Pooled Analysis of Tobacco Use and Risk of Parkinson Disease

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Context: Epidemiologic studies have reported that cigarette smoking is inversely associated with Parkinson disease (PD). However, questions remain regarding the effect of age at smoking onset, time since quitting, and race/ethnicity that have not been addressed due to sample size constraints. This comprehensive assessment of the apparent reduced risk of PD associated with smoking may provide important leads for treatment and prevention.

Objective: To determine whether race/ethnicity, sex, education, age at diagnosis, and type of tobacco modify the observed effects of smoking on PD.

Design, Setting, and Participants: We conducted the first ever pooled analysis of PD combining individual-level data from 8 US case-control and 3 cohort studies (Nurses’ Health Study, Health Professionals Follow-Up Study, and Honolulu-Asia Aging Study) conducted between 1960 and 2004. Case-control studies provided data for 2328 PD cases and 4113 controls matched by age, sex, and ethnicity; cohort studies contributed 488 cases and 4880 controls selected from age- and sex-matched risk sets.

Main Outcome Measure: Incident PD.

Results: We confirmed inverse associations between PD and smoking and found these to be generally stronger in current compared with former smokers; the associations were stronger in cohort than in case-control studies. We observed inverse trends with pack-years smoked at every age at onset except the very elderly (>75 years of age), and the reduction of risk lessened with years since quitting smoking. The risk reductions we observed for white and Asian patients were not seen in Hispanic and African American patients. We also found an inverse association both for smoking cigars and/or pipes and for chewing tobacco in male subjects.

Conclusions: Our data support a dose-dependent reduction of PD risk associated with cigarette smoking and potentially with other types of tobacco use. Importantly, effects seemed not to be influenced by sex or education. Differences observed by race and age at diagnosis warrant further study.

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EARLY CASE-CONTROL STUDIES SUGGESTING THAT PATIENTS WITH PARKINSON DISEASE (PD) ARE LESS LIKELY TO BE SMOKERS WERE CRITICIZED AS BIASED. THE OBSERVATION IS COUNTERINTUITIVE; CIGARETTE SMOKE HAS LONG BEEN RECOGNIZED AS A CAUSE OF ADVERSE HEALTH EFFECTS. Thus, selective survival of PD cases and reporting bias were suggested as possible explanations. In the 1990s, reports from prospective cohort studies lent more credibility to the assertion that smoking may play a protective role in PD. Recent studies also suggested that PD risk is particularly low in active smokers with a long history of intense smoking; some even suggested dose-related risk reductions with increasing pack-years of smoking. This prompted speculation as to whether and how these observations might inform PD treatment and prevention. The small size of most PD studies and the aggregate nature of meta-analytic data, including the most recent meta-analysis, limit our ability to answer important questions about the role smoking plays in PD. These questions include the importance of smoking intensity vs duration, the influence of age of starting or quitting, the time interval after smoking cessation and before disease onset, and the type of tobacco product (cigarettes, cigars, pipes, or chewing tobacco). Furthermore, no single PD study to date has had adequate sample size or diversity to address the influence of race/ethnicity, sex, education, or age at diagnosis on the observed smoking effects. Here, we address these issues in the first ever pooled analysis of PD where we combine individual-level data from 8 US case-control and 3 cohort studies.

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†Deceased.
STUDY DESIGN

Detailed smoking data were obtained from lead investigators of 8 population-based or nested case-control studies and 3 cohort studies. The pooled data set included a total of 2328 PD cases and 4113 controls from case-control studies and 488 cases and 4880 controls selected in a nested case-control manner from cohort studies. For our pooling effort, we asked that each cohort identify 10 controls per case from age- and sex-matched risk sets of all unaffected subjects at the time of case diagnosis. Methods of identifying subjects and diagnosing cases have been described previously. We included in our analyses only those cases considered newly diagnosed such that data were collected via interview within 3 years of diagnosis in all studies contributing data and the number of subjects per stratum.

