Diagnosis and Initial Management of Parkinson’s Disease

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A 62-year-old man presents with an intermittent tremor in his left hand and some vague discomfort in the left arm. Physical examination shows a minimal rest tremor in the left hand that disappears with use of the limb, mild rigidity at the left wrist and elbow, slowness of finger tapping with the left hand, and decreased arm swing on the left while walking. How should he be evaluated and treated?

The Clinical Problem

Parkinsonism, the syndrome, is a common movement disorder, and Parkinson’s disease, the most common cause of parkinsonism, is the second most prevalent neurodegenerative disease after Alzheimer’s disease. Parkinson’s disease is estimated to afflict about 1 million Americans, or about 1 percent of the population over 60 years of age.1,2 As the U.S. population ages, this number is likely to double in the next 15 to 20 years.3 The disease is uncommon before the age of 40; both the prevalence and the incidence increase steadily thereafter.3,4 The incidence is higher among men than among women.5 All races and ethnic groups are affected.2 Although therapy can ameliorate the symptoms of Parkinson’s disease and improve both the quality of life and life expectancy, Parkinson’s disease continues to be associated with progressive disability and increased mortality.6,7

Parkinson’s disease is caused by the disruption of dopaminergic neurotransmission in the basal ganglia. On pathological examination, the dopaminergic neurons in the substantia nigra are markedly reduced, and Lewy bodies (cytoplasmic inclusions) are present in the residual dopaminergic neurons.

More than 10 autosomal dominant and recessive genes or gene loci have been linked to Parkinson’s disease, but mutation in a single gene is an uncommon cause.8 Nevertheless, 10 to 15 percent of people with Parkinson’s disease will have an affected first-degree or second-degree relative.9 No clear environmental determinants of Parkinson’s disease have been identified.2

Strategies and Evidence

Diagnosis

The diagnosis of Parkinson’s disease is based on the presence of the core features of slowness and paucity of movement (bradykinesia and akinesia) and tremor when the limb is at rest or resistance to passive movement of the joints (rigidity), or both.10,11 Postural abnormalities are often included in the definition but generally occur later in the course of the disorder and are nonspecific, making them of little clinical usefulness in early disease.11 There are four common presentations of Parkinson’s disease: tremor,
a weak and clumsy limb, a stiff and aching limb, and a gait disorder (Table 1).

The classic tremor of Parkinson’s disease is a resting tremor in a limb, most commonly one hand, that disappears with voluntary movement. It frequently emerges in a hand while the person is walking. (A video clip can be viewed in the Supplementary Appendix, available with the full text of this article at www.nejm.org.) Rest tremor is virtually pathognomonic of Parkinson’s disease. However, the diagnosis may be complicated by nonclassic findings, such as tremor when the person is holding the arms out or using the hands in voluntary movement or the absence of a tremor (about 20 percent of cases).12

Essential tremor is the entity that is most commonly confused with early Parkinson’s disease.13 Patients with essential tremor frequently report difficulty drinking from a cup because of their tremulous hands. Essential tremor generally causes a symmetric tremor in the hands, often accompanied by head and voice tremor. If the tremor of Parkinson’s disease affects the cranial musculature, it is generally as tongue, jaw, and chin tremor, not as head tremor. Handwriting may differentiate the two conditions: in essential tremor, the handwriting is large and tremulous; in Parkinson’s disease, it is small and irregular. Rigidity and bradykinesia are not associated with essential tremor.

The bradykinesia of Parkinson’s disease begins asymmetrically in about 75 percent of patients.11 It is often described by the patient as a weakness of a hand or leg, but strength testing reveals no abnormalities. However, assessment of dexterity by finger tapping and toe tapping shows slowing, reduced amplitude of movement, and irregular cadence that become more apparent as the patient continues the movement (see video clip in the Supplementary Appendix). Fine movements are affected more than large movements, so that the patient first notices difficulty using small tools and fastening buttons. Repetitive movements also suffer; for example, brushing the teeth may be difficult.

