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Parkinson's Disease

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Parkinson's disease is a condition of neural degeneration. It affects approximately 1% of people 65 years and older, and 0.4% of those older than 40 years. It occurs across all ethnic and racial groups, and also approximately equal sex distribution. The most common form of Parkinsonism (idiopathic Parkinsonism) develops between 45 and 65 years of age.

The etiology of Parkinsonism may be multifactorial. Exposure to certain toxins (for example manganese dust, carbon disulfide) and severe carbon monoxide poisoning may play a role. It is also seen in people who took MPTP recreationally – which converts to a neurotoxin in the body. Other drugs and medication can cause a reversible form of this disease. Postencephalitic parkinsonism is becoming more rare, and parkinsonism can also be related to a brain tumor or some other progressive space-occupying lesion. The most common form of Parkinsonism is idiopathic, in which dopamine is depleted and an imbalance in neurotransmitters is created. Treatment in this case is directed and redressing the imbalance.

Symptoms

Symptoms of Parkinson's Disease include shuffling gait, slowness of movement, tendency for falling, resting tremors (which usually affect

one limb or those on one side of the body before becoming more generalized, if they occur at all, and can be aggravated by stress or fatigue), rigidity of muscles, postural instability, mask-like facial expression, drooling, softness of voice, depression, and a decline in mental functioning. Seborrhea of the scalp and face is common.

Diagnosis

Diagnosis of Parkinson's Disease is via clinical and physical examinations for the signs and symptoms noted above. Health conditions which can mimic the signs of Parkinson's need to be effectively ruled out, including depression, Wilson's Disease, Huntington's Disease, Shy-Drager syndrome, Creutzfeldt-Jakob disease, and other neurological disorders and dysfunctions.

Diet & Lifestyle

Environment and lifestyle can play a large role in the etiology of Parkinson's Disease. HOC physicians may utilize detoxification therapies to remove heavy metal and toxin buildup in the body which may be contributing to Parkinsons' development and progression. The results from these therapies alone can show dramatic improvement in cognitive and motor functioning. Dietary changes and nutritional supplementation can also alleviate the symptoms of this disease, restoring function and improving quality of life. Physical therapies assist in maintaining range of motion and physical capabilities.

Studies

Research suggests that glutathione, a critically important brain chemical, is deficient in Parkinson's patients and may play a significant role in the treatment of this disease. Glutathione is a powerful antioxidant, and helps to prevent free radical damage to brain tissue. So far, the intravenous use of glutathione has shown promising results in reducing tremors and improving movement and balance.

Ongoing clinical trials suggest that multi-modality therapy, combining intravenous glutathione with Hyperbaric Oxygenation Therapy (HBOT) and nutritional supplementation, may be more effective than glutathione alone. HOC is currently conducting clinical trials on combination therapy for Parkinson's disease and is looking for participants. Please contact Dr. Tasreen Alibhai, ND at 604-520-3941 for further information.

Idiopathic Parkinson's Disease (PD) and Pesticides: an Argument for Rational Therapy Based on Known Epidemiological Studies.

By Dr. Zayd Ratansi

Although by strict criteria, the etiology of Parkinson's Disease (PD) is still considered idiopathic, one cannot ignore the very large body of epidemiological evidence linking long term herbicide, fungicide and pesticide exposure to the pathogenesis of Parkinson's disease.

