





the hand. As the condition progresses, tremors may involve the arms, legs, head or jaw. The tremor is more noticeable when relaxing, but reduced when moving or sleeping.

Bradykinesia, which simply means 'slowness of movement', is also a recorded symptom: patients experience difficulty initiating movement (akinesia), often referred to as freezing, or movement taking longer to perform. Walking can become progressively difficult and slow, with patients needing to make a conscious effort to lift their feet to prevent shuffling or falling.

Mobility problems occur due to a stiffness or rigidity of muscles, which can also result in falls. As different muscles become affected, facial expression may be affected, speech may become quiet or rapid and small or difficult handwriting is noted by some.

Additional symptoms may occur of anxiety or low mood. Memory and reasoning ability can also become part of the symptom picture, particularly as the condition progresses.

There is no specific test currently available that can confirm the presence of the condition: diagnosis is made on symptom observations and after tests have eliminated other potential causes or conditions.

NHS National Guidelines advise that Parkinson's should be suspected in people presenting with tremor, stiffness, slowness and balance or gait problems. Doctors should refer patients prior to treatment to a specialist in differential diagnosis of Parkinson's disease. The condition should be diagnosed clinically and based on the UK Parkinson's Disease Society Brain Bank Criteria. Regularly reviews of the diagnosis of PD should be undertaken.

## Treatment

Currently there is no cure for Parkinson's disease: treatment focuses on the use of medication to control the symptoms with a variety of drugs, including:

- Drugs which replace dopamine
- Drugs which mimic the action of dopamine
- Drugs which prevent the breakdown of dopamine
- Drugs which inhibit the action of acetylcholine

As the symptoms of the condition vary between individuals, patients'



## A Multi-factorial condition

One area on which most agree is that Parkinson's is a multi-factorial condition with toxic exposure, genetic predisposition and diet playing a potential part for the onset of the condition. Susceptibility, it appears, may also be influenced by some rather surprising factors: one well-known toxin, nicotine, may well offer some protection from Parkinson's, and whilst smoking would not be recommended as a preventative treatment, the authors of this research suggest that nicotine may be of potential therapeutic value.<sup>7</sup>

## Nutrition

Parkinson's disease, as with many conditions, is believed to have links with diet in both the development of the condition and control of symptoms. A dietary study carried out with both males and females and followed up after sixteen years found that, 'Dietary patterns with a high intake of fruit, vegetables, legumes, whole grains, nuts, fish, and poultry and a low intake of saturated fat and a moderate intake of alcohol may protect against PD'.<sup>8</sup> Much of the interest in neurological conditions such as Parkinson's and nutrition looks at the impact of exposure to free radicals or pro-oxidants and the corresponding lack of antioxidants in the individual's diet. The cells of the brain are considered particularly susceptible to oxidative stress, including the cells in the substantia nigra, the dopamine-producing area of the brain.

Antioxidants have the ability to protect cells from damage, and many studies have been carried out in this area with papers dating back to 1998 considering the part that oxidative stress might play in the development of diseases such as Parkinson's disease.<sup>9</sup>

Inhibition of the oxidation of dopamine by antioxidants was the subject of research which found that certain plant-derived antioxidants can inhibit dopamine oxidation, with ascorbic acid (vitamin C) having the most effect.<sup>10</sup>

## Iron

Research for the aetiology of Parkinson's disease has evidenced a potential disrupted iron metabolism together with the presence of increased iron levels found within the substantia nigra of Parkinson's disease patients. Oxidative damage to cells resulting from the Fenton reaction of iron and the accumulation of iron in the substantia nigra are associated with neuronal loss and Lewy body pathology.<sup>11,12,13</sup>



- Resveratrol and quercetin are considered protective of dopaminergic neurons, diminishing apoptotic neuronal cell death by acting on the expression of pro- and anti-apoptotic genes.<sup>25</sup>
- The mulberry fruit has demonstrated neuroprotective effects in vitro and in vivo for Parkinson's disease models, providing a source of the anthocyanins. The mulberry was found to significantly protect the cells from neurotoxicity in a dose dependent manner.<sup>26</sup>
- Curcumin has demonstrated the ability to reduce reactive oxygen species and protect cells against apoptosis; the ability for curcumin to cross the blood brain barrier makes this particularly interesting for neurological conditions, with the potential therapeutic value for treating Parkinson's disease and other neurodegenerative diseases highlighted.<sup>27</sup> Curcumin and antioxidants have been identified as a potential pre-symptom therapeutic intervention in blocking or delaying the onset of Parkinson's disease.<sup>28</sup> Animals pre-treated with curcumin or naringenin, a citrus flavonoid, also showed clear neuroprotective properties in a model of Parkinson's disease.<sup>29</sup>
- Researchers identified extracts of tangerine peel, described as 'rich in polymethoxylated flavones', cocoa, a specific 'rich in procyanidins', and red clover providing isoflavones as protective of the dopaminergic neurons with short term supplementation in a rat model of Parkinson's disease.<sup>30</sup>

