

# Parkinson's Disease: An update on Pathophysiology, Epidemiology, Diagnosis and Management

## Part 1 : Background and Epidemiology

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## Abstract

The relationship between Atopic dermatitis and food allergies remain controversial, it is not uncommon for patients and their care givers to question the possibility of allergy to food items acting as triggers for flare ups. This article seeks to examine the relationship between atopic dermatitis and food

allergies and discusses the diagnosis of food allergy in patients with atopic dermatitis.

**Key words:** Parkinsons, epidemiology, pandemic

## Prologue to Parkinson's Disease

Parkinson's disease is the most widely recognized neurodegenerative condition, and it has a profound effect on the social and health related aspects of patient, family and caregiver quality of life. To tackle the disease effectively, a large number of healthcare professionals need to work together, organized as an interdisciplinary team, in which patients and their families play a vital part in preparation, knowledge, and involvement. It especially includes the loss of nigral dopaminergic neurons. The characteristics of the cardinal motor are rigidity, bradykinesia, tremor in rest and postural instability. Non-motor symptoms are typical both early and late in the course of the disease and include autonomic, neuropsychiatric and cognitive disability.

Parkinsonism is a clinical condition portrayed by at least two of four cardinal characteristics: bradykinesia (slowness and intermittent movement), rigidity, resting tremor (trembling), and a loss of postural equilibrium contributing to disruption of gait and fall (Lang & Lozano

(1998). The most prevalent form of parkinsonism is idiopathic Parkinson's disease (PD), first identified as agitans paralysis (the trembling palsy) by James Parkinson, an English physicist, in 1817. Dr Parkinson identified the disease's main symptoms which would bear his name later on. Scientists investigated the causes and treatment of the disease for the next century and a half, describing its spectrum of symptoms, its population distribution and its prospects for cure.

PD's pathological characteristic is a depletion of substantia nigra pars compacta's pigmented, dopaminergic neurons in the brain, with the introduction of intracellular inclusions known as Lewy bodies (Gibb, 1992, Fearnley & Lees, 1994). Researchers identified a fundamental defect in the early 1960s that is a characteristic of the disease: the loss of brain cells that produce significant chemical, dopamine, that helps guide muscle function. Gradual loss of dopamine-containing neurons is a common aging feature; however, most people do not lose the 70-80% of the dopaminergic neurons required to cause symptomatic PD (Braak & Braak 1994).

Without treatment, PD progresses to a static, akinetic state within 5 to 10 years, in which patients are unable to care for themselves. Death may result from immobility complications, such as aspiration pneumonia and pulmonary embolism.

Pharmacological endeavors to reestablish dopaminergic action with levodopa and dopamine agonists have been fruitful in easing a significant number of the clinical features of PD. An alternative but supplementary strategy was to restore the natural balance of cholinergic and dopaminergic effects with anticholinergic drugs on the basal ganglia. The development of successful pharmacological care has dramatically altered PD prognosis; strong functional independence can be preserved for several years in most cases, and the life expectancy of appropriately managed patients is significantly increased.

Progress has been made in understanding the underlying pathophysiology of this disorder, though the cause is still unclear, and no remedial treatment is available. Treatment remains difficult over the course of the disease, and should be individualized at each point of the disease depending on the quality of life of the patient. Some advancements have been made in treating Parkinson's disease and there is ongoing studies looking at novel management approach.

## Epidemiology

After Alzheimer's disease Parkinson's disease is the second most common neurodegenerative condition (Dorsey et al., 2005). The estimated prevalence of PD in the general population in developed countries is 0.3 percent. Parkinson's disease usually progresses from age 55 to age 65. The prevalence is 1.0 percent for people over the age of 60 and 3.0 percent for people over the age of 80; incidence rates of PD are estimated to range from 8 to 18 per 100,000 person years (Lee & Gilbert, 2005). Estimated prevalence and occurrence rates for PD in Europe range from 65 to 12,500 per 100,000 and from 5 to 346 per 100,000 person years respectively (VonCampenhausen et al., 2005). Age is the disease's most significant risk factor; male gender carries a moderate risk (Gillies et al, 2014).