Dozens of studies using 1-methyl-4-phenylpyridinium (MPTP) and Rotenone, both herbicide analogues, have helped to elucidate the biological cascade that leads to selective cell death of dopaminergic neurons of the substantia nigra of PD patients. Present day treatment of this refractory neurological disease consists mainly of replacement of dopamine through decarboxylation of levodopa, and promotion of its uptake through the BBB by peripheral inhibition of this conversion by carbidopa. Other approaches have included slowing the breakdown of dopamine by MAO inhibition through the use of Deprenyl (Selegiline), and inhibiting glutamate (excitatory neurotransmitter) induced neuronal apoptosis through NMDA receptor antagonists. A couple of common themes that these well accepted treatments share are a significant amount of side effects, and the fact that they highly concentrate on curtailing the end products of the Parkinsonian biochemical inhibition, replacing dopamine and avoiding oxidative neuronal cell destruction. These are logical treatment strategies and necessary for preventing the patients' clinical decompensation. However, reviewing the medical literature and a good number in vivo and in vitro studies, it is clear that many safe, intermediary natural interventions exist to prevent the initial loss of dopamine (DA) neurons in the first place. The rest of this paper will focus on some of these interventions. One of the main focuses of the paper will be considering the hypothesis that PD may be linked to pesticide exposure and that treating the causative factor with detoxification regimens can lead to long lasting clinical improvement in Parkinson's patients.

First, a quick review of the biochemical defects postulated to underlie PD. It is agreed that the main pathogenic defects center along the function of the mitochondrial complex I of the electron transport chain in the DA cells of the substantia nigra. In normal function, extra cellular NADH reduces FMN. The reduced FMNH2 transfers a pair of electrons to a series of between 6-8 Iron sulfur (thiol) centers; the final result is the reduction of Ubiqinone or Coenzyme Q10. Down through another major series of steps and through complex 3 results in the oxidative phosporylation of ATP. (Biochemistry, Mckee). It is postulated that, pesticides, herbicides and fungicides, analogues of MPTP/MPP+ can start the process of DA substantia nigra apoptosis by binding to NADH dehydrogenase multienzyme complex [1]. The process of neuromelination or the auto oxidation of DA cells [2]occurs presumably when these iron sulfur centers, failing to be reduced by FMNH2, start to accumulate [3]. The highly neurotoxic byproducts of the inhibition of the ferredoxin-thioredoxin system and the iron/melanin interaction: hydrogen peroxide (H2O2), and nitrous oxide (NO) [4] [5] [6], rapidly depletes glutathione reductase to its oxidized form of GSSG [7] [8]. Gamma GT/dipeptidase hydrolyses GSSG to its constituent amino acids: glutamate, glycine and cysteine [9]. The severe rise in excitatory glutamate levels in addition to the above mentioned reactive oxygen species (ROS) lead to further formation of highly neurotoxic peroxynitrite (ONOO-) and hydroxyl radicals (OH-) [10] causing lipid peroxidation and subsequent cell death of DA neurons in the striatum and substantia nigra [11].

Next, is the implication of pesticides, herbicides and fungicides involved in the etiological pathogenesis of PD? Numerous retrospective studies have been done showing a very high correlation between Parkinsonian incidence and rural living, pesticide exposure, drinking from well water (presumably contaminated from pesticide soil run off) [12] [13] [14-16] [17-19]. Furthermore, postmortem double blind studies of PD patients have detected selectively high quantities of

Dieldrin, hexachlorocyclohexane (lindane), PCB's, and DDE in PD tissues [20] [21]. Animal studies have confirmed that the well-known fungicide Paraquat directly causes DA cell death:

"The data indicate that paraquat like MPTP elicits a dose-dependent decrease in substantia nigra dopaminergic neurons assessed by a Fluoro-gold prelabeling method, a decline in striatal dopamine nerve terminal density assessed by measurement of tyrosine hydroxylase immunoreactivity; and neurobehavioral syndrome characterized by reduced ambulatory activity. Taken together, these data suggest that systemically absorbed paraquat crosses the blood- brain barrier to cause destruction of dopamine neurons in the substantia nigra, consequent reduction of dopaminergic innervation of the striatum and a neurobehavioral syndrome similar to the well characterized and bona fide dopaminergic toxin MPTP." [22]

A study showed the combined effects of herbicides: paraquat and Maneb had synergistic effects in inhibiting nigrostriatal dopamine systems in a study with mice [23].