## Glutathione

An important antioxidant produced in the body, the levels of which are known to fall with aging, has been proposed for the pathogenesis of Parkinson's disease with decreased glutathione concentrations in the substantia nigra observed in preclinical stages.<sup>31</sup>

## CoEnzyme Q10

Has been assessed in a double blind trial for the ability to slow functional decline in Parkinson's disease. Patients selected were those in the early stages of disease, not requiring treatment for their condition. At follow-up, less disability was found to have developed in those receiving CoQ10, with the greatest benefits linked to the higher doses of 1200mg per day.<sup>32</sup>

## Vitamins

### B6

A review for the dietary intake of vitamins for the incidence of Parkinson's disease indicated a low intake of vitamin B6 being independently



## Dietary pattern

A study of dietary pattern and the risk of Parkinson's disease after a sixteen year follow-up identified two dietary patterns, 'prudent' containing high intakes of fruit, vegetables and fish, and the 'Western diet', characterised by a high intake of red meat, processed meats, refined grains, desserts and high fat dairy. On analysis, the prudent diet was found to be inversely associated with the risk for Parkinson's disease.<sup>38</sup> The similarity for the prudent diet and that of the Mediterranean diet, with the high intakes of fruit and vegetables, is also evident. A meta-analysis for adherence to the Mediterranean diet found a significant improvement in health, with a reduction in overall mortality from cardiovascular disease, cancer and reduced incidence of Parkinson's and Alzheimer's disease.<sup>39</sup> The beneficial impact of a Mediterranean style diet, improving nutritional balance of the diet and gastro-intestinal dysfunction, were also highlighted as providing an improved response to pharmacological treatment. The positive effects on levodopa pharmacokinetics were seen to be mainly due to the increased fibre intake from the plant derived foods.<sup>40</sup>

The diet that is low in processed foods and contains an increased intake of fruit and vegetables, nuts, seeds, natural wholegrains, healthy oils and lean proteins such as white meat and fish has much support for its health benefits across a wide range of research. The processed Western diet is associated with an excess of calories, increased saturated fats plus low nutrient and fibre intakes and a resultant decreased digestive and bowel function, leading to an increasing incidence of constipation. The improved pharmacokinetics of the Parkinson's drug identified with increased fibre intake and improved gastro-intestinal function,<sup>40</sup> become relevant when the presence of constipation is considered. This is a frequently reported problem amongst Parkinson's patients, often considered an inevitable part of the disease or of the aging process. A study reported in 2009 applies an interesting view to this, with constipation preceding Parkinson's disease seen in research, the association was significant and their findings suggest that constipation occurring as early as twenty years or more before the onset of motor symptoms is associated with an increased risk of Parkinson's disease.<sup>41</sup>

Ensuring a healthy digestive tract would therefore provide a further potentially preventative strategy with dietary assistance to alleviate constipation, also offering beneficial factors for those receiving treatment for Parkinson's.



- Nutrient/Drug interactions are important, and due to the varied and increasing number of new drugs used it is important that this is considered. For example, Levodopa, when prescribed alone, can be adversely affected by vitamin B6.
- Undesirable response to dietary changes: for example, those with poor motility may require a gradual dietary change to a natural, higher fibre diet. Those with conditions such as Diverticulitis may not be suitable for higher levels of fibre or some of the natural constipation preparations.
- In the elderly, consider issues such as food preparation and difficulties with eating a natural, higher fibre diet.