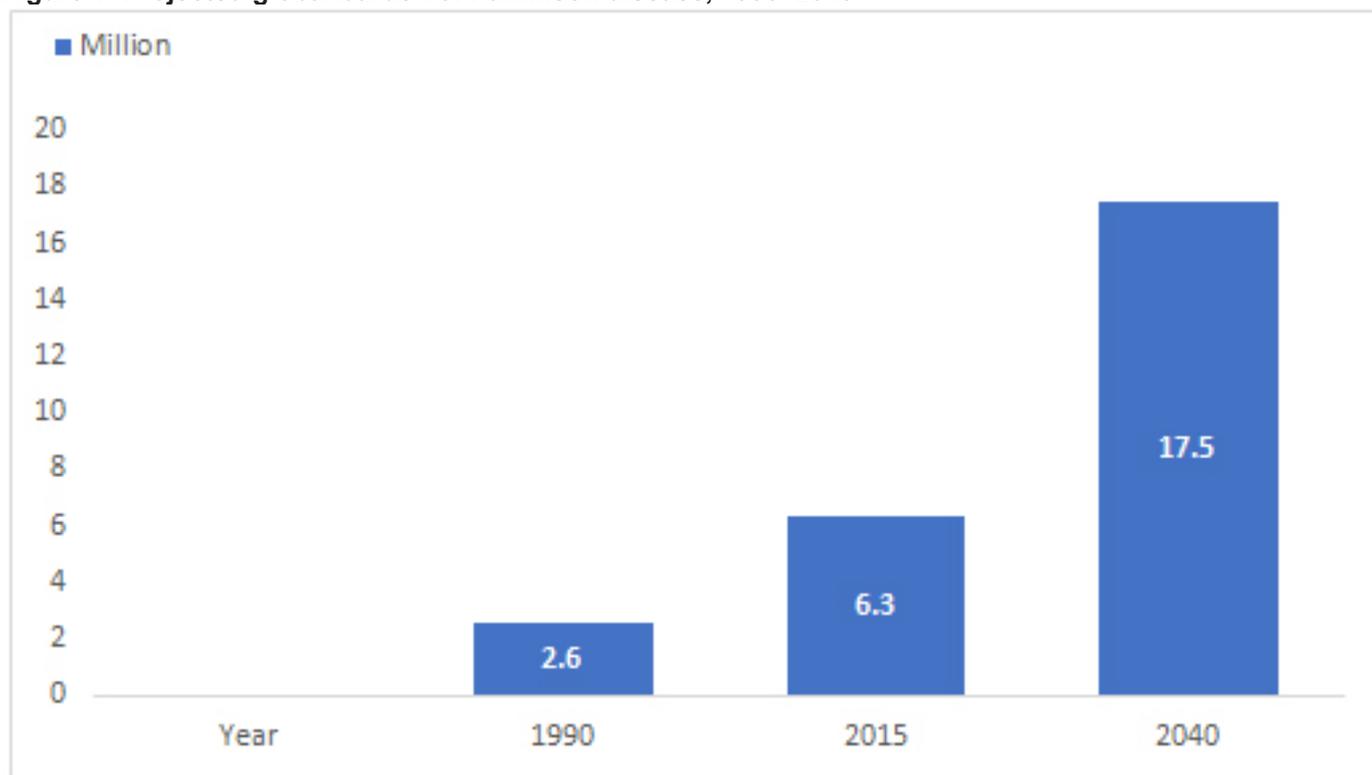
Neurological disorders are currently the leading cause of disability worldwide, according to the Global Burden of Disease report, and Parkinson's disease is the fastest growing of such disorders (in age standardized prevalence, impairment, and death rates) (GBD 2015). The number of people with Parkinson's disease rose globally from 1990 to 2015 by 118 per cent to 6.2 million (GBD 2015). Studies over time on the prevalence of Parkinson's disease yielded contradictory findings (Savica et al., 2016, Darweesh et al., 2016, Akushevich et al., 2013, Isotalo et al., 2017). Nonetheless, the latest Global Burden of Disease report showed that age standardized Parkinson's disease levels increased between 1990 and 2016 for every area of the world. Generally speaking, age-standardized prevalence rates rose by almost 22 per cent

worldwide (GBD 2016). Joining proof from investigations of worldwide reviews (GBD 2016), clinical records of huge organizations (Savica et al., 2017), national registration agencies (Rossi et al., 2018), and demise declarations (Darweesh et al., 2018) indicates that the incidence of Parkinson disease might be rising. It requires prospective cohort studies and comprehensive registries (GBD 2016) to better understand these patterns.

