Parkinson's Disease

A Guide for Patient and Family

Roger C. Duvoisin, M.D.

Raven

Parkinson's Disease

A Guide for Patient and Family

Roger C. Duvoisin, M.D.
Professor of Neurology
The Mount Sinai School of Medicine
The City University of New York
and
Attending Neurologist
The Mount Sinai Hospital
New York, New York

Raven Press ■ New York

Raven Press, 1140 Avenue of the Americas, New York, New York 10036

Made in the United States of America

Library of Congress Cataloging in Publication Data

Duvoisin, Roger C
Parkinson's disease.

Includes index.
1. Parkinsonism. I. Title.
RC382.D94 616.8'33 76-19845
ISBN 0-89004-205-5

PARKINSON'S DISEASE

A Guide for Patient and Family

Preface

Appreciable advances have taken place during the past 10 to 15 years in our understanding of the nature of parkinsonism and more specifically of Parkinson's disease. Treatment has become much more effective but also more complicated. Consequently, the success of treatment depends more than ever on the cooperation of the patient and the family. The best cooperation is built on intelligent understanding of the disease process itself, of what the doctor is trying to do, and of how the treatment actually works. But, alas! There is too little time in the daily bustle and rush of medical practice to explain all that needs explaining and to answer all the questions asked by every patient. Then too, patients often think of the most important questions after they have left the doctor's office, and forget them by the time of the next visit. Some questions are difficult to ask, and perhaps the patient does not know how or what to ask. It is often preferable and easier to find the answers in private, in a book.

Many pamphlets and monographs have been offered to the Parkinson patient over the years with a view to explaining the symptoms or providing a system of exercises or a method of treatment. Many of these are excellent, but most are out of date, and few have attempted to provide a comprehensive account. Patients often complain of the saccharin quality of much of this material. One of my older patients, after reading an especially benign review, growled that its author had "made the disease sound like it was a pleasure to have." Like most patients, this fellow did not want an inspirational message or psychotherapy. He wanted and needed a simple, forthright account about what was going on in his body, what could be done about it, and how to do it. The late Dr. Lewis Doshay's popular

monograph *Parkinson's Disease: Its Meaning and Management* served this purpose when it was written nearly 20 years ago. Subsequently, however, the treatment of parkinsonism has been radically changed by the development and availability of levodopa and then by the enzyme-inhibitor drugs carbidopa and bensarizide. The surgical treatment of parkinsonism has been largely abandoned. Newer forms of treatment undreamed of when Dr. Doshay wrote his book are even now under clinical study. Thus there seems to be a genuine need for an up-to-date book on the subject addressed to patients and their families in adequately detailed but nontechnical terms.

I have tried to answer this need in the present volume and to give the lay reader a comprehensive account of current concepts of the basic nature of Parkinson's disease and other forms of parkinsonism, some understanding of its treatment, and explanations of its more common symptoms. I have done this in essentially the same manner in which I discuss these subjects with patients and their families in the privacy of my office.

It was not without some trepidation that I set out on this task for I was uncertain of the wisdom of dealing with all the major and many of the minor symptoms of Parkinson's disease in a single volume. So numerous and varied are the symptoms that few patients experience them all. I feared that it would be impossible to avoid telling more about the disease than the reader would care to know or perhaps should know. Patients with a particular set of symptoms might be dismayed to learn of still others they had not yet experienced and perhaps never would. In short, I was worried that the burden of full knowledge might be too great for some to bear. Such, after all, was the concept of the physician's responsibility to the patient taught to the medical profession over the past century and persuasively stated by the great physician-teacher Sir William Osler in his essay entitled *Equanimitas.*

The past quarter-century, however, has seen important changes in these stern old Victorian attitudes toward sickness and health. Patients now want to know all they can about their

diseases, and we recognize their right to complete access to the medical truth. We no longer need to write our prescriptions in Latin so that the patients may not know what medicines they are taking. The fear that patients may not be prepared by training and experience to accept the truth has not been vindicated. The new openness has proved in many ways to be unexpectedly healthy. It is obvious in practice that patients fare better and can face their problems with equanimity and intelligence when they gain a reasonable understanding of their affliction, of what their doctor is trying to do for them, and of what can be done with treatments currently available.

