

very thorough  
"Inheritance and Treatment of Parkinson's Disease"  
by Leann Gama

Parkinson's disease is a neurological disorder that affects the brain. It was named after a London physician named James Parkinson. In 1817, he was the first to describe this disease in one of his papers titled, "An Essay on the Shaking Palsy." In the United States alone, nearly one million people suffer from Parkinson's disease and each year there are about 50,000 new cases.<sup>1</sup> Yet, there is still no known cure. Because symptoms usually occur later in life, after the age of 40, the number of people with Parkinson's is expected to grow. Parkinson's is a disease that is found not only in the United States, but all over the world and seems to affect more men than women.

This neurological disorder slowly progresses as nerve cells degenerate and the levels of a neurotransmitter, dopamine, decreases. The decrease of dopamine in the brain causes uncontrollable movements. It has been observed that the small amounts of dopamine that remain are destroyed by the chemical in the synapse known as MAO-B. This large loss of dopamine causes an imbalance between the dopamine and acetylcholine, another neurotransmitter, hence, causing a lack of coordination.<sup>2</sup> The trembling of a limb at rest is often the first symptom.<sup>3</sup> Other symptoms may include bradykinesia, akinesia, reduced facial expression, and muscular rigidity. With time the symptoms only worsen causing depression, memory loss, concentration difficulties, dementia, personality changes, and sleep disturbances.<sup>4</sup>

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<sup>1</sup> "Background Information: Parkinson's Disease." Division of Intramural Research. Research News: Parkinson's Disease. 3 Nov. 2002.

[http://www.nhgri.nih.gov/DIR/LGDR/PARK/about\\_parks.html](http://www.nhgri.nih.gov/DIR/LGDR/PARK/about_parks.html).

<sup>2</sup> "What Happens in Parkinson's Disease." About Parkinson's Disease. 1997. Somerset Pharmaceuticals, Inc. 1 Nov. 2002. <[http://www.parkinsonsinfo.com/about\\_parkinsons/whathappens.html](http://www.parkinsonsinfo.com/about_parkinsons/whathappens.html)>.

<sup>3</sup> [http://www.nhgri.nih.gov/DIR/LGDR/PARK/about\\_parks.html](http://www.nhgri.nih.gov/DIR/LGDR/PARK/about_parks.html).

<sup>4</sup> "Parkinson's Disease." *The Columbia Encyclopedia*. Sixth ed. 2001. 2 Nov. 2002.

<http://www.bartleby.com/65/pa/Parkinson.html>.

There is no exact known cause for Parkinson's disease. Some researchers have reported families who have inherited the disease and others have provided a theory that suggests that environmental factors play a big role in the cause for Parkinson's. Several people suffering from Parkinson's, developed the disease after consuming an illegal drug which contained a certain chemical known as MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine).<sup>5</sup> Other people who have developed the disease, were those who during an epidemic in the early 1900s contracted a severe form of influenza. However, those researchers who have studied the disease in an inherited form, have discovered two of the chromosomes that seem to cause Parkinson's disease. These chromosomes are the 4q chromosome and the 2p13 chromosome. Chromosome 4q encodes the alpha synuclein gene.<sup>6</sup> This particular gene produces a small presynaptic protein which exact function still remains unknown. The gene in the 2p13 chromosome is yet to be identified. Its locus has only been mapped to this particular chromosome. The alpha synuclein gene suggests that Parkinson's disease is inherited in an autosomal dominant manner. Mutations in a single base pair of this gene seems to cause this neurodegenerative disease. A mutation in the alpha synuclein protein causes it to aggregate and to form a deposit by attracting other proteins.<sup>7</sup> As a result, this deposit damages the cell and eventually leads to its destruction. The deposits that are formed in the substantia nigra of the brain, in the cytoplasm of the neurons, are called Lewy bodies.<sup>8</sup> These Lewy

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<sup>5</sup> [http://www.nhgri.nih.gov/DIR/LGDR/PARK/about\\_parks.html](http://www.nhgri.nih.gov/DIR/LGDR/PARK/about_parks.html).

<sup>6</sup> Nussbaum, Robert L. "Human genetics: Putting the Parkin into Parkinson's." 9 April 1998. *Nature*. 3 Nov. 2002. [http://www.nature.com/cgi-taf/DynaPage.taf?file=/nature/journal/v392/n6676/full/392544a0\\_r.html&filetype=&dynoption=](http://www.nature.com/cgi-taf/DynaPage.taf?file=/nature/journal/v392/n6676/full/392544a0_r.html&filetype=&dynoption=).

