Slowing the Progress of Parkinson's Disease

There are lots of choices for medication to manage the symptoms of PD, very little that is proven to slow the progress of PD and nothing that cures it. Though that may change in the next decade. A lot of research is being done, with the most promising approaches being in the area of genetic manipulation — this is the new frontier in medical science, a substantial step beyond the magic bullet.

In the middle of the 20th century, the wonder drug, penicillin, changed what we could expect from our doctors. Before then, if you were sick and then got better it was because your body's defenses were stronger than the disease. Penicillin was a magic bullet, a substance which stops the disease in its tracks, needing no assistance from the patient's immune system, and doing it without harming the patient. Infectious diseases that were often fatal could now be cured. The list includes pneumonia, blood poisoning, strep throat, scarlet fever, diphtheria, syphilis, gonorrhea, meningitis, tonsillitis, rheumatic fever.

Where PD differs from infectious diseases is that the agent that caused our condition is frequently long gone by the time our symptoms show up – so there is nothing for a magic bullet to knock out. What is needed is some sort of rebuilding process, which is why the genetic approach is most promising.

Slowing progress of the condition is another matter. Much of what is happening to us is just natural aging that is proceeding a little faster than is the case with healthy people. Anything which slows aging is likely to slow the progress of PD. There is no magic bullet which stops the aging process but anything which helps your body's natural defenses is going to slow it down a little.

From the time I was diagnosed, I have paid special attention to hints about what could be done to slow the progress of PD. And while there is nothing that comes with a guarantee there is no shortage of unproven possibilities. I meet my neurologist every six months and always have something to check out with him. His typical response is that there is probably no harm in it and there has been some scientific interest but supporting evidence is weak or non-existent. Even when a treatment sounds good in theory and is backed up by experimental evidence, the supporting evidence always seems to be insufficient. This may mean the theory is wrong. Or it may just mean that further experimentation is required to demonstrate a clear benefit.

Most of the research on PD is concentrating on find a cure. Slowing the progress of PD is a lower priority. I don't have a quarrel with this. Fortunately, if something can be shown to slow PD it tells us something about the nature of PD so it may be useful in a general way as well as being of practical use to those of us with PD. So some research on slowing PD is being done.

While there are many things which appear to slow PD progress, ever so slightly, none of them are so effective that the benefit is easily measured. For a substantial effect it is probably necessary to employ many of them together. A comprehensive list of things that have been claimed to slow PD would be 20 to 50 items long. Following is my top 10 list of the possibilities that strike me as the most interesting.

[1] Eliminating Neurotoxins

In the scientific papers I have read to date, I have found no mention of eliminating neurotoxins. I find this quite surprising. It seems to me this ought to be a first step. Since just about all treatments aim to repair the brain (or at least maintain the status quo), a neurotoxin would get in the way.

Many treatments have worked quite well on PD rats but produced indifferent results when tested on humans with PD. A key difference between lab rats and the average human is that lab rats live in a toxin free environment whereas humans are exposed to a wide range of neurotoxins. A PD-rat is created by exposing it to a neurotoxin like MPTP. This toxin does a lot of damage in a short time but then the toxin is metabolized and clears the body. By the time the rat takes part in a PD experiment there is no residual toxin to interfere with whatever is being tested.

Most humans, on the other hand, have idiopathic PD (cause unknown) and while the exact cause may be unknown, some sort of neurotoxin is usually the main suspect. If the responsible neurotoxin is still present when the patient is treated, the neurotoxin will interfere with the treatment. Furthermore, if a different neurotoxin is present which was not the primary cause of your PD, it is also likely to interfere with treatment.

If there are neurotoxins in the workplace as with welders (manganese fumes), farmers (herbicides, insecticides) and many industrial workers (solvents and various process gases), a researcher doing a trial should determine that the subject is no longer exposed to such toxins before enrolling him in the trial. And of course if you discover you have PD and your occupation exposes you to neurotoxins, you should get the hell out of there, even if you are not taking part in an experiment. Don't wait for irrefutable proof that a particular toxin caused your PD. Even if it wasn't the primary cause of your PD, you are not in a healing atmosphere.

