

**Feasibility of Conducting a Prevalence Survey
of Parkinson's Disease in the Bipyridil Cohort at Widnes**

Philip Cole, Jack Mandel, Dimitrios Trichopoulos, Hans Olov Adami

These comments are based primarily on a series of notes provided by Syngenta, on several papers relating to the potential study group and on the epidemiology of Parkinsonism and Parkinson's Disease (hereafter collectively, "PSD").

A retrospective cohort study of incident cases of PSD is not feasible because of the lack of a national database to retrospectively ascertain cases of PSD among members of a study cohort. However, a prevalence survey is a feasible study design. In such a survey cases would be ascertained from among those members of the study cohort who can be located and who are willing to provide information on PSD. Because PSD is a relatively uncommon disease that is difficult to diagnose, such surveys are challenging. In addition it is unlikely that both the study group and the comparison group would have been subjected to the same, or nearly the same, criteria of diagnosis and that equal ascertainment of PSD will have occurred.

It is difficult to estimate with any precision a prevalence that is inherently low. For example, the prevalence of PSD among persons 50+ years old varies considerably based on published estimates. It is probably less than 1% and perhaps less than 0.5%. Such a low prevalence can be estimated accurately only in a study of several thousand people. Further, any selection on the part of cohort members (e.g., the self-exclusion of persons who consider themselves too elderly or ill (for any reason) to participate would render findings extremely difficult to interpret. So any prevalence estimate that is based on self-reported diagnoses or on physical exams conducted *ad hoc* are, in effect, the result of screening and are not truly comparable with a prevalence estimate based on documented, patient-initiated medical complaints and subsequent clinical diagnosis.

Considerable thought has gone into estimating the size of the available bipyridil cohort. From information provided to us, it appears that the cohort initially consisted of 729 male employees and 32 female employees who were mainly packers. The vital status of 573 employees was ascertained through the Company's personnel systems and pension fund records. Vital status for 188 workers who had left the company was obtained using the UK National Health Service Central Register (UKNHSCR). Follow-up for cancer incidence was through 31 December 1985. In the early 1990s further concerns were raised about whether there might be an ongoing skin lesion problem in the low temperature sodium (LTS) plant. Consequently, it was decided to extend the Widnes cohort to include workers who had started work on the LTS plant after 1983. Following the plant closure in 1995 the cohort was extended to include all workers who had worked on the LTS plant up to its closure. Therefore, the extended Widnes cohort included 928 male employees including 721 of the male employees included in the original Widnes cohort. This cohort of male workers includes 13 people who have very incomplete records including no date of birth (12 of these were included in the original Widnes cohort).

While there may have been as many as 900 men who were ever included in the cohort, the actual number willing and able to be evaluated for PSD is likely to be considerably fewer because of attrition and willingness to participate in a study. Of the approximately 900 potential subjects, some are deceased and some are no longer under surveillance. However, it is reasonable to assume that some of these men may be found and be willing to participate in the survey. An unknown number, say 10%, or 90, will be lost to follow-up. It seems likely that of any subjects invited to participate at least 30% would unwilling to participate, especially if a physical examination were required. Thus, it seems reasonable to consider that about 500 men would contribute findings to a new study.

Among 500 men, age 50+ in the general population, approximately 3 to 4 prevalent cases of PSD would be expected. Thus, an actual finding of any number of cases from 0 to 5 would be entirely unremarkable and unpersuasive as to the presence or absence

of anything unusual. It would take at least six cases to suggest a borderline, but not persuasive, excess of cases. The study would not be persuasively negative even if zero cases were found.

In summary, a prevalence survey of an uncommon, difficult-to-diagnose condition in a small, possibly select, cohort is most unlikely to produce informative results.