For primary analyses involving smoking status and pack-years, we excluded 1 study at a time from the pooled data set to examine the influence of each study group and the consistency of patterns of estimated effects. Trend tests for categorical variables were conducted using the mean (for continuous) or midpoint of each category. Finally, we examined the influence of the time interval after smoking cessation in categories (never smoker; current smoker or quit smoking within past year; quit smoking >1t o5, 5 to 15, 15 to 25, or >25 years prior to reference date). Through pooling we assembled enough data to assess effect measure modification of pack-years smoked by major racial/ethnic categories (African American, Asian, Hispanic, and white), age at diagnosis (<75 years, ≥75 years), and time elapsed since quitting (0-4, 5-24, ≥25 years).

DATA ANALYSIS

Relative risks (odds ratios [ORs]) with 95% confidence intervals (CIs) and dose-response trends, where applicable, were estimated for pack-years of cigarette smoking, smoking status (current, former, never), and cigar-pipe smoking (ever regularly vs never). The logistic regression models were adjusted for sex, ethnicity/race (white, African American, Hispanic, Asian, Native American, other), education (<12 years, 12 years, 13-15 years, ≥16 years), and an indicator variable for each study. For unaffected subjects, we used time/age at which the matched case had been diagnosed as the reference date for assessing smoking. Subgroup analyses were conducted after stratification by sex, age at diagnosis, race/ethnicity, and education. Stratum selection for subgroup analyses was guided, and often limited, by the level of detail in each of the studies contributing data and the number of subjects per stratum.

For primary analyses involving smoking status and pack-years, we excluded 1 study at a time from the pooled data set to examine the influence of each study group and the consistency of patterns of estimated effects. Trend tests for categorical variables were conducted using the mean (for continuous) or midpoint of each category. Finally, we examined the influence of the time interval after smoking cessation in categories (never smoker; current smoker or quit smoking within past year, quit smoking ≥t o5, 5 to 15, 15 to 25, or >25 years prior to reference date). Through pooling we assembled enough data to assess effect measure modification of pack-years smoked by major racial/ethnic categories (African American, Asian, Hispanic, and white), age at diagnosis (<75 years, ≥75 years), and time elapsed since quitting (0-4, 5-24, ≥25 years).

RESULTS
New York City study and the cohort study of Asian males. In case-control studies, about half the subjects reported ever having smoked cigarettes regularly and men reported smoking more often than women (Figure). Most participants initiated smoking in their late teens (mean age, 18 years in men, 21 years in women), and most smokers who had quit did so between the ages of 40 and 50 years. For both sexes, the percentage of subjects who smoked peaked at age 30 years and declined steadily thereafter. Smoking initiation and quitting followed the same general age pattern for cases and controls, but a smaller percentage of patients with PD reported having ever smoked regularly and those who stopped did so on average 2 to 5 years earlier than control subjects (men, 43 vs 49 years; women, 44 vs 49 years). Our cohort data generally confirmed these patterns (results not shown). The average pack-years of cigarettes consumed by smokers varied considerably between studies (16-46 pack-years), reflecting both differences in the average amount of cigarettes smoked per day (0.6-1.3 packs per day) and the average duration of smoking (25-35 years).

While almost one-fifth of study participants reported regular cigar and/or pipe smoking (Table 1), this tobacco use was almost exclusively reported by men (30% vs 0.7%) and was more prevalent among cigarette smokers: only 19% of regular cigar/pipe smokers did not report regular cigarette smoking. In the 5 case-control studies that ascertained use of chewing tobacco, the reported lifetime prevalence was generally low (4%-5% of all subjects; 7% of all men, but only 1% of nonsmoking men).

Our pooled-risk estimates for current and former vs never smoking suggest a similar sized risk reduction for PD among men and women but a stronger reduction in current than former smokers and in cohort studies com-
pared with case-control studies (Table 2). When combining information on quantity and duration of cigarette smoking, we observed inverse trends for PD with increasing pack-years of cigarettes smoked: ie, an average 5% to 8% reduction in relative risk per 10 pack-years (Table 3). Dose-response patterns were similar in both sexes and not affected by restriction of comparisons with smokers (results not shown). Excluding 1 study at a time from the pooled data set did not change the results. For smokers, we also observed inverse trends for quantity of cigarettes and duration of cigarette smoking separately.