The Parkinson pandemic is energized by aging demographics, rising fertility, dropping smoking levels and industrialization by-products. Parkinson's disease incidence increases with age and rises sharply at around the age of 65 (Van Den eta, 2003). The population of the planet is getting older, as the number and proportion of people over 65 is increasingly growing. The consolidated result of these two causes is an extraordinary rise in the number of Parkinson's disease sufferers. By 2040, the number of Parkinson's disease sufferers worldwide is estimated to reach 12 million (Dorsey & Bloem, 2018). Significantly, Parkinson's disease affects not only older people, and those under 50 are developing the disorder.

Notwithstanding aging, different variables are expected to raise the global burden of Parkinson's disease beyond existing projections. The quantity of individuals with an illness is a result of disease incidence and the survival of those with the disorder. Rising survival can lead to a greater disease burden for those with and without Parkinson's disease. Regardless of Parkinson's disease, in the last two decades global life expectancy has risen by six years (GBD, 2013). According to a new report by Wanneveich and colleagues, between 2010 and 2030 demographic changes in life expectancy would improve the longevity of 65-year old people in France with Parkinson's disease by about three years. This longevity rise would result in an increase of 12 per cent over 20 years in the age standardized prevalence rate (Wanneveich et al., 2018). Moreover, expanding life span will undoubtedly increase the number of people with advanced Parkinson's disease who are more difficult to treat and who currently have much less access to treatment.

Though a global health boost, declining smoking levels may contribute to a higher incidence of Parkinson's disease in some countries. Various studies have discovered that the danger of Parkinson is diminished among smokers by roughly 40% (Scheperjans et al., 2015). If the correlation is causal, which remains to be confirmed, lower smoking rates may lead to higher Parkinson's disease levels. Indeed, a 2018 report by Rossi and colleagues projected that decreasing U.S. smoking levels could raise the number of people with Parkinson's disease by 10 percent beyond estimates that predict only the impact of aging (Rossi et al., 2018). Another investigation reported an increased incidence of Parkinson's disease between 1976 and 2005, especially in men over 70 years of age, which may be partly due to decreasing smoking in previous decades (Savica et al., 2017).

**Figure 1: Projected global burden of Parkinson disease, 1990–2040**

Lastly, industrialization by-products may lead to increasing levels of Parkinson's disease. Various by-products of the Industrial Revolution have been related to Parkinson's disease, including particular pesticides, solvents and heavy metals (Goldman, 2014). Nations that have experienced the most rapid industrialization have witnessed the largest increment in Parkinson's disease rates. For instance, adjusted Parkinson's disease prevalence rates in China increased more than in any other country from 1990 to 2016, and more than doubled (GBD2016). The global use of pesticides, meanwhile, is at or near its highest levels (Roser & Ritchie 2020). There is also frequent use of particular pesticides associated with Parkinson disease. For example, albeit 32 nations have restricted the utilization of paraquat, which is emphatically connected to Parkinson malady, the United States keeps on utilizing paraquat in ever more prominent amounts (Mercola, 2017). A few nations that have banned the pesticide, for example, England, keep on trading the pesticide to different nations, including Brazil, Columbia, South Africa, Taiwan, and the United States (Hakim, 2016).

Many neurotoxic compounds that are associated with Parkinson's disease, such as trichloroethylene, also see continuing use. More than half of U.S. Superfund sites, including one located under Google's headquarters in Mountain View, CA, where titans such as Fairchild Semiconductor and Intel used the chemical in the semiconductor industry, are contaminated (Fairchild Semiconductor Corp, 2018). However, global use of the solvent is expected to increase by 2 percent per annum and by 4 percent per annum in China, even though there are several records of the "trichloroethylene toxicity" dating back to at least 1932, including a letter published in the *Journal of the American Medical Association* (McCord, 1932).

Together, these elements of aging populations, increasing mortality, declining smoking levels, and industrialization by-products, alone or in combination—may underlie the enormous number of people influenced by Parkinson's disease. Assuming an increase of 12 percent due to increased longevity, an increase of 10 percent due to reduced smoking, and that about half (10 percent) of the observed rise in age-adjusted prevalence levels persists due to environmental factors, the burden of Parkinson's disease could reach 17 million by 2040 (Fig. 1). (GBD, 2016, Rossi et al., 2018, Wanneveich et al., 2018). Although those predictions are obviously optimistic, they emphasize the Parkinson pandemic's potential development. However, as Strickland and Bertoni noted in 2004, "It's important that as methods improve, prevalence rates (of Parkinson's disease) are increasing, indicating that undercounting is the main problem in counting Parkinson's patients" (Strickland & Bertoni, 2003).