Mercury is a special case. You don't have to go to work to be exposed. It might be in the fish you eat. And your dentist may have filled cavities in your teeth with it. And your doctor may have given you vaccinations containing mercury as a preservative. The amounts from all of these sources are small enough to be handled by the heavy metal defenses of the average human. But not all of us have defenses that are in perfect working order. There is growing evidence that the amount of mercury absorbed from amalgam fillings alone is sufficient to cause harm to somewhere between 1% and 10% of the human population. It is possible, though not proven, that mercury causes PD in some of the mercury sensitive people. But even if mercury was not the primary cause, it would almost certainly interfere with brain repair.

Getting amalgam fillings replaced with some sort of composite is an obvious first step and better than doing nothing at all. However a nasty characteristic of mercury and other heavy metals that act as neurotoxins is that they get stored in all our organs, including the brain, and natural removal from the body is a very slow process. Chelation might be worthwhile but there is no general agreement on the best way to do this. My personal choice is the protocol recommended by Andrew Cutler but I know of no independent trials which have tested and evaluated the various chelation methods.

For a review of some of the mercury chelation methods used by mainstream medicine, see

- Rooney, The role of thiols, dithiols, nutritional factors and interacting ligands in the toxicology of mercury

General Maintenance

Some things that have been recommended for PD are also recommended for many other ailments. While it is possible that some of these act directly on the brain, it is also possible, assuming there is a genuine benefit, that they are good for PD because they improve the health of the body as a whole.

[2] Good Diet

A good diet, by itself, is no guarantee of good health. But a good diet is the foundation upon which good health is built. Without a balanced diet, the other things described below are unlikely to have much effect.

Diet is a huge subject and I will not try to deal with it here beyond the general observation that your diet should include the major food groups with lots of fibre, fruit and vegetables; and you should go easy on red meat, deep fried food, sugar and salt. Overall, more is not better – there is some evidence that fewer calories (short of starvation) increases longevity.

- For a comprehensive discussion of diet and PD, see Kathrynne Holden's website

[3] Physical Exercise

Not all exercise is beneficial but there will be some sort of physical exercise that is good for just about everybody whether you are sick or not. In the case of PD it is not clear whether exercise actually slows the progress of PD or whether it just makes the physical disabilities of PD less debilitating by improving overall health.

[4] Vitamin C

Our body manufactures many of the chemicals that are essential for good health. Vitamins, by definition, are essential food chemicals which our body needs but doesn't manufacture. If they are not part of our diet, we get sick. In the case of vitamin C (ascorbic acid), the deficiency disease is scurvy. When vitamins were first discovered (less than a century ago), the recommended daily allowance (RDA) was the amount necessary to keep us from getting sick. For example, it takes about 10 mg vitamin C per day to prevent scurvy. The RDA was initially set at 60 mg to allow for a generous margin of error.

It wasn't long before some scientists began to wonder if there would be any benefit from amounts of vitamins in excess of what was required to prevent disease. In the case of vitamin C, there is a special reason for thinking there might be health benefits from much larger daily doses. For most living beings, ascorbic acid is not a vitamin because almost all animals, birds and reptiles manufacture their own ascorbic acid. And the amount they manufacture is equivalent (in human terms) to a range from 4000 mg to well over 10,000 mg.

Somewhere in the evolutionary past, all primates lost the ability to make ascorbic acid – presumably during a period (of a million years or so) when our primate ancestors had a mega-C diet of fruit and berries; so the mutation loss of the ability to make ascorbic acid went unnoticed so to speak. This loss is a trait which primates share with guinea pigs and very few other living species.

When we are compared, in other respects, to rats, mice and rabbits (all of which still make their own ascorbic acid), our metabolism is close enough to their metabolism that rats, mice and rabbits can be used in lab experiments where the end objective is to learn about some aspect of human metabolism. Since these otherwise-very-similar animals manufacture and use megadoses of ascorbic acid, we have to wonder what mega-C would do for us. Clearly, we get by very nicely on relatively small amounts of vitamin C. But if a large amount became available, would we make use of it?

Skeptics said no. And in an early experiment proved their case by giving subjects a large dose of vitamin C – then they measured the ascorbic acid in the urine 14 hours later and discovered that most of the dose was in the urine. This was a silly experiment and should have been an embarrassment for the perpetrators. But skeptics are easily satisfied when an experiment seems to prove them right, so the experiment was widely accepted. The problem with the experiment is that it failed to take into account that while our digestive system is very adaptable, it can't turn on a dime. If the skeptics had continued their experiment for a few

days, with a high dose given every day, they would have found less and less ascorbic acid discarded in the urine as the digestive systems of their subjects mobilized the enzymes necessary to make use of the new found wealth.

