symptoms appear to become less severe when patients are placed on low-protein diets. In one study, patients taking L-dopa were placed on a high-protein diet of 1.6 g/kg or a low-protein diet of 0.8 g/kg, with most of the protein consumed during the evening meal. Symptoms, such as tremors, tapping, and amount of time that a patient had difficulty in walking all were reduced in severity on the lower protein diet.<sup>1</sup> Another study that was double-blinded arrived at the same conclusions, i.e., that symptoms become less severe when patients are placed on low-protein diets.

It was also found that these results did not correlate with L-dopa levels. Thus, it was conjectured that high dietary protein influences L-dopa's central nervous system effects, directly or indirectly, as a result of blood-brain barrier interference.<sup>2</sup> Closely monitoring and adjusting L-dopa dosage may be necessary because the required therapeutic range may become reduced when the dietary protein is raised.

### *Predisposing Foods*

In one study, there appeared to be an increased risk of Parkinson's disease that manifested in newly diagnosed patients who had consumed diets that were high in animal fat. Additionally, consuming foods high in vitamin D may increase the risk of a patient manifesting the disorder. This study also concluded that there appears to be a significant correlation

with vitamin A supplementation and an increased risk of contracting Parkinson's disease.<sup>3</sup>

### *Food Restriction*

Although the scientific literature is glaringly limited with regard to human studies involving food restriction and Parkinson's disease, animal models have offered interesting insights into possible human applications. In rodent studies, food restriction extends the animals' lifespans and decreases oxidative damage to lipids, proteins, and DNA. Excitotoxicity and mitochondrial impairment are believed to play major roles in neurodegenerative conditions such as Parkinson's, Alzheimer's, and Huntington's diseases. In rodent populations, alternate day-feeding regimens for 2-4 months have shown the ability to increase resistance to brain insults and protect against excitotoxicity.<sup>4</sup> Conceivably, human applications could involve using modified fasting or alternating caloric intakes.

### *Antioxidant Rich Diets*

There is growing evidence that diets that are high in antioxidants may help to confer some degree of protection against the neurodegenerative processes involved in the progression of Parkinson's disease. Representative of the growing belief behind this hypothesis, a study, conducted in the Netherlands, demonstrated that a high intake of dietary vitamin E may protect individuals against the occurrence of Parkinson's disease.<sup>5</sup>

## Environmental Factors

A leading hypothesis of the pathogenesis of Parkinson's has associated excessive oxidative damage of the substantia

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nigra dopamine-containing cells.<sup>6</sup> There are currently numerous predisposing etiologies under investigation as either triggering or contributing factors to the onset of Parkinson's disease. Among the most commonly held factors include infections, industrial exposure, pesticides, head injuries, low dietary antioxidant intakes, and not smoking.<sup>7,8</sup> Although the reason for a greater risk for contracting Parkinson's disease among nonsmokers has yet to be delineated, it may involve differences in premorbid personality traits.

Occupational exposures to manganese, copper, lead, and iron have been associated with the development of Parkinson's disease.<sup>9</sup> It also appears that organophosphate poisoning can lead to acute, yet reversible parkinsonism.<sup>10</sup> This sensitivity most likely represents a genetic susceptibility or another type of predisposition.

There is no question that environmental factors play a crucial role in the predisposition, development, and progression of the Parkinson's disease. Although all the evidence required for the creation of an all-inclusive list of epidemiologic factors has not been created, there is no question that external factors are intimately involved in the etiology of this disease. This is clearly illustrated by a study, conducted in 1992, in southwestern Finland with an urban and rural population of 196,864 subjects as a follow-up to a similar study conducted in the same area in 1971. The conclusions reached were that a significant male and rural predominance was present that was not seen in 1971, suggesting a probable environmental causative factor.<sup>11</sup>

### Supplementation Factors

There are a number of supplements that are important to our understanding of Parkinson's disease.

#### *Coenzyme Q10*

Although the research is preliminary, animal models have shown that Co Q10 may be useful in the treatment of Parkinson's disease. The effects appear to arise from Co Q10's ability to protect against neurotoxicity.<sup>12</sup>

#### *Copper*

Supplementation with copper should probably be avoided, including the copper that may be found in multivitamins. There is evidence that copper levels in the cerebrospinal fluid may become elevated in patients with Parkinson's disease, leading to increased oxidative damage.<sup>13</sup>

#### *Essential Fatty Acids*

Administration of essential fatty acids (EFAs), such as evening primrose oil, has been shown to help in controlling tremors.<sup>14</sup> It is believed that, through regulation of prostaglandin pathways and displacement of harmful fatty acids, EFAs support overall neurologic health.

#### *Folic Acid*

There is some evidence that a deficiency of folic acid may be associated with Parkinson's disease.<sup>15</sup> This trigger may result either from a clinical deficiency or from a genetic folic-acid metabolism error. Measuring serum folic acid levels and ensuring that mean corpuscular value red-blood-cell indices stay within 3 points of 90 is worth consideration.

#### *Iron*

There is a strong correlation in animal models between dietary intake of iron and brain iron concentrations. In addition, there is a significant increase in oxidized glutathione and a decrease in total glutathione levels. Iron alone does not appear to have a causative effect on triggering Parkinson's disease. However, this supplement appears to set the stage for future oxidative insults that could trigger

neurodegeneration that may, in turn, ultimately manifest as degenerative disease.<sup>16</sup>

There may be a synergistic relationship between the consumption of dietary animal fat and a systemic defect in iron metabolism with regard to the progression of lipid peroxidation in Parkinson's disease.<sup>17</sup>

#### *Magnesium*

Evidence suggests that a localized reduction in the caudate nucleus occurs in patients who are suffering from Parkinson's and other neurodegenerative diseases.<sup>18</sup> Because only 1 percent of all body magnesium is found in the serum, a standard chemistry panel with magnesium will not give an accurate physiologic read on true available levels. Instead, a cellular magnesium level test may provide a more accurate benchmark for checking supplementation efficacy.