The rigidity of Parkinson’s disease may be experienced as stiffness associated with vague aching and discomfort of a limb suggesting musculoskeletal syndromes, particularly bursitis and tendinitis. In the arm, this rigidity may progress to a frozen shoulder.14

Early Parkinson’s disease may cause slowing of gait, dragging of the foot, and decreased arm swing on the affected side that can suggest a mild hemiparesis (see video clip in the Supplementary Appendix). Patients may notice difficulty getting out of cars, rising from deep chairs, and rolling over in bed. However, a shuffling gait, freezing, and falls are rare in early disease. The separation of the feet in Parkinson’s disease is normal or even narrow; a wide-based gait suggests other diseases. Shuffling gait disorders with other causes were the second most common misdiagnosis of Parkinson’s disease in general practice.13

The diagnosis of Parkinson’s disease is based on a careful history taking and physical examination. There are no laboratory tests or imaging studies that confirm the diagnosis. Magnetic resonance imaging of the brain or other tests may be appropriate in some patients, particularly those with prominent gait abnormalities, to exclude other conditions, but are seldom necessary in a typical case. Ligands that bind the dopamine transporter and are visible on single-photon-emission computed tomography provide a measure of the density of dopamine nerve terminals; such ligands are available in Europe and

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<tr>
<th>Presentation</th>
<th>Parkinsonism</th>
<th>Differential Diagnosis</th>
<th>Distinguishing Signs</th>
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</thead>
<tbody>
<tr>
<td>Tremor</td>
<td>Asymmetric rest tremor</td>
<td>Essential and other tremors</td>
<td>Symmetric postural and action tremor</td>
</tr>
<tr>
<td>Clumsy or weak limb</td>
<td>Bradykinesia</td>
<td>Carpal tunnel syndrome, radiculopathies, and stroke</td>
<td>Altered reflexes, sensation, and strength</td>
</tr>
<tr>
<td>Stiff or uncomfortable limb</td>
<td>Rigidity</td>
<td>Musculoskeletal syndromes</td>
<td>Pain and limitation of movement</td>
</tr>
<tr>
<td>Gait disorder</td>
<td>Asymmetric slowness, shuffling, reduced arm swing, minimal or no imbalance</td>
<td>Multiple ischemic lesions in the brain, hydrocephalus, and musculoskeletal disorders</td>
<td>Symmetric shuffling, retained arm swing, wide-based gait, prominent imbalance, limited movement at knee and hip</td>
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</tbody>
</table>
are undergoing testing in the United States. Dopamine-transporter imaging may provide useful diagnostic information for treatment when clinical findings are subtle or equivocal. The patient’s response to a trial of levodopa has been suggested as a diagnostic test for Parkinson’s disease but is of questionable value, particularly if the severity of symptoms does not justify long-term therapy with levodopa.

**DIFFERENTIAL DIAGNOSIS**

There is a long list of causes of parkinsonism that includes toxins, infections of the central nervous system, structural lesions of the brain, metabolic disorders, and other neurologic disorders. Most of these causes are rare and are generally suggested by atypical features in the history or examination. In practice, the clinician routinely needs to consider two alternative diagnoses: drug-induced parkinsonism and “parkinsonism-plus” syndromes.

Drug-induced parkinsonism is important to recognize because it is reversible, although reversal may require weeks or months after the offending medication is stopped. Drug-induced parkinsonism accounted for 20 percent of cases of parkinsonism in a population-based study. Dopamine antagonists, including neuroleptic agents, atypical neuroleptic agents, antiemetic drugs, and calcium-channel antagonists (flunarizine and cinnarizine), can induce parkinsonism. Other drugs, such as amiodarone, valproic acid, and lithium, may also cause parkinsonism, but uncommonly and by uncertain mechanisms. Dopamine antagonists also exacerbate Parkinson’s disease and should be avoided, if possible, in the treatment of patients with the disease.

Approximately 25 percent of patients who received an initial clinical diagnosis of Parkinson’s disease are found to have parkinsonism as part of another disorder, such as one of the so-called parkinsonism-plus syndromes. Features suggesting other conditions include falls or dementia early in the course of the disease, symmetric parkinsonism, wide-based gait, abnormal eye movements, Babinski signs, marked orthostatic hypotension, urinary retention, and the development of marked disability within five years after the onset of the symptoms. The parkinsonism-plus syndromes respond poorly to antiparkinsonian medications and have a worse prognosis than does idiopathic Parkinson’s disease. Neurologic consultation is warranted if the clinical features suggest these other diagnoses.

**NONPHARMACOLOGIC MANAGEMENT**

Support and education of patients are critical when giving a diagnosis of Parkinson’s disease. Patients should understand that Parkinson’s disease often has a course over decades, the rate of progression varies greatly from one person to another, and many approaches are available to reduce symptoms. Support groups that include patients with more advanced disease may be alarming rather than helpful to persons with newly diagnosed disease. Patients should be counseled about exercise, including stretching, strengthening, cardiovascular fitness, and balance training, although only small, short-term studies suggest that these may improve activities of daily living, gait speed, and balance.