When vitamin C is ingested in very large amounts it causes diarrhea. The amount necessary for this effect varies from 5,000 mg to 25,000 mg, depending on the individual. This amount is sometimes called the bowel tolerance threshold. Somewhere short of that threshold, the stool becomes soft. I have never seen mega C recommended as a cure for constipation, but since constipation is a common problem in PD, and since mega C is probably good for PD anyway….why not.

[5] Vitamin E

Vitamins C and E are antioxidants. Our bodies use both oxidation and reduction processes in productive ways. But destructive processes are mainly ones of oxidation, so antioxidants tend to be the good guys. And vitamins C and E are two of the most beneficial of the antioxidants.

Harvard researchers gathered data on 76,890 women and 47,331 men for more than a decade. A few years ago, the researchers reported on 371 subjects who had developed PD symptoms. They found a correlation between diets high in Vitamin E and a low risk of PD. They found no benefit from supplements of Vitamins C or E (I wasn't able to discover whether the supplements were small or large). More tests will have to be done to confirm the benefit of Vitamin E in the diet and also the lack of benefit of vitamin supplements. This trial is concerned with risk of getting PD rather than slowing progress of PD but one would expect a connection.

[6] CoQ_{10}

CoQ_{10}, another antioxidant, is present in all human cells and is responsible for the production of the body's energy. Food is converted into energy in the mitochondria of each human cell with the aid of CoQ_{10}. We make our own CoQ_{10} but most people lose part of their CoQ_{10} production capacity as they get older.

A preliminary trial in 2002 showed that megadoses (1200 mg/day or more) of CoQ_{10} slows PD progress.

A recent trial reported in July, 2007 failed to show any benefit. But the dose was small (300 mg/day) and the trial was short (3 months).

Of all the supplements that might slow PD progress, CoQ_{10} has received the most publicity. It is expensive, it is probably beneficial, but it has yet to be proven in a full-fledged study.

[7] Tobacco

Every study which has looked at smoking and PD has found an inverse correlation. In other words, smokers are less likely to get PD than nonsmokers. The studies have been repeated enough times (with the same results) to establish beyond any reasonable doubt that smokers are less likely to get PD. But this doesn't necessarily mean that tobacco is beneficial. It could just mean that something smokers have in common is doing the trick.

In order to determine, beyond doubt, that tobacco slows PD, a large group of parkies would have to be randomly assigned to be smokers or non-smokers. This is an experiment we are unlikely to see in the near future. In the meantime, it's a pretty good assumption that, from a PD perspective, smoking is good for you.

There's a downside, of course. In many other ways, smoking is bad for you. This is one possibility I will not be trying. But if I were already smoking and having some difficulty giving it up…

Direct Effects on the Brain

Since the brain is a part of the body, anything which improves the health of the body will have some benefits for the brain. Those things listed above are of that sort. Following are some measures which act directly on the brain

[8] Mental Exercise

Years ago, before I had a personal reason for thinking about the health of the brain, I was impressed by the report of a woman (in a care facility) with advanced Alzheimer's who still played a pretty good hand of bridge. Either the bridge part of the brain was resisting the advance of AD or that woman's brain was doing some rewiring to allow her to continue her favourite pastime.

It is now generally accepted that activities which involve using the brain (work that requires thought, most games, as well as playing a musical instrument) reduce your chances of developing AD and slow the progress of AD in those who do get it.

But what about PD? As a life long gameplayer (bridge, chess, go, scrabble, sudokus) I can attest that mental exercise by itself is not sufficient to prevent PD. Nevertheless, researchers working with PD mice have determined that mice with puzzles to solve are healthier than mice who just watch TV.

[9] Levodopa

Many of the symptoms of PD arise from a shortage of dopamine in the brain. Levodopa, the most effective medication for relieving PD symptoms, gets converted to dopamine when it reaches the brain. There is a honeymoon period with levodopa when its effects are mainly positive. But after a few years, levodopa becomes less effective and there are negative side effects. Since the good effects of levodopa appear to be time limited, some PD patients (with the blessing of their doctor) put off using levodopa until they really need it.