For both sexes, a strong inverse dose-response trend was observed for the number of years from cessation of smoking to PD diagnosis (Table 4). This did not change when we excluded never smokers from the comparison group such that the reference group consisted only of former smokers who had quit 25 years ago or more (results not shown). In analysis of pack-years stratified by age at PD diagnosis, we observed a possible trend with age, especially in men (Table 5). When stratifying by age at PD diagnosis and time since quitting, the negative trend with pack-years was still observed in younger age groups but not among persons aged 75 years and older (age <75 years per 10 pack-years, OR=0.92 [95% CI, 0.88-0.96]; age ≥75 years, OR=1.00 [95% CI, 0.96-1.06]).

The negative associations with pack-years of cigarette smoking were not influenced by educational status; ie, effect estimates were similar in different educational strata (results not shown). However, we noticed some race/ethnicity-specific effect measure modification: the inverse association of pack-years on PD risk was observed in white patients and possibly in Asian patients but was not seen in African American (99 cases, 226 controls) and Hispanic patients (130 cases, 160 controls) (OR per 10 pack-years: African American, 1.01 [95% CI, 0.93-1.11]; Hispanic, 1.02 [95% CI, 0.92-1.12]; Asian, 0.92 [95% CI, 0.70-1.20]; white, 0.94 [95% CI, 0.91-0.97]; P value for interaction, .01 comparing white patients with African American and Hispanic patients).

A strong inverse association was suggested for regular smoking of cigars and/or pipes in our pooled male cohorts (OR=0.46 [95% CI, 0.28-0.76]); cigar/pipe smoking data was not available for the female cohort. In our case-control studies, an inverse association with regular lifetime cigar/pipe smoking was seen only among persons who did not smoke cigarettes (cigarette nonsmok-

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### Table 2. Pooled Adjusted Odds Ratios (and 95% CIs) for Parkinson Disease for Current/Former/Ever Smokers Compared With Never Smokers

<table>
<thead>
<tr>
<th>Study</th>
<th>Women</th>
<th>Men</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases, No.</td>
<td>Controls, No.</td>
<td>Odds Ratio (95% CI)a</td>
<td>Cases, No.</td>
</tr>
<tr>
<td>Case-control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>737</td>
<td>1240</td>
<td>0.48 (0.36-0.64)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>880</td>
<td>1442</td>
<td>0.67 (0.55-0.82)</td>
</tr>
<tr>
<td>Ever smoking</td>
<td>955</td>
<td>1694</td>
<td>0.61 (0.51-0.72)</td>
</tr>
<tr>
<td>Cohort</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>95</td>
<td>904</td>
<td>0.28 (0.14-0.56)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>148</td>
<td>1319</td>
<td>0.71 (0.50-1.00)</td>
</tr>
<tr>
<td>Ever smoking</td>
<td>157</td>
<td>1565</td>
<td>0.59 (0.43-0.83)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.
a Adjusted for race, education, and original study.
b Adjusted for sex, race, education, and original study.

### Table 3. Pooled Adjusted Odds Ratios (and 95% CIs) for Parkinson Disease and Pack-Years of Cigarette Smoking in Case-Control Studies

<table>
<thead>
<tr>
<th>Time Smoking</th>
<th>Women</th>
<th>Men</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases, No.</td>
<td>Controls, No.</td>
<td>Odds Ratio (95% CI)a</td>
<td>Cases, No.</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>512</td>
<td>715</td>
<td>1.00 [Reference]</td>
</tr>
<tr>
<td>Continuous (per 10 pack-years)</td>
<td>727</td>
<td>1218</td>
<td>0.93 (0.88-1.00)</td>
</tr>
<tr>
<td>0 to &lt;9 pack-years</td>
<td>92</td>
<td>153</td>
<td>0.82 (0.61-1.11)</td>
</tr>
<tr>
<td>9 to &lt;29 pack-years</td>
<td>51</td>
<td>110</td>
<td>0.73 (0.47-1.13)</td>
</tr>
<tr>
<td>29 to &lt;59 pack-years</td>
<td>37</td>
<td>118</td>
<td>0.53 (0.33-0.85)</td>
</tr>
<tr>
<td>≥60 pack-years</td>
<td>35</td>
<td>122</td>
<td>0.52 (0.31-0.89)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.
a Adjusted for race, education, original study, and time since quitting.
b Reference group.