**PHARMACOLOGIC THERAPY**

The diagnosis of Parkinson’s disease is not necessarily cause to begin drug therapy. Drug therapy is warranted when the patient is sufficiently bothered by symptoms to desire treatment or when the disease is producing disability; patients’ preferences are critical to making this decision.

If the patient needs treatment for motor symptoms, efficacious agents for initial therapy include levodopa, dopamine agonists, anticholinergic agents, amantadine, and selective monoamine oxidase B (MAO-B) inhibitors (Table 2). Except for comparisons of individual dopamine agonists with levodopa, there are no robust comparisons of efficacy among these agents, but clinical experience suggests that the dopaminergic agents are more potent than the anticholinergic agents, amantadine, and selective MAO-B inhibitors. For this reason, dopaminergic drugs are often the initial therapy recommended for patients with troublesome symptoms. Guidelines from the American Academy of Neurology and the evidence-based review of the Movement Disorder Society indicate that initiating therapy with levodopa or a dopamine agonist is reasonable.

**Levodopa**

Levodopa, a dopamine precursor, is considered the most effective antiparkinsonian agent. In randomized trials comparing levodopa and a dopamine agonist, activities of daily living and motor features of Parkinson’s disease improved with levodopa by about 40 to 50 percent (as compared with approximately 30 percent with dopamine agonists). Levodopa, combined with a peripheral decarboxylase inhibitor such as carbidopa to reduce the decarboxylation of levodopa to dopamine in the peripheral nervous system, produces the most consistent improvement in symptoms. The combination of levodopa and carbidopa is available in a variety of dosing forms, making it possible to adjust the ratio of levodopa to carbidopa to optimize the patient’s response on the basis of the individual need for dopaminergic and anticholinergic effects. When levodopa is administered in combination with carbidopa, the anticholinergic side effects are minimized, while the beneficial effects of levodopa are increased. As the disease progresses, the need for levodopa increases, and the response to levodopa therapy diminishes, and levodopa dose requirements increase. Many patients require levodopa supplements at least once daily, and some may require multiple daily doses. In older patients, the absorption of levodopa may be poor, and the levodopa dose may need to be increased. In some patients, especially those with advanced disease, the side effects of levodopa become severe, and the need for levodopa may be reduced to once-daily dosing or eliminated altogether.

**ANTICHOLINERGIC THERAPY**

Anticholinergic agents are used to reduce rigidity and tremor and are often used with levodopa. The anticholinergic agents with the best reduction in tremor are trihexyphenidyl, benztropine, procyclidine, and amantadine. In the past, anticholinergic agents were used frequently to reduce the motor complications of levodopa therapy, particularly in patients who had been treated for several years. However, the use of anticholinergic agents to treat the motor complications of levodopa therapy cannot be recommended. There is a risk of hallucinations, confusion, delirium, and cognitive impairment.

**SELECTIVE MAO-B INHIBITORS**

Selegiline and rasagiline are selective MAO-B inhibitors approved for treatment of Parkinson’s disease. They serve the same function as levodopa in the treatment of Parkinson’s disease but have fewer side effects than levodopa and dopamine agonists. Selegiline is used to reduce levodopa dosage requirements and is also available in combination with levodopa. Rasagiline is used alone and in combination with levodopa. Both selegiline and rasagiline are associated with a lower risk of developing motor complications than levodopa or dopamine agonists. However, the use of selective MAO-B inhibitors is limited by their potential to cause peripheral vasoconstriction and agitation, particularly in patients with a history of cardiovascular disease or hypertension.

**DOPAMINE AGONISTS**

Dopamine agonists include bromocriptine, apomorphine, quinpirole, cabergoline, pergolide, and pramipexole. Dopamine agonists are used during the early stages of Parkinson’s disease and in patients who have responded poorly to levodopa therapy. Dopamine agonists may also be used to substitute for levodopa in patients who experience motor fluctuations or dyskinesias with levodopa therapy. Dopamine agonists are associated with fewer motor complications and less risk of developing motor fluctuations than levodopa and dopamine agonists. However, the risk of developing motor fluctuations is lower with dopamine agonists than with levodopa and dopamine agonists.