Thus I have tried to present a plain, unvarnished account of Parkinson's disease and other forms of parkinsonism, realistically describing the nature of the disease, the various symptoms, the side effects (as well as the good effects) of current drug therapies, and the limits of our present knowledge. In the blunt language of our time, I have tried to "tell it like it is." I must add one word of explanation: In describing the signs and symptoms, I relied on my observations of patients made before the advent of levodopa. The efficacy of this drug is such that many of these manifestations are now quite rare or, when they do occur, are relatively mild. Nevertheless I thought it important to present as complete a picture as possible.

Because I believe that patients with chronic disorders who must take medication for indefinite periods should know what drugs they are taking, why they are taking them, and what the side effects are, I devoted a large part of this book to describing the various drugs used in treating parkinsonism. In describing the drugs, I used the generic names and indicated the trademark names in parentheses. When several trade names exist, I indicated the one which is most familiar or most commonly used. I do not mean thereby to recommend one product over another. The generic equivalent drugs are, to my knowledge, indistinguishable in their effects and serve equally well. I mentioned the trade names employed in the United States and Canada. The same drugs are available in most countries but sometimes under

different proprietary (trade) names.

To a limited extent I ventured into the scientific knowledge underlying the present concepts of parkinsonism. Because these concepts are not fixed but are in constant flux, I thought it important as well as interesting to try to put our present concepts and knowledge in some historical perspective. I also tried to share with the reader the hopes of research and prospects for still better treatment in the years ahead.

Much of the material in this volume has been presented in various lectures I have given over the years to patient groups, nurses, physical therapists, social workers, and lay audiences. To a very considerable extent this book reflects the many things I have learned from my patients and their families. I humbly acknowledge the great debt I owe them for all they have taught me, not only about their disease but about themselves as people, about life itself, of courage in the face of long adversity, and of the remarkable strength of the human spirit. I trust that I have been able to convey what I have learned from them to others who may benefit from this collective experience.

Finally I wish to acknowledge the encouragement of Dr. Alan Edelson, my publisher, the able editorial assistance of Virginia Martin and Laura Kosden of Raven Press, the helpful criticism of my son Marc, whose journalist's eye caught many a syntactical fault, and of my friends Charles and Rhoda Kaufman.

Roger C. Duvoisin

Contents

1

What Is Parkinsonism?

The word parkinsonism refers not to a particular disease but to a commonly recognized condition marked by a characteristic set of symptoms. Chief among these are trembling of the limbs, muscular stiffness, and slowness of bodily movement. To this triad may be added a tendency to stand in a stooped posture; to walk with short, shuffling steps; and to speak softly in a rapid, even tone.

The trembling usually affects the hands and feet but sometimes also the lips, tongue, jaw, abdomen, and chest. It tends to occur in the affected hand or foot when it is at rest and to disappear during a movement. For example, trembling in the hand ceases while reaching out to pick up an object but reappears when the hand is returned to a position of rest. The trembling, or *tremor*, is thus a *resting tremor*, unlike tremors in other disorders.

The muscular stiffness is also of a particular kind. It is called a "plastic *rigidity*" because a doctor examining an affected person finds a constant, uniform resistance to passive manipulation of the limbs. The affected muscles seem unable to relax and are in a state of contraction even at rest.

The third element of the triad, the slowness of bodily movement, is called *bradykinesia* (from the Greek *brady*, meaning slow, and *kinesis*, meaning movement). It is a very complex phenomenon comprising hesitancy in initiating a new movement or activity, slowness in its execution, and rapid fatiguing. The term bradykinesia also encompasses a lack of spontaneity and a diminution in the performance of the automatic movements of which we are usually unaware, such as eye blinking, the swing of

the arms while walking, expressive gestures of the hands while talking, facial expressive movements, etc.