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ers, OR=0.78 [95% CI, 0.58-1.05]; cigarette smokers, OR=1.13 [95% CI, 0.93-1.37]). Chewing tobacco was rare especially among nonsmokers, and we did not see any association with PD in analyses that included women. However, after adjustment for all other types of smoking, an inverse association for use of chewing tobacco was suggested for men (OR=0.66 [95% CI, 0.43-1.02]).

The large data set of this pooled analysis enabled us to investigate aspects of cigarette smoking and subgroup-specific associations that could not be addressed adequately in previous studies. Our analyses confirmed prior reports of an inverse association between cigarette smoking and PD similar in size to those reported in a recent meta-analysis.9 We also showed that associations did not differ by sex or educational status. Although we found that current smokers and those who had continued to smoke to within 5 years of PD diagnosis exhibited the lowest risk, a decrease in risk (13%-32%) was also observed in those who had quit smoking up to 25 years prior to PD diagnosis. This later observation suggests that the risk reduction is unlikely to be attributable to recent changes in smoking habits resulting from behavior modifications related to incipient disease onset.

Inverse associations with smoking were stronger in our pooled analyses of cohort data. In cohort studies, smoking is assessed repeatedly and prior to disease onset. Thus, smoking information in these studies is likely more accurate and not influenced by recall bias. Better exposure assessment reduces misclassification bias; thus, smoking might be more strongly negatively related to PD than estimates from case-control studies suggest.

Women are generally less likely to be affected by PD.10,13,15 We found that both elderly female patients and controls reported a lower lifetime prevalence of ever having smoked (20% vs 32% smoked at the peak age of 30 years) compared with their male counterparts (44% vs 54% smoked at age 30 years). Female smokers generally smoked less than male smokers (female patients and controls on average smoked 56 and 64 pack-years; men, 64

### Table 4. Estimated Effects (Odds Ratios and 95% CIs) for Number of Years Since Subjects Quit Cigarette Smoking in Case-Control Studies

<table>
<thead>
<tr>
<th>Cigarette Smoking</th>
<th>Women (Cases, No.)</th>
<th>Women (Controls, No.)</th>
<th>Odds Ratio (95% CI)b</th>
<th>Men (Cases, No.)</th>
<th>Men (Controls, No.)</th>
<th>Odds Ratio (95% CI)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsmoker/stopped &gt;25 years ago</td>
<td>591</td>
<td>855</td>
<td>1.00 [Reference]</td>
<td>707</td>
<td>994</td>
<td>1.00 [Reference]</td>
</tr>
<tr>
<td>Stopped &gt;15 to 25 years ago</td>
<td>38</td>
<td>87</td>
<td>0.66 (0.44-0.99)</td>
<td>109</td>
<td>185</td>
<td>0.87 (0.66-1.13)</td>
</tr>
<tr>
<td>Stopped &gt;5 to 15 years ago</td>
<td>44</td>
<td>100</td>
<td>0.62 (0.42-0.91)</td>
<td>93</td>
<td>181</td>
<td>0.76 (0.58-1.01)</td>
</tr>
<tr>
<td>Stopped &gt;1 to 5 years ago</td>
<td>10</td>
<td>62</td>
<td>0.23 (0.12-0.46)</td>
<td>19</td>
<td>57</td>
<td>0.57 (0.33-0.98)</td>
</tr>
<tr>
<td>Current smoker or stopped ≤1 year ago</td>
<td>45</td>
<td>127</td>
<td>0.55 (0.38-0.80)</td>
<td>59</td>
<td>174</td>
<td>0.48 (0.34-0.66)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

a Case-control studies excluding the “Northern California 1” study for which no time of quitting was available.

b Adjusted for race, education, and original study.

c Reference group.

