# The Age of Onset of Parkinson's Disease: Etiological Implications

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**ABSTRACT:** We have conducted a hospital-based survey of the age-specific prevalence of Parkinson's disease in 551 patients from Helsinki and Vancouver. We conclude that the disorder may be starting earlier than previously and we discuss the implications of this finding for the etiology of Parkinson's disease.

**RÉSUMÉ: Age de début de la maladie de Parkinson: implications étiologiques** Nous avons procédé à une enquête en milieu hospitalier de la prévalence par âge de la maladie de Parkinson chez 551 patients de Helsinski et Vancouver. Nous concluons que cette affection commence peut-être plus tôt que par le passé et nous discutons des implications de cette observation en ce qui a trait à l'étiologie de la maladie de Parkinson.

*Can. J. Neurol. Sci. 1986; 13: 317-319*

Speculations of the etiology of Parkinson's disease focus on three main issues: aging of the nervous system, genetic predisposition and environmental risk factors. Eldridge and Rocca[1] have argued that Parkinson's disease cannot be secondary to an environmental cause which is changing or is limited to a small geographic area because the mortality and morbidity rates have been stable over time and place for a period of at least 35 years, without any established clusters or demonstrated risk factors. They speculate that the initial number of dopamine neurons at birth is the critical determinant of whether Parkinson's disease will develop in later life.

Because of a clinical impression that we are seeing a larger proportion of young patients than previously, and the implications that a change in age-specific incidence rates would have for etiological hypotheses, we have surveyed our patient population and have compared our findings with earlier reports.

## Patients and Methods

The age of onset of symptoms was obtained from patients with Parkinson's disease living in the main population centers referring patients to the University of British Columbia Health Science Centre Hospital, Vancouver, Canada (Lower Mainland: population 1,527,852) and University Central Hospital, Helsinki, Finland (cities of Helsinki, Espoo and Vantaa: population 794,604). The age-specific rates calculated here are based on population projections for 1985 for the Lower Mainland (Statistics Canada) and Finland (National Pension Institute).

The age of onset was obtained in 196 out-patients examined in Helsinki from July 1982 through June 1985. This information was ascertained from the patient and in most cases also from the relatives. The data in Vancouver were based on retrospective analysis of files of 355 out-patients examained from January 1982 through July 1985. In both places, only patients living at the last day of the collection period were included. From the data, we were able to calculate minimal prevalence ratios, since patients seen only by other medical care providers, or those not coming to medical attention would not be counted. In both Helsinki and Vancouver there are no financial restraints from seeking medical attention. In both cities the patients were ascertained from what may be regarded as the main referral center for movement disorders though not necessarily the largest general neurological service.

## Results

Figure 1 shows the age of onset in patients alive on June 30, 1985 in Helsinki and July 31, 1985 in Vancouver. The findings were remarkably similar in both cities. Patients whose age of onset was 70 years or more were less frequent in Helsinki than in Vancouver; this finding probably derives from a Helsinki policy that directs elderly patients (>80 years) to another hospital specializing in geriatric care. Despite this administrative bias towards younger age groups in Helsinki compared to Vancouver, the mean age of onset, variation, and range, were quite similar: 57.8 + 11.3 (mean + SD) years in Helsinki (range 21-83) and 57.9 + 11.2 (range 24-85) in Vancouver.

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Two of the patients with age of onset before 40 years in Helsinki each had one sibling with young onset parkinsonism, suggesting that they represented a genetically determined subset. There were no familial cases in Vancouver.

Calculated point prevalence in the present survey was 23.3 per 100,000 for Vancouver and 24.7 per 100,000 for Helsinki. The usual prevalence figures for North America and Europe are in the region of 120 per 100,000.[2-5]

Higher prevalence ratios for Parkinson's disease have been published. Figures of 217 (men) and 267 (women) per 100,000 have been reported, but the population studied was aged 40 years or older, so the overall figures would clearly be much lower.[6] A figure of 200 per 100,000 has been published for the general population,[7] but no supporting observations are provided. Table 1 shows the prevalence figures calculated from the present observations, and compared with previous studies.

## Discussion

From our observations, the mean interval between the age of onset and the age at which the prevalence was recorded amounted to 4.6 years.

Our findings support our impression that we are seeing more patients with a relatively younger age of onset than would be expected from the epidemiological literature. Referrals to hospital may be biased towards younger age groups, but comparison with previous hospital-based surveys also indicate that we are seeing more young subjects with Parkinson's disease.[8,9] For Helsinki, and to a lesser extent for Vancouver, the data in Table 1 demonstrate relatively higher prevalence ratios compared to population based statistics for those under age 60, than for those aged 60 years or over; these figures are readily evident if the proportion of patients in each age group is compared for each survey.