One study concluded that ongoing depletion of GSH implied the continued local presence of a (xenobiotic) neurotoxin [24]. Environmental studies in Israel have confirmed abundant pesticide traces of carbamates and organophosphates in areas where there were unusually high incidence of PD and preparkinsonian symptoms [25]. Systemic ability to breakdown hydrogen peroxide, also elevated in the substantia nigra of PD, was compromised by the inhibition of superoxide dismutase (SOD) through the administration of the herbicides MCPA and Aniten I in an animal study [26].

This is not to imply that PD has solely, exogenous causative determinants. Many of the epidemiological studies show that family history is the most highly correlated risk factor for the development of Parkinson's disease. [16, 17]. One could hypothesize from a quick review of the literature, that a combined ecogenetic factors are both necessary for the development of PD. This is evidenced by the different polymorphisms of GSTP1-1 and CYP2D6 genes that can make individuals more susceptible to quicker GSH depletion and problems with xenobiotic metabolism[17, 27]. In other words, both hereditary susceptibility and mild environmental exposure or just frequent and intense exposure till GSH systems are overwhelmed are required for PD development. This is consistent with the epidemiological studies.

In addition to pesticides, heavy metal exposure can be another compounding environmental factor in the development of PD, specifically: iron, copper, and manganese [28-30]. Manganese (Mn++) and Iron (Fe++/+++) both catalyze the auto oxidation of dopamine. They do this by there production of hydroxyl and cysteine derived thyl radicals [6]. These reactions have been confirmed in vitro [31]. Manganese toxicity can occur as a result of exhaust fumes from the antiknock, fuel additive Methylcyclopenadienyl Mn tricarbonyl (MMT). While iron overload, hemochromotosis, can be due to genetic HLA markers that predispose to increased Fe++ absorption, dietary iron overload, sideroblastic anemia, occupational exposure, and iron supplementation (Robbins, Pathologic basis of disease).

The aforementioned review of PD development will now

serve as background for the rational for the predopaminergic cell death natural interventions presented hereafter. These interventions are stressed because the current medical literature supports their promise, they are preventative in the sense that they preserve the integrity of the substantia nigra rather than focus on replacing dopamine, and they are by and large, non-toxic. L-dopa itself, the mainstay treatment for PD, has been shown to increase free radical production, which is ameliorated by high dose antioxidants [32]. The limitations of these natural interventions must also be stressed in that they do not treat the actual *cause* of the disease if indeed Parkinson's has an ecogenetic etiology. This would be better addressed by environmental medicine and medical genetics. The former will also be discussed and considered in this paper in the scope of natural treatment for PD.

One natural way to overcome the mitochondrial respiratory compromise in PD is to overcome its deficits through mass action of respiratory chain inducers. Two substances with this ability that have been studied are Nicotine Adenine Dinucleotide (NADH) and Acetyl-L Carnitine. NADH can stimulate the natural production of Levodopa via its activation of tyrosine hydroxylase (TH), the rate limiting enzyme in levodopa production [33]. Birkmayer et al has demonstrated both clinical and objective improvements in PD patients in both large and small open trials using IV NADH [34, 35]. Acetyl-L-Carnitine, by its ability to cross mitochondrial membranes and supply precursor to pyruvate to the Krebs cycle has also been postulated to aid in PD. Acyl L- Carnitine has been shown to protect DA neurons from MPTP induced cytotoxicity [36] and showed clinical improvement in aiding PD patients in sleeping and ambulation [37].