### Table 5. Estimated Effects (Odds Ratios and 95% CIs) for Pack-Years of Smoking by Age and Sex

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Women (Cases, No.)</th>
<th>Women (Controls, No.)</th>
<th>Odds Ratio (95% CI)a</th>
<th>Men (Cases, No.)</th>
<th>Men (Controls, No.)</th>
<th>Odds Ratio (95% CI)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>719</td>
<td>1218</td>
<td>0.94 (0.88-1.00)</td>
<td>964</td>
<td>1564</td>
<td>0.95 (0.92-1.00)</td>
</tr>
<tr>
<td>&lt;60 y</td>
<td>105</td>
<td>165</td>
<td>0.83 (0.65-1.07)</td>
<td>161</td>
<td>174</td>
<td>0.90 (0.75-1.08)</td>
</tr>
<tr>
<td>60-74 y</td>
<td>346</td>
<td>567</td>
<td>0.91 (0.83-0.99)</td>
<td>496</td>
<td>826</td>
<td>0.94 (0.89-0.99)</td>
</tr>
<tr>
<td>≥75 y</td>
<td>268</td>
<td>486</td>
<td>0.96 (0.87-1.07)</td>
<td>307</td>
<td>564</td>
<td>1.01 (0.95-1.07)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NC, not calculated.

a Adjusted for race, education, original study, and time since quitting; 10-year increments of pack-years.

b Interaction of age at diagnosis and pack-years.
and 71 pack-years). Yet, we observed very similar inverse associations by pack-year in both sexes. Thus, smoking behavior cannot explain the sex difference in PD risk.

Interestingly, while we confirmed the dose-response relationship between pack-years of smoking and PD, the inverse association was not seen in subjects older than 75 years of age at diagnosis, regardless of whether we restricted this analysis to smokers or included nonsmokers. A lack of protection due to smoking in older-onset patients with PD had previously been noted by Mayeux et al and in the EUROPARKINSON study, while a 2003 meta-analysis corroborated but did not replicate the finding. Tzourio et al pointed out that many previous studies had been restricted to patients younger than age 75 years. Thus, we calculated the average age at disease onset for all case-control studies included in the meta-analysis by Hernan et al and found that in studies reporting strongly protective ever-smoking odds ratios (OR range, 0.32-0.60) the average age at PD onset/diagnosis was lower (38 years) compared with studies reporting odds ratios in a less protective or no association range (OR between 0.7 and 1.1; average age at onset, 68 years). However, PD case-control study results can be affected by selection bias, in part because the adverse effects of smoking on total mortality are more pronounced among people without PD than among patients with PD, while cohort study results are sometimes limited by small numbers of older individuals. Nevertheless, these findings are consistent with the hypothesis that smoking may delay rather than prevent the onset of PD, and confirmation with larger numbers in prospective studies will be important.

In our analyses of racial/ethnic subgroups, we did not detect any association of smoking and PD in Hispanic or African American subjects, although we did observe an inverse association in white and Asian American subjects; an association in Chinese subjects has been reported previously. Therefore, the risk reduction observed in this pooled study seems to be attributable to white and Asian subjects. Possible explanations include differential diagnosis and genetic diversity. Genetic polymorphisms are known to be differentially distributed among racial groups and diversity of genetic variants may be responsible for observed racial differences. A number of genes may modify the effect of smoking on dopaminergic neurons, including monoamine oxidases (MAO A and B), cytochrome P450 enzymes, glutathione S-transferases, N-acetyl transferase, dopamine and serotonin receptor and transporters, and cannabinoid and opioid receptors. Functional variations in enzymes metabolizing cigarette smoke products may create variations in the risk profiles for PD in different racial groups if the underlying genetic variants are differently distributed among racial groups. Gene-environment interaction studies of MAO B, smoking, and PD have been equivocal, but genetic influences on smoking behavior and dopamine metabolism may be too complex to be addressed in population studies targeting a single gene or polymorphism. The apparent lack of a smoking-PD association in African American and Hispanic individuals may suggest gene-environment interactions but needs to be confirmed in future studies that target racially/ethnically mixed populations.

CONCLUSIONS

Our results for cigar and pipe smoking suggested a 54% risk reduction for PD in our male cohort studies and a 22% reduction among non–cigarette smokers assembled in case-control studies, further corroborating the findings for cigarettes. While our results for the use of chewing tobacco are based on a very small number of regular users, it too suggests a protective effect, at least in men. Similarly, a recent study reported that current and former snuff use had a protective effect in male never-smokers.