#### *Manganese*

Measuring the body for elevated levels of manganese can offer insights regarding the presence of this possible causative, and promoting, metal in patients with Parkinson's disease. Elevated manganese levels have been attributed to neurodegeneration. When toxic levels arise from inhalation, accumulation occurs in the nasal ganglia.<sup>19</sup> It appears that the neurotoxicity leads to dopamine depletion and the production of neurotoxins.<sup>20</sup>

#### *Methionine*

Treatment with L-dopa reduces S-adenosyl-methionine (SAME) levels, yet supplementation with L-methionine, an essential amino acid, can cross the blood-brain barrier and be converted into SAME.<sup>21</sup> A large majority of patients treated with 1 g and working up to 5 g of methionine experienced a dramatic reduction in symptom severity.<sup>22</sup> Responses seen included increased activi-

## Use of phenylalanine may reduce the severity of some symptoms of Parkinson's disease.

ty levels, less rigidity, and improvements in attention span, concentration, voice control, muscular strength, and sleep and mood.

### Niacin

Treatment with L-dopa, when given with carbidopa or other decarboxylase inhibitors, may increase the risk for the development of niacin deficiency.<sup>23</sup> In turn, supplementation with niacin may extend the elevation of dopamine levels that result from the treatment with L-dopa.<sup>24</sup> In addition to niacin, 1-N-methylnicotinamide and the reduced form of nicotinamide adenine dinucleotide can also help to maintain dopamine levels.

### Phenylalanine

Use of this amino acid may reduce the severity of some symptoms of Parkinson's disease without helping to control tremors. Phenylalanine should not be taken with, or near the time of, consumption of L-dopa because phenylalanine will compete for absorption with the therapeutic agent. In one study, after suspending the conventional medication regimen, 15 patients were given diphenylamine, 100–250 mg, 2 times per day. Four weeks later, reexamination revealed significant improvements in speech and ability to walk as well as significant reductions in depression and rigidity.<sup>25</sup>

### Pyridoxine

It is well documented that a deficiency of vitamin B<sub>6</sub> can lead to decreased activity in the pathway responsible for the conversion of building-block tryptophan into serotonin.

In turn, treatment with L-dopa and a decarboxylase inhibitor may lead to a pyridoxine deficiency that increases the likelihood for the development of depression in patients with Parkinson's disease.<sup>23</sup> Correction of a marginal

Coenzyme Q10	25–100 mg per day
Evening primrose oil	1000 mg 2–3 times a day
Folic acid	400 mcg 2–3 times a day (with vitamin B <sub>12</sub> )
Magnesium	250 mg 1–2 times a day
Methionine	5000 mg per day (not at the same time as L-dopa)
Niacin	50 mg 2–3 times a day (watch for flushing)
Phenylalanine	100–1000 mg per day
Vitamin B <sub>6</sub>	50–250 mg per day (not at the same time as L-dopa)
Tryptophan	100–1000 mg per day (not at the same time as L-dopa)
Vitamin C	1000 mg 3 times a day
Vitamin E	800–1200+ international units per day

deficiency of the vitamin may help to control tremors and may improve muscular control.<sup>26</sup>

### Tryptophan

Supplementation with this mood-enhancing amino acid, when given at different intervals than when L-dopa is administered, to avoid competitive absorption interference, can help to control Parkinson's disease-associated depression and may improve functional ability.<sup>27,28</sup>

### Vitamins C and E

Dopamine-containing cells in the substantia nigra may become damaged from increased lipid peroxidation. Protecting against, and slowing, oxidative damage can delay the need for starting conventional drug therapy. In one study, 15 patients were administered 3000 mg of vitamin C and 3200 international units of vitamin E gradually. These patients were able to delay the start of drug therapy by 2.5 years.<sup>29</sup>

### Zinc

It may be worth actively avoiding supplements, including multivitamins, with zinc unless there are definitive signs of zinc deficiency. Research has

shown that zinc levels are often elevated in the caudate nucleus, lateral putamen, and substantia nigra in Parkinson's disease. Until further evidence about the role that elevated zinc levels play is discovered, cautious use is highly warranted.<sup>30</sup>

### Possible Interactions

There are three important interactions with L-dopa that should be avoided.

#### Alcohol

Limiting the intake of alcohol is important because it can antagonize the effects of dopamine and result in diminished control of symptoms.

#### Kava-Kava

Known as *Piper methysticum*, this popular treatment for anxiety and mild depression may decrease the effectiveness of L-dopa as a result of a dopamine antagonistic action.<sup>31</sup>

#### Protein

Consumption of large quantities of protein containing foods, can compete with L-dopa, an amino acid for transport through the intestine, and blood-brain barrier. A diet that varies greatly in protein content

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can result in difficulty in controlling symptoms.

Although other significant interactions are likely to exist, these examples serve as reminders that vitamins, minerals, herbs and food can alter the effectiveness of conventional treatments significantly at times and must be considered when determining therapeutic doses.

### Summary

As with so many degenerative conditions, often, the difference between the manifestation of a disease or its symptoms is largely dependent on a person's overall wellness and total physical burdens. Examining risk factors of patients with strong family histories of Parkinson's disease or with early signs of the disorder can allow meaningful changes in one's exposure risks and greatly improve prognosis. Once, dietary and environmental variables have been controlled, nutritional and supplementation intervention protocols can improve the quality of life and clinical outcomes for patients who are suffering from Parkinson's disease and other progressive neurodegenerative conditions. □

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