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Joseph H Friedman has been active in clinical research on Parkinson's disease for many years, focussing on the behavioral aspects. He has been clinical director of the American Parkinson's disease Association's Information and Referral Center in Rhode Island (RI, USA) for over 20 years, and is Director of the Movement Disorders Program of Butler Hospital and Professor (Clinical) of Neurology and Chief of the Division of Movement Disorders of the Alpert Medical School of Brown University (RI, USA). He is on the editorial board of *Parkinsonism and Related Disorders*, and had served on the executive committee of the Parkinson Study Group and the board of editors of Movement Disorders. He is editor in chief of *Medicine and Health*, Rhode Island, the state's medical journal.

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Foreword

Advances in Parkinson's disease management

Joseph H Friedman

Parkinson's disease (PD) is the second most common neurodegenerative disorder in the western world. Our understanding of this condition has undergone dramatic changes. Until recently, it was considered a paradigm for nongenetic disorders, whereas recent data have implicated a large number of genes, most of which have an uncertain relationship to disease causation. While it is still classified as a 'movement disorder', it is clearly more than this, and more accurately may be considered a neurobehavioral disorder. The behavioral aspects, less well understood than the motoric, appear to be the major determinants of quality of life. While James Parkinson described "the senses and the intellect being uninjured," separate studies have demonstrated that by the time of death, 80% of PD patients are demented, undoubtedly the worst of all symptoms.

Parkinson himself proposed his description of this disorder as a tentative classification, knowing that pathology would be required to prove him correct. But, with time, clarity has come and gone. What took almost 150 years to define, that is the loss of pigmented cells in the brainstem and the presence of Lewy bodies in these same cells or tombstones of these cells, may be falling apart. It is likely that we will ultimately be reading about multiple PDs, each defined by their etiologies, rather than their pathologies or purely clinical characteristics. For example, many of the recessively inherited disorders that meet the clinical criteria for the diagnosis of PD have not been studied post-mortem. Of the few that have, not all have Lewy bodies. Furthermore, the continuing debates about whether dementia with

Lewy bodies is a variant of PD, or is actually the same disease in which the disease begins in the cortex and works its way down, attest to, perhaps, the simplest of the problems we face in studying PD, nosology. Making things even more complicated is the fact that neuropathology itself is a field making rapid advances, so that new ways of identifying pathology not yet available are in development. Looking back on the first description of Lewy bodies in the cortex, a singular event 50 years ago, is now seen routinely with the help of histopathological advances.

Treatment for PD has evolved significantly, although, unfortunately, not at a pace that parallels the advances in basic science. James Parkinson advocated standard remedies of his time, blood letting, purging, the application of poultices to induce blisters on the neck, then surgical incisions in the posterior neck, to produce pus, in order to drain the toxins acting on the presumed site of injury, the medulla. Anticholinergics were used in the 19th century and remained the standard treatment until the development of levodopa in the late 1960s. Subsequent developments, with the exception of deep brain stimulation and stereotactic surgery, have not been as significant. Deep brain stimulation, while a remarkable advance, is useful for only a small percentage of patients. We still lack medication to arrest or even slow disease progression. We lack biomarkers to accurately diagnose and measure disease progression. And we have no important therapies to treat the symptoms that are not dopamine based. Yet progress is being made.

Everything written about clinical disorders is subject to change and journal articles are often outdated by the time they are published. A hard-learned observation has been that the more we understand, the more complicated the problems appear to be.

This book is an attempt to provide an update on the state of our understanding of PD from a clinician's perspective. The chapters are relatively brief so that they can be easily digested at one sitting, and cover a wide variety of topics, both clinical and basic translational. The use of electronic media allows a quick publication, to reduce the risk of being outdated.

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