## References

1. [www.parkinsons.org.uk/research/current\\_research/what\\_causes\\_parkinsons.aspx](http://www.parkinsons.org.uk/research/current_research/what_causes_parkinsons.aspx)
2. [www.parkinsons.org.uk/default.aspx?page=10057](http://www.parkinsons.org.uk/default.aspx?page=10057)
3. Beate Ritz, Fei Yu.2000. Parkinson's disease mortality and pesticide exposure in California 1984–1994. *International Journal of Epidemiology* 29:323-329
4. Dana B Hancock, Eden R Martin, Gregory M Mayhew, Jeffrey M Stajich, Rita Jewett, Mark A Stacy, Burton L Scott, Jeffery M Vance, William K Scott.(2008) Pesticide exposure and risk of Parkinson's disease: A family-based case-control study. *BMC Neurology*, 8:6 doi:10.1186/1471-2377-8-6
5. Rebecca L. Miller, Marilyn James-Kracke, Grace Y. Sun Albert Y. Sun.(2009) Oxidative and Inflammatory Pathways in Parkinson's Disease. *Neurochemical Research* 34:pg 55–65.DOI 10.1007/s11064-008-9656-2
6. Jeffrey S. Gillette, and Jeffrey R. Bloomquist 2003. Differential up-regulation of striatal dopamine transporter and  $\alpha$ -synuclein by the pyrethroid insecticide permethrin. *Toxicology and Applied Pharmacology* Volume 192, Issue 3, 1 November Pages 287-293
7. Karen Riveles, Luping Z. Huang, Maryka Quik.2008 Cigarette smoke, nicotine and cotinine protect against 6-hydroxydopamine-induced toxicity in SH-SY5Y cells *NeuroToxicology* Volume 29, Issue 3, May, Pages 421-427
8. Gao X, Chen H, Fung TT, Logroscino G, Schwarzschild MA, Hu FB, Ascherio A. 2007. Prospective study of dietary pattern and risk of Parkinson disease. *Am J Clin Nutr.* Nov;86(5):1486-94.
9. A. T. Diplock J.-L. Charleux<sup>2</sup>, G. Crozier-Willi, F.J Kok, C. Rice-Evans, M. Roberfroid, W. Stahl. and J. Vina-Ribes. Functional food science and defence against reactive oxidative species. *British Journal of Nutrition* (1998), 80, Suppl. 1, S77-S112 577



23. O Weinreb, S Mandel, T Amit, MBH Youdim.(2004). Neurological mechanisms of green tea polyphenols in Alzheimer's and Parkinson's diseases. *The Journal of Nutritional Biochemistry*, Volume 15, Issue 9, Pages 506-516
24. Silvia Mandel, Tamar Amit, Lydia Reznichenko, Orly Weinreb, Moussa B. H. Youdim. (2006) Green tea catechins as brain-permeable, natural iron chelators-antioxidants for the treatment of neurodegenerative disorders. *Molecular Nutrition & Food Research* Volume 50, Issue 2, Date:, Pages: 229-234
25. Julie Bournival, Patrik Quessy, Maria-Grazia Martinoli. (2009) Protective Effects of Resveratrol and Quercetin Against MPP -Induced Oxidative Stress Act by Modulating Markers of Apoptotic Death in Dopaminergic Neurons. *Cell Molecular Neurobiology* 29:pg 1169–1180 DOI 10.1007/s10571-009-9411-5
26. Hyo Geun Kim. Mi Sun Ju. Jin Sup Shim. Min Cheol Kim. Sang-Hun Lee. Young buhm Huh.Sun Yeou Kim. Myung Sook Oh.(2010) Mulberry fruit protects dopaminergic neurons in toxin-induced Parkinson's disease models. *British Journal of Nutrition*, 104. Pg 8-16 doi:10.1017/S0007114510000218
27. Min S Wang, Shanta Boddapati. Sharareh Emadi and Michael R Sierks. (2010) Curcumin reduces reduces  $\alpha$ -synuclein induced cytotoxicity in Parkinson's disease cell model. *Bio Med Central Neuroscience* , 11:57 doi:10.1186/1471-2202-11-57
28. Gladson Muthian, Jennifer King, Veronica Mackey, Kedar Prasad, Clive I Charlton. (2008) Blockage of the Proposed Precipitating Stage for Parkinson's Disease by Antioxidants: A Potential Preventative Measure for PD. *The FASEB Journal.*;22: 715. 2.abstract only available.
29. Virginia Zbarsky, Krishhna P Datla,Shabnam Parkar,deepal K Rai, Okezie I Aruoma, David T Dexter.(2005) Neuroprotective properties of the natural phenolic antioxidants curcumin and naringenin but not quercetin and fisetin in a 6-OHDA model of Parkinson's disease. *Free Radical Research*, 39(10): pg.1119-1125
30. Krishna P. Datla, PhD, Virginia Zbarsky, PhD, Deepal Rai, BSc, Shabnam Parkar, BSc,Naomi Osakabe, PhD, Okezie I. Aruoma, DSc, and David T. Dexter, PhD.(2007) Short-Term Supplementation with Plant Extracts Rich in Flavonoids Protect Nigrostriatal Dopaminergic Neurons in a Rat Model of Parkinson's Disease. *Journal of the American College of Nutrition*, Vol. 26, No. 4,pg 341–349.
31. Jörg B. Schulz, Jörg Lindenau, Jan Seyfried and Johannes Dichgans.(2000). Glutathione, oxidative stress and neurodegeneration. *European. Journal. Biochemistry.* 267, pg 4904-4911
32. Shults CW, Oakes D, Kiebertz K, Beal MF, Haas R, Plumb S, Juncos JL, Nutt J, Shoulson I, Carter J, Kompoliti K, Perlmutter JS, Reich S, Stern M, Watts RL, Kurlan R, Molho E, Harrison M, Lew M;( 2002). Parkinson Study Group. Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. *Archives Neurology.* Oct;59(10):pg1541-50.