The literature has seemingly reached a consensus that the neuronal cell death in PD is due to oxidatative stress. In particular, GSH depletion has been targeted as the source of this increased oxidative stress [8, 38]. Many studies have focused on the repletion of GSH as a means to prevent the oxidative death of DA neuronal cells. This accomplished in a variety of ways. First, there is direct GSH IM or IV replacement. Sechi et al. demonstrated clinical improvement in all PD patients in a small study of infusion of IV GSH [39, 40]. The same results were shown in an in vivo animal study involving rat brains [41]. A second, seemingly equally effective way to increase GSH concentration is through the administration of GSH precursors: Selenium, and specifically N-acetylcysteine (NAC). NAC provides the sulfhydyl groups in the iron sulfur centers of mitochondrial complex I in addition to being a GSH precursor [42] Offen et al, in a animal study, demonstrated the protective effect of NAC, GSH and other thiol containing compounds against nigrostriatal apoptosis [43]. In another study, Martinez Banaclocha demonstrated that NAC maximized mitochondrial complex I activity in aging mice [44]. In a recent human trial by De Rosa et al, NAC demonstrated a direct unequivocal increase in GSH levels of HIV patients [45]. Selenium showed in vivo increases in both SOD and GSH and protected against Amphetamine induced nigrostriatal toxicity in a study of mice [46].

One other very practical way to increase intracellular GSH is through the intake of dietary or supplementary cruciferous vegetables, which contain a natural abundance of thiol groups. The efficacy of this approach has also been shown in vivo studies [47] [48]. Vitamin D3, cholecalciferol has also been purported to enhance the intracellular GSH concentration in the CNS [49].

A third, indirect way of enacting nigrostriatal protection is to

supplement with other antioxidants shown to protect these cells from ROS. Melatonin and Vitamin C have been shown to be potent neurological antioxidants. Melatonin quenches the free radicals of literally all the known ROS active in PD: hydroxyl radicals, superoxide anions, peroxynitrite, and peroxyl radicals. In addition to these scavenging effects, melatonin also inhibits nitric oxide synthase and stimulate mRNA for SOD, glutathione peroxidase and glutathione reductase. Melatonin, in vivo and in vitro studies, has been shown prophylactically to reduce oxidative damage in several models of Parkinson's disease (dopamine auto-oxidation, 1-methyl-4-phenyl-1,2,3,6- tetrahydropyridine and 6-hydroxydopamine), and to protect against glutamate excitotoxicity. [50]. [51]. Vitamin C has been shown to inactivate DA quinones, which are severely neurotoxic [2].

Another method for the prevention of nigrostriatal cell death in PD is to remove the inducers of ROS, mainly heavy metals, especially if they are detected to be elevated in RBC, UA or ferritin labs. The traditional treatment for this is heavy metal chelation with DMSA, DMPS, BAL or Deferoxamine for iron overload. Rat studies with Deferoxamine prevented the 6-OHDA induced loss of dopamine [4]. In another animal study, deferoxamine allowed the survival of MPTP poisoned rats while all of the control animals died [52].

Finally, if PD has such great correlation with environmental exposure, and these xenobiotics can accumulate and store in the adipose, liver, and CNS, the most rational top down approach aiming at a causal intervention involves active detoxification. Conventional medicine uses hemodialysis for acute poisonings, but this will only clear extracellular blood and not toxins stored intracellularly in adipose, CNS and liver. If PD patients show labs or history indicating herbicide, pesticide, fungicide or heavy metal exposure, a simple, natural, active detoxification regimen has been shown to be the most effective method for clearance of stored xenobiotics. The regimen that has been repeatedly shown to be effective in the literature is known as the *Hubbard method*. It is a natural regimen designed to alter the metabolism and to increase excretion of xenobiotics through the body's 5 natural organs of detoxification and excretion: the liver, the kidneys, the lungs, the bowels and the skin. The program consists of the following given in a 3 week regimen:

- PUFA EFA Supplement.
- Daily aerobic exercise. 30 minutes –1 hour/day
- ½ hr. sauna at 60-82 degrees C
- Vitamin and mineral support centered around gradually increasing nicotinic acid levels
- Cal/Mag supplement.
- Filtered water and electrolyte replacement.
- Orderly schedule with light, easily digested organically grown foods.
- Adequate sleep.
- No medications, ETOH or recreational drugs during the regimen unless specifically prescribed by the Physician.

Also specific to detoxification and PD, dietary restriction or short periods of clinical fasting were found to be detoxifying and reducing to oxidative stress in animal induced models of PD [53].