THE UNDERLYING DYSFUNCTION

This complex of symptoms we call parkinsonism reflects the dysfunction of a particular region of the brain—in fact, of a particular system of nerve cells in a center or nucleus known as the *substantia nigra.* It is called the substantia nigra, a Latin expression meaning "black substance," because it is deeply pigmented and may readily be seen by the naked eye on examining specimens of human brain (Fig. 1). It can be seen under the

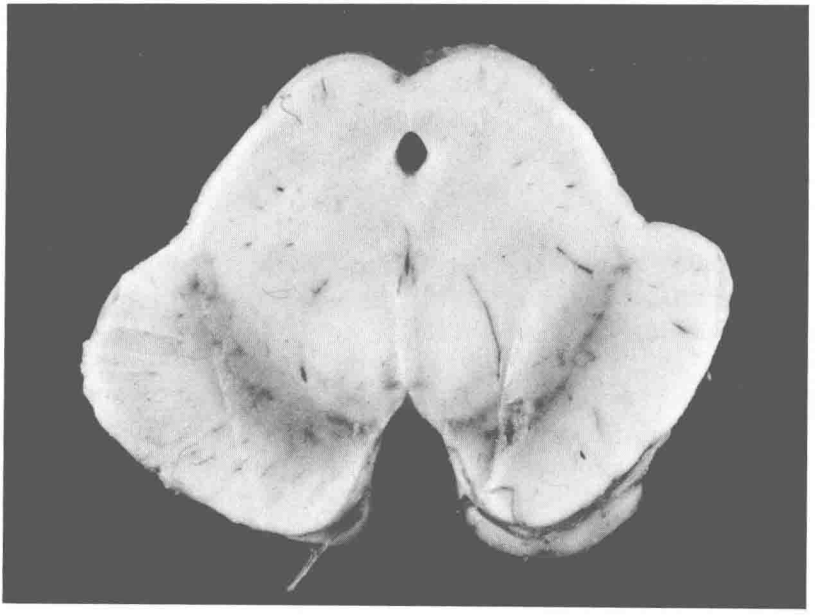

FIG. 1. Specimen of human brain cut transversely through the upper brainstem to show the substantia nigra. This is the appearance in a normal brain.

microscope that the dark color of the substantia nigra is due to pigment granules densely packed within the nerve cells that reside in that nucleus. This pigment seems to be chemically

similar to the melanin pigment responsible for the color of our skin and eyes, and so it has been called neuromelanin. We do not know its chemical structure precisely nor what its function may be. However, we believe that this pigment is related in some way to the fact that these nerve cells produce and store a specific chemical substance called *dopamine.* Similar pigment granules are also found in other nerve cells, mainly in cells which produce and store dopamine and the closely related substances adrenaline[1] and noradrenaline.

The nerve cells of the substantia nigra send long, thin fibers upward to connect with other nerve cells in the deep gray matter of the cerebral hemispheres known as the *corpus striatum* (Fig. 2), or *striate body*. Dopamine made in the cells of the substantia nigra travels up these fibers to the corpus striatum, there to act as a chemical messenger transmitting signals to the nerve cells of the striatum. When the substantia nigra cells are injured or for some reason cannot produce or store dopamine, there results a deficiency of dopamine in the striatum. If the deficiency is sufficiently severe, symptoms of parkinsonism begin to appear. Some neuroscientists have defined parkinsonism in chemical terms as a state of brain dopamine depletion.

A deficiency of brain dopamine can come about in various ways. The nerve cells of the substantia nigra may deteriorate for one reason or another. They may be injured by a tumor, a stroke, a chemical agent, or a virus infecting the brain (encephalitis). Brain dopamine deficiency can also be caused by certain drugs. A functionally comparable state can be caused by drugs which block the action of dopamine in the striatum. The dopamine is then unable to deliver its chemical message, and the end result is the same as when dopamine is deficient. Similarly, if the nerve cells of the striatum which normally receive the chemical messenger dopamine lose their ability to receive the message, the effect is the same as when dopamine is absent. This is believed to be the situation in certain disorders. Without going into fur-

[1]Adrenaline is the common name for this substance. Scientists frequently refer to it as epinephrine. Adrenaline and epinephrine are one and the same.

