

# Editorials

## Pantethine: Potential Treatment for Parkinson's Disease

Parkinson's disease is a degenerative neurological disease that results from the loss of dopamine-producing cells in the substantia nigra. Symptoms include tremor, rigidity, slowing of movement, impaired balance and coordination, and depression. While the cause of Parkinson's disease is not known, it is believed to result from exposure to endogenous or exogenous (such as some pesticides) compounds that are toxic to substantia nigra cells, possibly in combination with various genetic defects that impair the capacity to detoxify such compounds.

A number of medications and some natural substances (L-methionine, DL-phenylalanine, octacosanol) have been used to relieve the symptoms of Parkinson's disease, but these treatments do not appear to slow the progression of the disease. Deprenyl (selegiline), a monoamine oxidase inhibitor, has been reported to delay the onset of disability in Parkinson's patients. High-dose vitamin E (3,200 IU/day) combined with vitamin C (3,000 mg/day) has also been found to slow the progression of the disease, presumably by inhibiting oxidative damage to brain cells. In addition, there is evidence that repeated intravenous administration of glutathione can relieve symptoms and slow disease progression. Despite this array of treatment possibilities, however, results are unsatisfactory for many patients.

There is reason to believe, on theoretical grounds, that supplementation with pantethine (a normal metabolite of pantothenic acid and a precursor to coenzyme A) might be an effective treatment for Parkinson's disease. The evidence supporting that possibility is as follows:

1. A substantial body of research suggests that 3,4-dihydroxyphenylacetaldehyde (DOPAL) is a toxic metabolite of dopamine *in vivo* that contributes to the pathogenesis of Parkinson's disease (*Brain Res* 2003;989:205-13).

2. One strategy for decreasing the toxic effect of DOPAL on dopaminergic

neurons would be to increase the activity of aldehyde dehydrogenase (ALDH), a group of enzymes that catalyze the metabolism of aldehydes, including DOPAL. That approach may be especially useful, since ALDH activity is decreased in the substantia nigra of patients with Parkinson's disease, and the extent of the decrease correlates with the degree of neurological dysfunction (*Neurobiol Dis* 2003;14:637-47).

3. Pantethine appears to be capable of stimulating ALDH activity, as demonstrated by its capacity to reduce blood levels of acetaldehyde (a metabolite of ethanol) following ethanol ingestion by healthy volunteers (*Alcohol Clin Exp Res* 1985;9:272-276). Since pantethine did not reduce blood levels of ethanol in that study, the effect of pantethine appears to have been due to accelerated degradation, rather than reduced formation, of acetaldehyde. Further evidence of an aldehyde-detoxifying effect of pantethine is my clinical observations with medical students who were exposed to formaldehyde in the anatomy lab. Several students who reported becoming ill each time they went to the anatomy lab were advised to try 600 to 900 mg of pantethine per day. In each case, pantethine supplementation significantly reduced the adverse effects of formaldehyde.

4. Pantethine has been mentioned previously as a potential treatment for Parkinson's disease (*Prog Neuropsychopharmacol Biol Psychiatry* 1990;14: 835-62), for reasons other than its potential to increase ADH activity.

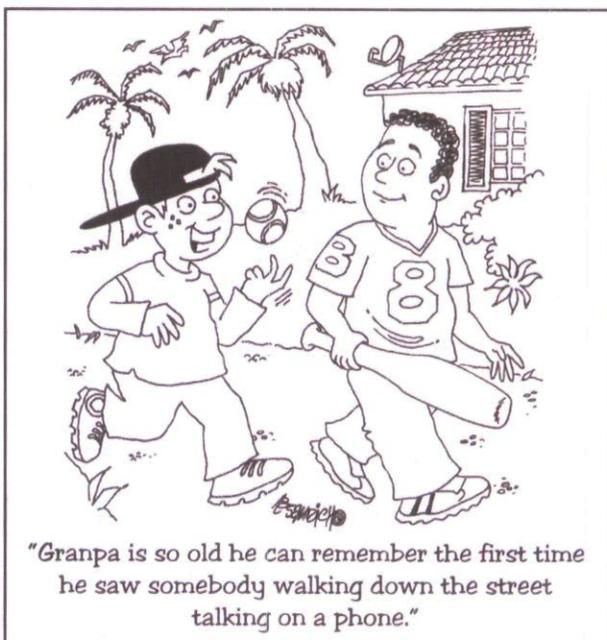
Pantethine has been extensively studied as a cholesterol-lowering agent, and it has been used for that purpose, primarily in Europe, for more than

20 years. Except for occasional, mild gastrointestinal side effects, no adverse effects have been reported. The usual dose of pantethine is 300 mg three times a day with meals.

It is possible that long-term administration of pantethine would slow the progression of Parkinson's disease, although it could take several years of supplementation before such an effect would be recognizable. It is also conceivable that pantethine supplementation could help "rescue" substantia nigra cells that have been rendered dysfunctional by the disease process, but are still living. If that were the case, then clinical improvement might be observed with pantethine after as little as a few weeks or a few months.

Readers who are interested in a trial of pantethine for patients with Parkinson's disease are requested to communicate their findings by email ([dragy@earthlink.net](mailto:dragy@earthlink.net)). For people with this debilitating disease, supplementation with pantethine appears to pose little risk, and it could result in substantial benefit.

Alan R. Gaby, MD



"Granpa is so old he can remember the first time he saw somebody walking down the street talking on a phone."

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