#### **Do we need to worry?**

Parkinson disease is on the rise and may be a result of our time. The burden of Parkinson's disease does the reverse, as opposed to other diseases whose burden decreases with increasing socioeconomic status. Disability caused by Parkinson's disease increases with the Socio-Demographic Index, a compound indicator of per capita employment, education and addition to do so (GBD 2016). As GDP per capita rises, so does Parkinson's disease levels. Although the correlation is small, the trajectory of the relationship is troubling and again highlights the role that human activities, especially industrialization, may play in raising Parkinson's disease burden. The lifetime danger of Parkinson illness, including for the perusers of this paper, is currently 1 out of 15 (Wanneveich et al., 2018, Driver et al., 2009).

Parkinson's disease wave is rising and multiplying. Parkinson's disease affects people with the disease and those around them with a massive human toll. The caregiving burden has its own negative health consequences (Schulz & Beach, 1999). The monetary expenses of Parkinson disease are also large, ready to rise, and, at least in the U.S., largely based on hospital treatment, which few desire (Kowal et al., 2013, Dieleman, 2016). Luckily the keys to the pandemic's origins is all around us. What we lack is a desire to act.

### How to fight and Act ?

Society has effectively tackled polio, breast cancer, and HIV pandemics over the past century. Vital to the accomplishment of these endeavors was unbridled activism From a March of Dimes to the White House for polio, to First Lady Betty Ford's brave declaration of breast cancer to a Quilt covering the National AIDS Mall, those with and affected by the disease made their voices heard and their faces remembered. This advocacy helped prevent polio and Aids lobby for more private and public funding, care for all affected people and manage the conditions with new therapies.

Given these examples, those at risk for Parkinson's disease may form a "PACT" for the prevention, advocacy, care and treatment of the illness. Where possible we can prevent Parkinson's disease by reducing the use of chemicals known to raise the risk of Parkinson's disease and in some cases eliminate it. We have the ability to prevent the possibly millions from ever suffering Parkinson's crippling symptoms. However, we do need to raise additional funds to better understand the root causes of the disease—environmental, genetic, and biological—and to develop new models of treatment that aim to deliver expert care to everyone (Ypinga et al., 2008). Last but not least, Parkinson's disease requires modern, highly effective therapies; the most effective treatment (levodopa) is now 50 years old. So the Parkinson pandemic is preventable and not imminent or inescapable.

### References

Akushevich I, Kravchenko J, Ukraintseva S, Arbeev K, Yashin AI (2013) Time trends of incidence of age-associated diseases in the US elderly population: medicare-based analysis. *Age Ageing* 42, 494-500.

Braak H, Braak E (1994). Pathology of Alzheimer's disease. In: Calne DB, editor. *Neurodegenerative Diseases*. Philadelphia, PA: WB Saunders; 1994. pp. 585-614.

Darweesh SKL, Raphael KG, Brundin P, Matthews H, Wyse RK, Chen H, Bloem BR (2018) Parkinson matters. *J Parkinsons Dis*. doi: 10.3233/JPD-181374.

Darweesh SKL, Koudstaal PJ, Stricker BH, Hofman A, Ikram MA (2016) Trends in the Incidence of Parkinson Disease in the General Population: The Rotterdam Study. *Am J Epidemiol* 183, 1018-1026.

Dieleman JL, Baral R, Birger M, Bui AL, Bulchis A, Chapin A, Hamavid H, Horst C, Johnson EK, Joseph J, Lavado R, Lomsadze L, Reynolds A, Squires E, Campbell M, DeCenso B, Dicker D, Flaxman AD, Gabert R, Highfill T, Naghavi M, Nightingale N, Templin T, Tobias MI, Vos T, Murray CJ (2016) US spending on personal health care and public health, 1996-2013. *JAMA* 316, 2627-2646.

Dorsey E, Bloem BR (2018) The parkinson pandemic—a call to action. *JAMA Neurol* 75, 910.

Dorsey ER, Constantinescu R, Thompson JP, et al. Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. *Neurology* 2007;68:384-6.

Driver JA, Logroscino G, Gaziano JM, Kurth T (2009) Incidence and remaining lifetime risk of Parkinson disease in advanced age. *Neurology* 72, 432-438.

Fairchild Semiconductor Corp. (2018). (Mountain View Plant) Mountain View, CA Cleanup Activities. US Environmental Protection Agency. <https://cumulis.epa.gov/supercpad/SiteProfiles/index.cfm?fuseaction=second.Clean+up&id=0901680#bkground>.