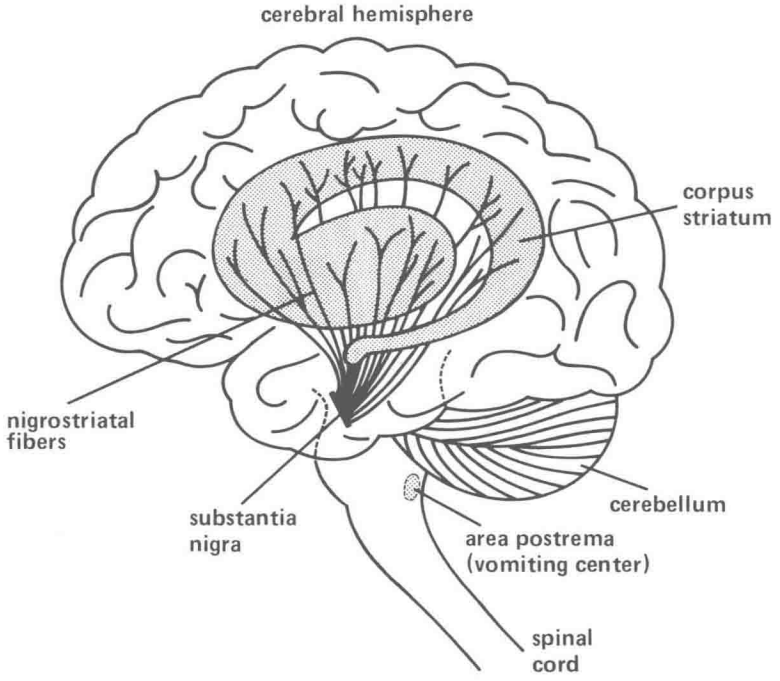

FIG. 2. Left side view of the human brain showing schematically the substantia nigra and the corpus striatum (*shaded area*) lying deep within the cerebral hemisphere. For simplicity, only one side is shown. Nerve fibers extend upward from the substantia nigra and, dividing into many branches, carry dopamine to all regions of the corpus striatum.

ther details, it is clear that there are many possible causes of parkinsonism, some more important than others and some very rare.

PARKINSON'S DISEASE

By far the most prevalent type of parkinsonism today is the condition first described by James Parkinson in 1817 in his *Essay on the Shaking Palsy*. It is generally known as Parkinson's disease. It was the first type of parkinsonism to be recognized and remains the prototype against which other types are

compared. It is sometimes called *idiopathic* parkinsonism or *paralysis agitans*. The term idiopathic means that the cause is unknown. Paralysis agitans is merely "shaking palsy" translated into Latin; it is the official name for the disease in the World Health Organization's International Statistical Classification of Disease.

The cause of Parkinson's disease is not known. Pathologists classify it as a *system* degeneration of the brain because specific groups or systems of nerve cells appear to be the target of some morbid process. The disease process seems to select very precisely only certain nerve cell systems. It is clearly not a random thing. The location of the affected cells is such that their deterioration almost certainly cannot be due to poor circulation or to arteriosclerosis. Nor is there any sign of infection or inflammation. The selective involvement of certain systems of nerve cells scattered through the brain and spinal cord suggest that an unknown toxin or a deficiency of some undiscovered nutrient may be responsible. Some think that there is merely a premature aging process which affects the cells of the substantia nigra. The truth is that the cause or causes are simply unknown.

The disease rarely affects people under the age of 40 years. The average age of onset seems to be about 60 to 61 years. The beginning is usually so insidious and the progression so gradual that it can rarely be dated precisely. Usually the first symptoms noted are, to quote James Parkinson, "a slight sense of weakness, with a proneness to trembling . . . in one of the hands and arms." These symptoms tend to increase very gradually year by year over a period of many years. Indeed, progression is so gradual that little if any change can be seen from one year to the next.

Parkinson's disease is believed to affect about a half-million persons in the United States, or approximately 1% of the population over age 50. It occurs with a similar prevalence in other countries in which good epidemiological studies have been done and appears in all races of mankind all over the world. It is difficult to make precise comparisons in different countries, how-

ever, owing to differences in medical care systems and in statistical methods. Some statistical data are available in England and Wales dating back to the middle of the last century and from various hospitals and university clinics in the United States and several European countries at least as far back as the 1890s. These data suggest that the prevalence of the disease has not changed appreciably over the past century.

There is a widespread suspicion that Parkinson's disease is genetically determined. Many patients ask whether their disease is hereditary or runs in families. The answer to this question seems to be "no." It is true that approximately 10 to 15% of patients report that they have an affected relative. When one actually examines these relatives, it turns out that many—more than half in my experience—have some other disorder. The remaining relatives who do in fact also have Parkinson's disease do not represent a greater number than would be expected by chance. After all, if everyone has at least six relatives who live beyond age 50, and the prevalence of the disease is 1% of the population over age 50, no fewer than six patients in a 100 would be expected to have an affected relative.