<sup>7</sup> "NIH Researchers Find First Parkinson's Disease Gene." Division of Intramural Research. NHGRI Media Release: Parkinson's Disease. 3 Nov. 2002. [http://www.nhgri.nih.gov/DIR/LGDR/PARK2/media\\_release.html](http://www.nhgri.nih.gov/DIR/LGDR/PARK2/media_release.html).

<sup>8</sup> [http://www.nature.com/cgi-taf/DynaPage.taf?file=/nature/journal/v392/n6676/full/392544a0\\_r.html&filetype=&dynoption=](http://www.nature.com/cgi-taf/DynaPage.taf?file=/nature/journal/v392/n6676/full/392544a0_r.html&filetype=&dynoption=)

bodies react with anti-ubiquitin antibodies and with antibodies against alpha synuclein. Due to the gene's mutation, the cell's mechanism for breaking down the proteins fails. The causes for the mutations have not been clearly identified. Some researchers suggest that an infection or virus may alter the gene in some way. Another hypothesis is that maybe some kind of environmental toxin causes the alpha synuclein to change shape and block normal protein breakdown. Likewise, a mere defect in the gene may be the problem.<sup>9</sup> Indeed, the cause for this disease remains unclear.

Although, there is also no known cure for Parkinson's disease, treatment is available. Patients who are experiencing the first symptoms of the disease usually do not require treatment until several years after diagnosis. Those patients who suffer severely from the disease are put on drug therapy. They are usually prescribed levodopa (L-Dopa), pramipexole (Mirapex), or ropinirole<sup>®</sup> (Requip).<sup>10</sup> Levodopa aids in replacing the dopamine in the brain. It helps to ease the trembling, rigidity, and slow movements. Injecting dopamine into the bloodstream is ineffective because the brain does not pick up the chemical from the blood. Whereas levodopa acts as a metabolic precursor and is able to enter the brain through the bloodstream.<sup>11</sup> After converting into dopamine, the brain is able to use it effectively. Mirapex and Requip are usually prescribed to delay the need for L-Dopa due to some of its side effects: nausea, loss of appetite, cardiac irregularities, and psychological changes.<sup>12</sup> Because of other serious side effects, patients must stop taking L-Dopa. When stopping the use of levodopa, after 5 to 10 years, the symptoms

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<sup>9</sup> [http://www.nhgri.nih.gov/DIR/LGDR/PARK/about\\_parks.html](http://www.nhgri.nih.gov/DIR/LGDR/PARK/about_parks.html)

<sup>10</sup> <http://www.bartleby.com/65/pa/Parkinson.html>

<sup>11</sup> "L-Dopa." *The Columbia Encyclopedia*. Sixth ed. 2001. 2 Nov. 2002.

<http://www.bartleby.com/65/pa/Parkinson.html>.

<sup>12</sup> <http://www.bartleby.com/65/pa/Parkinson.html>

return much worse.<sup>13</sup>

Brain surgery has been another approach in treating Parkinson's disease. Specifically, pallidotomy, a surgical operation that destroys the globus pallidus of the brain,<sup>14</sup> and the "implantation of an electrical stimulator to counteract the effect of the loss of dopamine-producing cells in the substantia nigra."<sup>1</sup> Another brain surgery involves, in particular, involves the transplantation of healthy neural tissue that is able to produce dopamine, hence restoring neurological function. Scientists have been able to take dopamine-producing cells from the adrenal glands of a patient with Parkinson's and have implanted them in the affected brain region. Others have used dopamine-producing human fetal tissue, from miscarriages, for transplants. Fetal tissue is preferred because it produces more dopamine and is more likely to survive in the affected area. PET scans have shown significant improvements in the brain's capability for producing dopamine.

Consequently, these patients required less and less L-Dopa.<sup>13</sup>

However, the end results of such transplants have been variable. Researchers need to work on increasing the survival and growth of the transplant tissue, as well as, on discovering a solution to prevent dopamine producing brain cells from dying. The fact that the chromosome responsible for the inheritance of this disease has been discovered, only provides us with the piece of the puzzle. There is a lot more needed to be discovered. Once there is a better understanding of what exactly causes this disease, then and only then, will scientists and researchers be able to develop better therapies or a cure.

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<sup>13</sup> Passer, Michael W. and Ronald E. Smith. Psychology: Frontiers and Applications. New York: McGraw-Hill, 2001.

<sup>14</sup> "Pallidotomy." Medical Dictionary. MedTerms.com. 21 Nov. 1999. 4 Nov. 2002. <http://www.medterms.com/script/main/art.asp?li=MNIP,ArticleKey=11437>.