Editors' Note: In response to "Incident parkinsonism in older adults without Parkinson disease," Mahlkecht et al. share their own experience of analyzing risk factors for parkinsonism in a separate population. They confirm and expand the study findings, providing additional single markers for prodromal Parkinson disease (PD). Commenting on the same article, Drs. Bohnen and Muller note that factors that contribute to parkinsonism in persons without PD are also likely to contribute to parkinsonism in persons with PD and that physicians need to take age-related pathology and medical comorbidities into consideration when treating gait and balance impairments in PD. Buchman et al., authors of the study, agree with both comments, stress the long subclinical phase in patients with PD, and ask physicians to consider coexisting conditions that may cause parkinsonism.

—Chafic Karam, MD, and Robert C. Griggs, MD

LETTER RE: INCIDENT PARKINSONISM IN OLDER ADULTS WITHOUT PARKINSON DISEASE

Philipp Mahlkecht, Stefan Kiechl, Johann Willeit, Werner Poewe, Klaus Seppi, Innsbruck, Austria:

We read with interest the article by Buchman et al.,¹ which reported that depressive symptoms, neuroticism, urinary incontinence, sleep complaints, and chronic health conditions were associated with incident parkinsonism (48.2% over 5 years) in the elderly. We previously reported on incidence and risk factors of mild parkinsonian signs, a similar concept to possible parkinsonism,¹ in the cohort of the prospective population-based Bruneck Study of 2005.² We now present an analysis of risk factors for parkinsonism according to the definition used by Buchman et al. in this population. Of 393 participants without parkinsonism at baseline undergoing 5-year follow-up, a markedly lower proportion of 16.0% (95% confidence interval [CI] 12.7%–20.0%) developed incident parkinsonism (excluding participants developing secondary parkinsonism). A logistic regression analysis adjusted for age and sex revealed that, out of single markers for prodromal Parkinson disease as defined per movement disorder society research criteria,³ assessed in the Bruneck study,⁴ substantia nigra hyperechogenicity on transcranial sonography (odds ratio 1.99; 95% CI

1.10–3.62, $p = 0.024$), probable REM sleep behavior disorder (6.88; 95% CI 1.10–43.10, $p = 0.039$), olfactory loss (1.96; 95% CI 1.01–3.81, $p = 0.047$), urinary dysfunction (5.15; 95% CI 1.65–16.14, $p = 0.005$), and depression/anxiety (2.85; 95% CI 1.28–6.36, $p = 0.011$) were significantly associated with incident parkinsonism, thus confirming and expanding the findings of Buchman et al.

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AUTHOR RESPONSE: INCIDENT PARKINSONISM IN OLDER ADULTS WITHOUT PARKINSON DISEASE

Aron S. Buchman, David A. Bennett, Chicago:

We thank Mahlkecht et al. for the interest in our study, which reported on risk factors for incident parkinsonism in community-dwelling older adults without Parkinson disease (PD).¹ Mahlkecht et al. confirmed and extended some of our findings, growing the literature that demonstrates that PD, like other chronic diseases of aging, has a long subclinical phase in which brain pathology develops without clinical signs or symptoms, followed by mild signs and symptoms of insufficient severity to warrant a diagnosis of PD, with PD representing a late manifestation.² Overall, this conceptual model is similar to the one currently used for Alzheimer disease (AD).³ However, parkinsonian signs are much more common than subclinical PD pathology and are associated with diverse brain pathologies.^{4,5} Thus, like AD dementia, the clinical phenotype of parkinsonism in older adults may be caused by diverse etiologies. A means for identifying the subset of persons with parkinsonian signs who have PD pathology and are therefore likely

to be at a higher risk for progressing to PD is urgently needed.

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LETTER RE: INCIDENT PARKINSONISM IN OLDER ADULTS WITHOUT PARKINSON DISEASE

Nicolaas I. Bohnen, Martijn Muller, Ann Arbor, MI:

We read with interest the article by Buchman et al.,¹ which reported on the frequency of parkinsonian signs over a 5-year period in older adults without Parkinson disease (PD). The authors showed that 48.2% of older adults who had no or only 1 parkinsonian sign at baseline had 2 or more parkinsonian signs at 5-year follow-up. The observed increase in gait impairment increasing from 19.9% at baseline to 87.4% at follow-up was particularly intriguing. Although the development of parkinsonian signs over time in older adults may signify the effect of age-associated nigrostriatal dopaminergic losses,² we agree with Buchman et al. that gait disturbances in the elderly, in particular, may also be explained by vascular etiology, frailty, medical comorbidities, side effects of medications, or other systemic factors in the absence of prototypical Lewy body parkinsonism.³ The findings of this study are also relevant for patients with PD, as age-related pathophysiology and medical comorbidities may contribute additively to motor impairments (gait and balance disturbances in particular).⁴ Physicians need to take age-related pathology and medical comorbidities into consideration when treating gait and balance impairments in PD.

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AUTHOR RESPONSE: INCIDENT PARKINSONISM IN OLDER ADULTS WITHOUT PARKINSON DISEASE

Aron S. Buchman, David A. Bennett, Chicago:

We thank Drs. Bohnen and Muller for their interest in our study on the high incidence of parkinsonism in community-dwelling older adults without PD.¹ They note, and we agree, that many factors other than PD pathology contribute to parkinsonian signs in older persons.^{2,3} Further, Drs. Bohnen and Muller make an excellent point regarding the implications of our findings for aging persons with PD; namely, the factors that contribute to parkinsonism in persons without PD are also likely to contribute to parkinsonism in persons with PD. This may have implications for treatment response and progression of PD. The situation is similar to that of Alzheimer disease (AD). In older persons, mixed pathologies are the most common cause of AD dementia and the coexisting non-AD pathology contributes to both the detection of AD and a more rapid rate of progression.^{4,5} We agree that physicians need to consider coexisting conditions that make an ever-larger contribution to many diseases with age.

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