This method was found to be safe with no side effects in a previous study with 103 individuals [54]. These are some of the results found studies utilizing Hubbard detoxification regimen:

- A study of seven individuals was evaluated pre and post treatment for the removal of 16 organohalides through the Hubbard detoxification method. 10 of the 16 measured pesticides showed significantly significant reduction at 1 and 4 mos. post treatment. There was no evidence of redistribution of toxins into different bodily compartments [54].
- In a case study of 23 yr old woman who had pesticide exposure, the Hubbard technique was prescribed and the physicians noted black substance being excreted by the sebaceous glands and sweat which was later identified as PCB's. The removal of the toxic substance was accompanied by the remission of her subjective complaints. [55]
- In a controlled study of electrical workers exposed to Hexochlorobenzene, PCB's, Deildrin, oxychlordane, heptachlor epoxide and dichlorophenyldichloroethylene, the Hubbard method was used to detoxify the experimental group while the control group received no treatment. At post treatment, all chemicals were significantly lowered in concentration in the treatment group, while most chemicals were insignificantly higher in the control group. Symptom scores greatly improved in the treatment group, while they stayed the same or worsened in the controls. [56]
- In a study of the general physiological effects, safety and clinical improvement of a detoxification regimen for the removal of adipose stored xenobiotics, the regimen was found to be safe and well tolerated by environmental patients exposed to recreational and iatragenically induced drug toxicity, occupational, and environmental exposures. Patients with high blood pressure had a mean reduction of 30.8 mm systolic and 23.3 mm diastolic. Cholesterol level mean reduction was 19.5 mg/100ml. The program resulted in improvements of Psychological and IQ test scores. There was also a plethora of clinical symptom improvement in 70% of all cases. [57]
- In a clinical study of symptomatic capacitor workers exposed to PCB's on the job, the Hubbard detoxification protocol brought about a mean reduction of adipose tissue PCB's of 37.4 mg/kg and in serum by 261 ug, a 63% and 49% reduction respectively. 90% of reported symptoms ceased after the treatment. Excretion of intact PCB's in

sebum was increased 5 fold during detoxification. [58]

- Another case study of 33 yr. old Vietnam vet who had a history of exposure also tested positive for DDE and PCB's. He was placed on a detoxification protocol and experienced full resolution of symptoms. levels of both DDE and PCB fell appreciably. [59]
- The Hubbard detoxification method was used in a study of Cocain attempt to detoxify their systems. Cocaine was found both in the swea the subjects during the study. Low levels continued to be excreted fo weeks after the regimen. [60]
- In the Healthmed study of chemically exposed workers undergoing detoxification protocol the symptoms reported pre and post treatment follows: [61]

Symptom	% of pretreatment group	% of post treatm
Rash	18	4%
Acne	16	4
Skin thickening	9	4
Parathesias	14	2
Weakness	16	4
Uncoordination	7	0
Dizziness	18	2
Fatigue	79	5
Nervousness	14	4
Disorientation	11	0
Headaches	40	9
Joint Pain	5	0
Muscle pain	42	5
Abdominal Pain	33	11
Constipation	26	2

In conclusion, PD can be seen as having a multifactorial etiology with epi evidence leaning toward hereditary and environmental causes. Through the bioch evident that present day treatments, albeit very sophisticated in pharmacology and are simply treating the symptoms of this dreaded neurological disease. As elucid a number of natural substances including: glutathione, NAC, Acyl-L-Carnitine, Vitar heavy metal chelators that can prevent the dopaminergic cell death and clinical dec Furthermore, a strong argument is made for intervention at the causal level of PD b safe, and effective method of detoxification demonstrated in the scientific literature. for Progressive Health has developed an even more sophisticated system of detox the latest in modern technology and comfort. (Please see attached detoxification F our hope to further the scientific inquiry into the etiology of chronic degenerative dis PD and to lessen the suffering or cure those afflicted with this malady. Thank you f consideration of our progressive hypothesis of PD. Your critique, input and experti welcome.

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