**AMANTADINE**

Amantadine is a pyridine derivative that has been used to treat Parkinson’s disease since the 1960s. Amantadine is used as an add-on therapy to levodopa or dopamine agonists in patients who have responded poorly to levodopa therapy. Amantadine is also used as monotherapy in patients who have not responded to levodopa therapy. Amantadine is associated with a lower risk of developing motor abnormalities than levodopa and dopamine agonists. However, the risk of developing motor abnormalities is lower with dopamine agonists than with levodopa and dopamine agonists.

**COMBINATION THERAPY**

Combination therapy with levodopa and a dopamine agonist is often used to treat Parkinson’s disease. Combination therapy is associated with a lower risk of developing motor complications than levodopa or dopamine agonists. However, the risk of developing motor complications is lower with dopamine agonists than with levodopa and dopamine agonists.

**EXERCISE**

Physical therapy and exercise are important components of the management of Parkinson’s disease. Exercise may improve motor function, balance, and quality of life. Exercise may also improve cognitive function and quality of life. Exercise may be beneficial for patients with mild to moderate Parkinson’s disease. However, exercise may be less beneficial for patients with severe Parkinson’s disease.

**SUPPORT GROUPS**

Support groups are critical for patients with Parkinson’s disease. Support groups may provide emotional support, information, and education. Support groups may also provide opportunities for patients to share their experiences and to learn from one another. Support groups may also provide a sense of community and a sense of belonging.

**MEDICAL SPECIALTY CLINICS**

Medical specialty clinics are critical for the management of Parkinson’s disease. Medical specialty clinics provide expertise in the diagnosis and management of Parkinson’s disease. Medical specialty clinics may provide a range of services, including consultation, treatment, and support.

**NEUROLOGIC CONSULTATION**

Neurologic consultation is critical for the management of Parkinson’s disease. Neurologic consultation may be needed to confirm the diagnosis of Parkinson’s disease or to determine the presence of other neurologic conditions. Neurologic consultation may also be needed to determine the course of Parkinson’s disease and to determine the need for treatment.

**PHYSICAL THERAPY**

Physical therapy is important for the management of Parkinson’s disease. Physical therapy may improve motor function, balance, and quality of life. Physical therapy may also improve cognitive function and quality of life. Physical therapy may be beneficial for patients with mild to moderate Parkinson’s disease. However, physical therapy may be less beneficial for patients with severe Parkinson’s disease.

**COUNSELING**

Counseling is critical for patients with Parkinson’s disease. Counseling may provide emotional support, information, and education. Counseling may also provide opportunities for patients to share their experiences and to learn from one another. Counseling may also provide a sense of community and a sense of belonging.
All antiparkinsonian drugs are started at low doses and increased slowly to reduce adverse effects. Likewise, slow withdrawal of these drugs after long-term treatment is prudent to avoid a marked worsening of parkinsonism or even the neuroleptic malignant syndrome (discussed by Keyser and Rodnitzky). MAO-B denotes monoamine oxidase B, SSRI selective serotonin-reuptake inhibitor, and NMDA N-methyl-D-aspartate.