33. K. Murakami, Y. Miyake, S. Sasaki, K. Tanaka, W. Fukushima. (2010) Dietary intake of folate, vitamin B6, vitamin B12 and riboflavin and risk of Parkinson's disease: a case-control study in Japan". *British Journal of Nutrition*. Published online doi: 10.1017/S0007114510001005
34. Zhang SM, Hernán MA, Chen H, Spiegelman D, Willett WC, Ascherio A.(2002) Intakes of vitamins E and C, carotenoids, vitamin supplements, and PD risk. *Neurology* 22;59(8):pg 1161-9.
35. M.L. Evatt, M.R. DeLong, N. Khazai, A. Rosen, S. Triche, V. Tangpricha.(2008) Prevalence of Vitamin D Insufficiency in Patients with Parkinson Disease and Alzheimer Disease. *Archives of Neurology*. Volume 65, Pages 1348-1352
36. David W. Anderson, Kristin A. Bradbury and Jay S. Schneider.(2006) Neuroprotection in Parkinson models varies with toxin administration protocol . *European Journal of Neuroscience*, Vol. 24, pp. 3174-3182,
37. Lonneke M. L. de Lau, Peter J. Koudstaal, Albert Hofman, and Monique M. B. Breteler. (2006) Serum Cholesterol Levels and the Risk of Parkinson's Disease. *American Journal of Epidemiology*. Vol. 164, No. 10.pg 998.1002 .DOI: 10.1093/aje/kwj283
38. Gao X, Chen H, Fung TT, Logroscino G, Schwarzschild MA, Hu FB, Ascherio A.(2007) Prospective study of dietary pattern and risk of Parkinson disease. *American Journal of Clinical Nutrition*. 86(5):pg1486-94.
39. Francesco Sofi, Francesca Cesari, Rosanna Abbate, Gian Franco Gensini, Alessandro Casini.( 2008) Adherence to Mediterranean diet and health status:meta-analysis. *BMJ*;337:a1344 doi:10.1136/bmj.a1344
40. Emanuele Cereda, Michela Barichella, Gianni Pezzoli. (2010) Controlled-protein dietary regimens for Parkinson's disease. *Nutritional Neuroscience* Vol 13 No 1 pg 29
41. R. Savica, MD, MSc, J. M. Carlin, BA, B. R. Grossardt, MS, J. H. Bower, MD, MSc, J. E. Ahlskog, PhD, MD, D. M. Maraganore, MD, A. E. Bharucha, MD and W. A. Rocca, MD, MPH . (2009). A case-control study. Medical records documentation of constipation preceding Parkinson disease. *Neurology* 2009;73:pg 1752-1758.
42. Juan J. García, Nélida Fernández, Ángela P. Calle, M. José Díez, Ana Sahagún, Matilde Sierra. (2009) Effects of *Plantago ovata* Husk on Levodopa (with Carbidopa) Bioavailability in Rabbits with Autonomic Gastrointestinal Disorders. *Drug Metab Dispos* 37:pg1434-1442; doi:10.1124/dmd.108.026229
43. Eduardo Tolosa MD.Carles Gaig MD Joan Santamaría MD.Yaroslau Compta MD.2009 Diagnosis and the premotor phase of Parkinson disease . *Neurology* 72(Suppl 2):S12-S20





## **CYTOPLAN LTD.**

**Unit 8 Hanley Workshops, Hanley Road,  
Hanley Swan, Worcestershire. WR8 0DX.**

**t: 01684 310099**

**f: 01684 312000**

**e: [info@cytoplan.co.uk](mailto:info@cytoplan.co.uk)**

**[www.cytoplan.co.uk](http://www.cytoplan.co.uk)**

**© Copyright - Cytoplan Ltd 2011**



**5060202183166**

**CYT HIS-10 Parkinson's Disease**