Fearnley J, Lees A. (1994). Pathology of Parkinson's disease. In: Calne DB, editor. *Neurodegenerative Diseases*. Philadelphia, PA: WB Saunders; 1994. pp. 545-554.

Kowal SL, Dall TM, Chakrabarti R, Storm MV, Jain A (2013) The current and projected economic burden of Parkinson's disease in the United States. *Mov Disord* 28,311-318.

Lee A, Gilbert RM. Epidemiology of Parkinson disease. *Neurol Clin* 2016; 34: 955-65.

Mercola J (2017) Paraquat-banned in EU while US increasing use of this toxic killer. *Take Control of Your Health, Mercola*.

GBD 2016 Parkinson's Disease Collaborators (2018) Global, regional, and national burden of Parkinson's disease in 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 17, 939-953.

GBD 2015 Neurological Disorders Collaborator Group (2017) Global, regional, and national burden of neurological disorders during 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Neurol* 16, 877-897.

GBD 2013 DALYs and HALE Collaborators (2015) Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. *Lancet* 386, 2145-2191

- Gibb WR. (1992) Neuropathology of Parkinson's disease-related syndromes. *Neurol Clin.* 10:361–376.
- Gillies GE, Pienaar IS, Vohra S, et al. Sex differences in Parkinson's disease. *Front Neuroendocrinol* 2014; 35: 370–84.
- Hakim D (2016) This pesticide is prohibited In Britain. Why is it still being exported? *The New York Times*, December 20, 2016. <https://www.nytimes.com/2016/12/20/business/paraquat-weed-killer-pesticide.html>
- Isotalo J, Vahlberg T, Kaasinen V (2017) Unchanged long-term rural-to-urban incidence ratio of Parkinson's disease. *Mov Disord* 32, 474-475.
- Goldman SM (2014) Environmental toxins and Parkinson's disease. *Ann Rev Pharmacol Toxicol* 54, 141-164.
- Lang AE, Lozano AM. (1998). Parkinson's disease. First of two parts. *N Engl J Med* ;339:1044–1053.
- McCord CP (1932) Toxicity of trichloroethylene. *J Am Med Assoc* 99, 409-409.
- Rossi A, Berger K, Chen H, Leslie D, Mailman RB, Huang X (2018) Projection of the prevalence of Parkinson's disease in the coming decades: Revisited. *Mov Disord* 33, 156-159.
- Roser M, Ritchie H, Fertilizer and pesticides. <https://ourworldindata.org/fertilizer-and-pesticides> ( accessed April 2020)
- Savica R, Grossardt BR, Bower JH, Ahlskog JE, Boeve BF, Graff-Radford J, Rocca WA, Mielke MM (2017) Survival and causes of death among people with clinically diagnosed synucleinopathies with parkinsonism: a population-based study. *JAMA Neurol* 74, 839-846.
- Savica R, Grossardt BR, Bower JH, Ahlskog J, Rocca WA (2016) Time trends in the incidence of parkinson disease. *JAMA Neurol* 73, 981-989.
- Scheperjans F, Pekkonen E, Kaakkola S, Auvinen P (2015) Linking smoking, coffee, urate, and Parkinson's disease – a role for gut microbiota? *J Parkinsons Dis* 5, 255-262.
- Schulz R, Beach SR (1999). Caregiving as a risk factor for mortality: The caregiver health effects study. *JAMA*. 282, 2215-2219.
- Strickland D, Bertoni JM (2003) Parkinson's prevalence estimated by a state registry. *Mov Disord* 19, 318-323.
- Van Den Eeden SK, Tanner CM, Bernstein AL, Fross RD, Leimpeter A, Bloch DA, Nelson LM (2003) Incidence of Parkinson's disease: variation by age, gender, and race/ethnicity. *Am J Epidemiol* 157, 1015-1022.
- von Campenhausen S, Bornschein B, Wick R, et al. Prevalence and incidence of Parkinson's disease in Europe. *Eur Neuropsychopharmacol J* 2005; 15: 473–90.
- Wanneveich M, Moisan F, Jacqmin-Gadda H, Elbaz A, Joly P (2018) Projections of prevalence, lifetime risk, and life expectancy of Parkinson's disease (2010-2030) in France. *Mov Disord*. doi: 10.1002/mds.27447.
- Ypinga JHL, de Vries NM, Boonen LHHM, Koolman X, Munneke M, Zwinderman AH, Bloem BR (2018) Effectiveness and costs of specialised physiotherapy given via ParkinsonNet: a retrospective analysis of medical claims data. *Lancet Neurol* 17, 153-161.