The biochemical basis for possible preventative effects of smoking, or of a substance delivered through cigarette smoke, is not well understood, but animal studies have indicated 2 possible mechanisms: chemical or biochemical processes may exist by which substances contained in cigarette smoke such as nicotine or carbon monoxide exert a protective effect and promote survival of dopaminergic neurons; or cigarette smoke alters the activity of metabolic enzymes or competes with other substrates for these enzymes and thereby alters the production of toxic endogenous (dopamine quinones) or exogenous (MPP+) metabolites.

Alternatively, behavioral characteristics or personality traits of patients with PD may be confounding the observed smoking association in that the same genetic or constitutional traits that increase susceptibility to PD may also prevent subjects from smoking. Thus, these traits would be the common cause for both smoking behavior and PD. Observations that smoking and personality are associated with dopaminergic functions lend support to this argument. Like others, we observed that a larger percentage of patients with PD never establish a smoking habit (%–10% fewer cases than controls depending on sex) and that patients with PD quit smoking, on average, 2 to 5 years earlier than control smokers. Both observations fit the personality trait hypothesis. However, to account for the observed dose-response relationship with pack-years in smokers, the trait hypothesis would have to claim that when the constitutional trait is not strong enough to prevent smoking completely, it causes future PD cases to smoke less.

If smoking behavior is influenced by the same underlying genetic factors that contribute to PD risk, one would expect the smoking-PD association to be diminished in twins discordant for PD. Twin studies, however, reported a 20% to 30% reduction of PD risk for ever or regular smoking in monozygotic and dizygotic same-sex male twin pairs discordant for PD. Both studies also found dose-response trends with smoking intensity or duration in male twins discordant for PD, casting doubt on the possibility that the smoking effect might be solely attributable to genetic confounding, at least in men.

Our analyses support a protective, dose-dependent role for cigarette smoking and potentially other types of tobacco use on PD risk. Importantly, estimated effects seemed unaltered by sex or education but were stronger among those with younger age at onset. Differences observed by race need to be further explored, especially to assess whether they might be attributable to differential...
underdiagnosis or whether they represent genuine differences in effect. Ultimately only randomized intervention trials can confirm that some components in tobacco are truly neuroprotective, negating the possibility that a premorbid personality influences smoking behavior among those who later develop PD.

These findings may have implications for the design of future randomized intervention trials. If the protective effect of nicotine on PD risk is limited to those with younger age at onset, trials would best be conducted in younger individuals. Considering that smokeless tobacco may be protective, the drug delivery system need not be inhalation, thus eliminating some of the dangers of smoking. Cigarette smoke is known to have thousands of chemicals; however, most research in PD treatment has focused on nicotine because it protects against nigral neuron damage from a variety of toxic insults in cell culture and in animal models of parkinsonism. In the meantime, there is more to learn from epidemiologic studies with enough statistical power to examine PD associations in subgroups such as users of chewing tobacco or nicotine gums and patches, people exposed to secondhand smoke, or groups that metabolize nicotine or other tobacco constituents at different rates.

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Drafting of the manuscript: Ritz, Checkoway, and Nelson.

Critical revision of the manuscript for important intellectual content: Ritz, Ascherio, Checkoway, Marder, Nelson, Rocca, Ross, Strickland, and Van Den Eeden.

Statistical analysis: Ritz, Ascherio, Checkoway, Nelson, Rocca, and Strickland.

Financial Disclosure: None reported.

Additional Information: The late Dr Gorell was the chair in Neurology at Henry Ford Hospital in Detroit, Michigan, and a movement disorder specialist and the director of the William T. Gossett Parkinson’s Disease Center.

Additional Contributions: We thank all coinvestigators, collaborators, and study subjects who participated in the original studies.

REFERENCES


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**Announcement**

**Calendar of Events: A New Web Feature**

On the new Calendar of Events site, available at http://pubs.ama-assn.org/cgi/calendarcontent and linked off the home page of the Archives of Neurology, individuals can now submit meetings to be listed. Just go to http://pubs.ama-assn.org/cgi/cal-submit/ (also linked off the Calendar of Events home page). The meetings are reviewed internally for suitability prior to posting. This feature also includes a search function that allows searching by journal as well as by date and/or location. Meetings that have already taken place are removed automatically.