There are no known examples of Parkinson's disease in identical twins. I have known several patients with identical twins, and not one of the twins was affected. This alone is rather strong evidence that Parkinson's disease does not have a genetic cause. There is also no evidence that the offspring of a patient with Parkinson's disease are at greater risk of developing the disease later in life than anyone else.

Occasionally one encounters a husband and wife who both have the disease, but the incidence of conjugal parkinsonism is less than 2%, approximately what might be expected by chance alone. This is good evidence that the disease is not contagious. Moreover, since it may be presumed that husbands and wives have shared a similar diet and environment for many years before the usual onset of parkinsonism, this observation is also additional evidence that neither a dietary factor nor an environmental pollutant is likely to be the cause of the disease. No dif-

ference in the incidence of the disease in men versus women has been found. Nor have studies of its incidence in different occupational or socioeconomic groups revealed any special concentration of cases. Parkinson's disease appears to be a democratic disease.

In summary, the cause of Parkinson's disease remains a profound mystery. There is no evidence that genetics, an infectious agent, or a poison in the environment might be responsible.

DRUG-INDUCED PARKINSONISM

Another common cause of parkinsonism today is the drug treatment of mental illness such as schizophrenia. There may be as many cases of drug-induced parkinsonism as there are cases of Parkinson's disease; however, they are almost entirely found among psychiatric patients. The powerful tranquilizing drugs used in treating mental illness block the actions of dopamine in the brain. The resulting disturbance of brain function is essentially the same as that caused by depletion of brain dopamine. The great value of these drugs is that they can tranquilize without causing sedation—that is, without making the patient feel drowsy, groggy, or sleepy. Introduced into medical practice during the mid-1950s, these drugs have revolutionized the treatment of mental illness. They quickly displaced the padded cell, straitjackets, water therapy, and the various coma therapies such as insulin coma, which had previously been the main methods of treatment available. However, these drugs also cause a Parkinson-like state which closely mimics Parkinson's disease and sometimes also presents features of postencephalitic parkinsonism. Efforts to find an effective major tranquilizer that does not cause parkinsonism have thus far failed. It appears that the tendency of these drugs to cause parkinsonism is linked in some fundamental way to their effectiveness in treating mental illness. Indeed, some psychiatrists believe that producing a very mild degree of parkinsonism is necessary to obtain good results in their patients. It has been said, partly in jest but with more than a grain of truth, that treatment with the major

tranquilizers represents a sort of "chemical straitjacket" more humane and more effective than the old physical methods.

The first of the major tranquilizers and probably still the most familiar is the drug chlorpromazine. Its proprietary name in the United States is Thorazine and in Europe Largactil. Many derivatives of chlorpromazine have been made and are widely used as tranquilizers. These include Stelazine, Permitil, Mellaril, and Prolixin, to cite a few of those in more common use by their trade names. One drug of this class, prochlorperazine (Compazine), is used mainly to combat nausea and vomiting. These drugs are known collectively as the phenothiazines.

A closely related chemical family includes the drug haloperidol (Haldol). This is one of the most potent of the major tranquilizers. It can induce a Parkinson-like state within 10 minutes of its injection into a vein!

One of the first tranquilizers found capable of causing parkinsonism was the drug reserpine derived originally from the Indian snakeroot plant *Rauwolfia serpentina.* It is commonly used today to treat high blood pressure. Although in large doses it can induce a state of parkinsonism, it very rarely does so in the small doses in which it is used to lower the blood pressure in hypertensive patients. Reserpine also causes a condition in animals which resembles parkinsonism, and it has consequently been used in experimental work to help find new treatments for human parkinsonism. Another drug used in treating hypertension, methyldopa (Aldomet), also, although very rarely, can produce a chemical parkinsonism. Both these drugs induce parkinsonism by causing a depletion of brain dopamine through chemical means. Several other agents are known that also induce a chemical parkinsonism, but they have been used only as experimental drugs and are not given in ordinary medical practice.

All of these forms of drug-induced parkinsonism are reversible. The Parkinson-like state they cause gradually disappears when the patient stops taking them or if the dose is simply lowered. It may take several days or perhaps 1 to 2 weeks for the