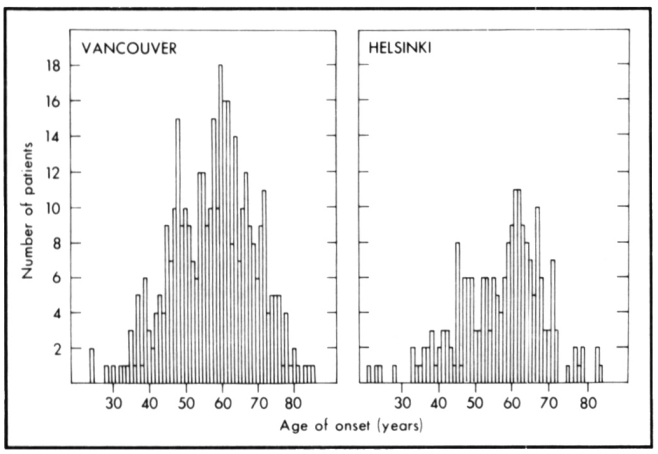


*Figure 1 — Age of onset of Parkinson's disease for patients in Vancouver and Helsinki. For the Vancouver group of 355 patients, 26 patients developed symptoms on or before the age of 40 years; for the Helsinki group of 196 patients, 18 started on or before the age of 40 years. For the entire population, 8% had onset on or before 40 years of age.*

One problem in the interpretation of our findings is the contamination of most previous studies of Parkinson's disease by patients with post-encephalitic parkinsonism; a condition that suddenly became common in the pandemic of 1919-1926, with survivors gradually disappearing over ensuing years. However, for post-encephalitic subjects to be included in surveys from 1935-1966 it is implicit that their age of onset would have been exceptionally young, so this confounding factor would strengthen our case for a trend towards a younger age of onset emerging in recent years.

Could this finding derive from an artefact in the ascertainment of patients because of changing interest in the disease, or altered criteria for diagnosis? We consider both possibilities unlikely because Parkinson's disease is so common that all physicians have to maintain a high level of awareness of the condition, and the basis for diagnosis remains clinical evaluation, as it has been since the time of James Parkinson.

Even if the present figures are biased because of selective referral to University Hospitals, the disparity from the Rochester data 1935-1966[5] is quite striking and the possibility that a real difference exists has to be considered. Our analysis (from previously published prevalence figures) shows that the age distribution of cases in Helsinki and Vancouver is only compatable with stable age-specific prevalence ratios if we have seen *all subjects* from the area of study with young onset Parkinson's disease, together with a disproportionally small fraction of patients whose age of onset was more than 50 years. It is clearly unlikely that these conditions prevail, so we consider it reasonable to conclude that Parkinson's disease may be starting earlier than previously.

Finally, what are implications of this conclusion for the etiology of Parkinson's disease? Twin studies indicate that for the majority of patients, genetic considerations are not relevant[10] and this view is supported by a recent survey of 60 young Parkinsonian patients.[11] An etiology based solely on ageing is rendered unlikely by the fall in incidence rates over the age of 75-80 years in previous studies.[2,4,5,12,13] The accuracy of incidence rates in older populations may be limited, but obser-

**Table 1: Age-Specific Prevalence Ratios**

| Location | Year | Author | Prevalence per 100,000 population age groups | | | |
|---|---|---|---|---|---|---|
| | | | <50 | 50-59 | 60-69 | >70 |
| Rochester | 1955 | Kurland et al, 1973 | 5.0 | 239.0 | 758.0 | 1535.1 |
| Carlisle | 1961 | Brewis et al, 1966 | — | 161.8 | 315.2 | 522.9 |
| Iceland | 1963 | Gudmundsson, 1967 | 9.4 | 162.0 | 932.0 | 1516.0 |
| Gibbsland | 1965 | Jenkins, 1966 | 6.2 | 166.0 | 297.0 | 923.0 |
| Turku | 1971 | Marttila and Rinne, 1976 | 4.5 | 118.9 | 500.5 | 751.9 |
| Vancouver | 1985 | Present* | 1.9 | 42.6 | 105.7 | 114.4 |
| Helsinki | 1985 | Present* | 4.8 | 54.7 | 115.3 | 30.5 |

*Minimal prevalence



https://doi.org/10.1017/S0317167100036647 Published online by Cambridge University Press

vations with monozygotic twins[10] also militate against a simple age-related etiology; inherited factors are generally acknowledged to be major determinants of ageing, yet identical twins have an extremely low concordance rate for Parkinson's disease.

It is difficult to avoid the conclusion that there is an environmental risk factor which is becoming more common. What might be its nature? Cigarette smoking is less frequent than 20 years ago and several reports have claimed an inverse relationship between Parkinson's disease and smoking.[14,15] This is a possible explanation but the inverse relationship is weak and has recently been queried.[16] Infection seems another improbable candidate because infectious disease is less prevalent now than hitherto. Perinatal nigral damage is a risk factor, as is low initial number of nigral neurons,[1] but the management of pregnancy and birth have certainly not deteriorated over the last 20 years, so this explanation also seems tenuous.

There has been recent interest in the possibility of a toxic etiology[17-20] and certain high risk groups have been proposed.[21-24] These suggestions will certainly have to be pursued.

Diet is also a factor to consider.[25] We believe this to be another area for future study; diet could contribute to etiology by either presenting diverse risks of exposure to a toxin, but it could alternatively operate conversely by contributing a variety of protective agents. Certainly diet has been changing over the last 20 years, and it is relevant to point out that the prevalence of Parkinson's disease in China is some 50% of that in Europe and North America, while in Japan it is some 35-45%.[26,27] One of the most obvious differences between the relevant environments is the impact of geography and culture on diet.

### Acknowledgements

We wish to thank the Dystonia Medical Research Foundation and the MRC of Canada for supporting this work. We are also grateful to Susan Calne, R.N. and Eileen Walsh, R.N. for their assistance.

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