A recent study suggests that this may not be a wise choice. In the study done by Fahn et al called *Levodopa and the progression of Parkinson's disease* (N Eng J Med, 2004 Dec 9; 351(24): 2498-508), 361 patients with early PD were given levodopa (small, medium or large doses) or a placebo, with nobody knowing who was getting what. After 40 weeks, medication was stopped for two weeks and then standard movement tests were used to evaluate PD progress. The placebo group had the worst scores; the large dose levodopa group had the best scores. This would be a clear vote for early levodopa medication if the experimenters had not also done a new analytical test called neuroimaging which showed maximum PD progression for the large dose levodopa. In other words, the opposite result. Because neuroimaging is new, the experimenters were inclined to place more credence on the movement tests. But the contradictory results made them somewhat tentative in their conclusions.

So nothing is proved with any certainty. Nevertheless, this trial raises the possibility that early use of levodopa slows PD – probably by relieving the strain on the brain's remaining dopamine production capacity which, without the levodopa supplement, would be working flat out trying to keep up with dopamine demand.

For those of us who prefer, whenever possible, to get our medication from natural sources, there are two

species of beans (fava and mucuna) which contain significant quantities of levodopa. The hitch is that in order to be effective, levodopa must be accompanied by carbidopa (or a similar enzyme inhibitor) to keep the levodopa from being converted to dopamine before it reaches the blood brain barrier – levodopa can cross into the brain, dopamine can't.

- For more information on using these beans see Medicinal Beans on this website.

Neurotrophic factors

Scientists have recently discovered a family of proteins called neurotrophic factors. These substances are responsible for the growth and survival of neurons during development, and for maintaining adult neurons. Neurotrophic factors also are capable of repairing damaged neurons in a test tube and in animal models. Because of this, they represent exciting possibilities for reversing devastating brain disorders, including Alzheimer's disease, Parkinson's disease and Lou Gehrig's disease.

Scientists are now looking for ways to harness neurotrophic factors to induce the regrowth of damaged neurons and improve symptoms of patients with neurological diseases. Targeting is one of the main problems. Just taking neurotrophic factor supplements doesn't do the job. Melatonin, however, has easy access to the brain and there is a neurotrophic factor connection.

[10] Melatonin

In addition to regulating sleep, melatonin is one of those supplements which is touted as good for whatever ails you. I didn't pay much attention until I ran across a trial in which a melatonin supplement was shown to stimulate GDNF production. That got my attention.

- See the abstract. Their conclusion: "In view of the potency of GDNF in promoting the survival of dopaminergic neurons, these novel findings have implications for the utilization of melatonin in neuroprotective strategies, especially in Parkinson's disease."

Melatonin is manufactured in our pineal gland and released as we go to sleep and then it goes to work in the resting brain. While we are still growing, melatonin may have a role to play in neuron growth. In the mature brain melatonin may have a role to play in neuron repair.

As we get older, the amount of melatonin produced by the pineal gland gradually decreases. A melatonin supplement clearly slows aging in rats and mice. A similar effect in humans has yet to be demonstrated. It is not an easy experiment to set up and complete in a reasonable time – humans age much more slowly than mice; and humans can't be kept in a controlled environment for any length of time to eliminate other influences.

Melatonin supplements are usually taken 30 minutes before bedtime. For most people there are no known side effects. The one exception is that some people find themselves inappropriately sleepy the following day. Melatonin is not a sedative. In the natural course of events, sleep triggers melatonin release and not the other way around. Nevertheless, our body comes to associate melatonin and sleep, so a melatonin supplement tricks the body into assuming it must be going to sleep. If it is necessary to stay awake, we are less groggy with melatonin than we would be with a sedative.

The most common tablet size is 3 mg but if you are going to try it out you should start with a smaller size. And, of course, you should discuss this with your doctor before doing anything.

Even though melatonin is available without a prescription, it is a potent drug and your doctor may know of some reason it is inappropriate for you.

Final Thoughts

I am not a medical professional so you should treat all of the above as food for thought which you will run past your doctor if you are inclined to act on any part of it. My take is that for those items which actually do slow the progress of PD, the individual benefit is too small to be easily measured. A significant effect would only come from the cumulative contribution of a number of such things.

Of the 10 items described above, I find melatonin the most intriguing. Realistically, if melatonin is actually beneficial, its contribution to slowing PD is probably small. But we can dream, can't we? The theoretical upside of melatonin is greater than for any of the others – if it does, in fact, activate GDNF and some of the other neurotrophic factors, it might be able to stop the progress of PD entirely. Though if that were possible, it would presumably only happen in an otherwise very healthy body because there is no evidence that melatonin acts like a magic bullet. It would have to work with our natural defenses, so anything that increases the health of the body would make melatonin more effective.

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