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Example</th>
<th>Initial Dosage</th>
<th>Usual Dosage</th>
<th>Side Effects</th>
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<tr>
<td><strong>First-line dopaminergic agents</strong></td>
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<tr>
<td>Carbidopa plus levodopa</td>
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<tr>
<td>Immediate release (Sinemet)</td>
<td>25 mg carbidopa, 100 mg levodopa</td>
<td>1/2 tablet three times daily</td>
<td>1 to 2 tablets three times daily</td>
<td>At initiation: anorexia, nausea, vomiting, dizziness, hypotension (a 1:4 ratio of carbidopa:levodopa reduces gastrointestinal symptoms), long-term therapy: motor fluctuations, dyskinesias, confusion, hallucinations</td>
</tr>
<tr>
<td>Controlled release (Sinemet-CR)</td>
<td>25 mg carbidopa, 100 mg levodopa</td>
<td>1 tablet three times daily</td>
<td>—</td>
<td>Same as for immediate-release preparations</td>
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<tr>
<td>Carbidopa plus levodopa plus entacapone (Stalevo)</td>
<td>50 mg carbidopa, 200 mg levodopa</td>
<td>1/2 tablet three times daily</td>
<td>1 tablet three times daily</td>
<td>Same as with preparations above, plus diarrhea</td>
</tr>
<tr>
<td>Carbidopa plus levodopa plus entacapone (Stalevo)</td>
<td>12.5 mg carbidopa, 50 mg levodopa, 200 mg entacapone</td>
<td>1 tablet three times daily</td>
<td>—</td>
<td></td>
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<tr>
<td>Carbidopa plus levodopa plus entacapone (Stalevo)</td>
<td>25 mg carbidopa, 100 mg levodopa, 200 mg entacapone</td>
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<td>—</td>
<td></td>
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<tr>
<td>Carbidopa plus levodopa plus entacapone (Stalevo)</td>
<td>37.5 mg carbidopa, 150 mg levodopa, 200 mg entacapone</td>
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<tr>
<td><strong>Dopamine agonists</strong></td>
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<td>Nonergot</td>
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<tr>
<td>Pramipexole (Mirapex)</td>
<td>0.125 mg three times daily</td>
<td>0.5–1.5 mg three times daily</td>
<td>Nausea, vomiting, hypotension, ankle edema, excessive daytime sleepiness, compulsive behavior, confusion, and hallucinations</td>
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<tr>
<td>Ropinirole (ReQuip)</td>
<td>0.25 mg three times daily</td>
<td>3–8 mg three times daily</td>
<td>Same as for pramipexole</td>
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<tr>
<td>Ergot</td>
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<tr>
<td>Pergolide (Permax)</td>
<td>0.05 mg three times daily</td>
<td>1 mg three times daily</td>
<td>Same as for nonergot drugs plus retroperitoneal, pulmonary, and cardiac fibrosis</td>
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<td><strong>Second-line alternatives</strong></td>
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<td>Anticholinergic agents</td>
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<tr>
<td>Trihexyphenidyl (Artane)</td>
<td>1 mg three times daily</td>
<td>2 mg three times daily</td>
<td>Impaired memory, confusion, constipation, blurred vision, urinary retention, xerostomia, and angle-closure glaucoma</td>
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<tr>
<td>Benztropine (Cogentin)</td>
<td>0.5 mg twice daily</td>
<td>1 mg twice daily</td>
<td>Same as for trihexyphenidyl</td>
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<tr>
<td>Selective MAO-B inhibitors</td>
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<tr>
<td>Selegiline (Eldepryl)</td>
<td>5 mg daily</td>
<td>5 mg daily</td>
<td>Insomnia, nausea, anorexia, hallucinations, potential for interactions with SSRIs and meperidine</td>
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<tr>
<td>NMDA antagonist</td>
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<tr>
<td>Amantadine (Symmetrel)</td>
<td>100 mg twice daily</td>
<td>100 mg twice daily</td>
<td>Dizziness, insomnia, nervousness, livedo reticularis, hallucinations, confusion</td>
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</table>

*All antiparkinsonian drugs are started at low doses and increased slowly to reduce adverse effects. Likewise, slow withdrawal of these drugs after long-term treatment is prudent to avoid a marked worsening of parkinsonism or even the neuroleptic malignant syndrome (discussed by Keyser and Rodnitzky). MAO-B denotes monoamine oxidase B, SSRI selective serotonin-reuptake inhibitor, and NMDA N-methyl-D-aspartate.
boxylation of levodopa before it reaches the brain, is available as immediate-release and controlled-release formulations. Carbidopa plus levodopa combined with a catechol O-methyltransferase inhibitor, entacapone, is another preparation designed to prolong the action of levodopa by preventing its O-methylation. Randomized trials have not found controlled-release preparations to be superior to immediate-release preparations as initial therapy.\textsuperscript{23,26} Trials with entacapone preparations are under way.

There are many causes of failure to respond to levodopa, including the use of an inappropriate index of response such as tremor, inadequate doses, inadequate duration of treatment, and drug interactions (e.g., concomitant treatment with metoclopramide or risperidone). A trial of levodopa should be given for three months with gradual titration upward to at least 1000 mg per day (immediate-release form) or until the appearance of dose-limiting adverse effects before concluding that a patient does not have a response to levodopa. Because failure to have a response to an adequate trial of levodopa occurs in less than 10 percent of patients with pathologically proved Parkinson’s disease,\textsuperscript{27} failure suggests the possibility of another disorder and indicates that no pharmacologic or surgical therapy is likely to be beneficial.

\textbf{Dopamine Agonists}

Although dopamine agonists are slightly less effective than levodopa, they are alternative first-line agents for Parkinson’s disease. The various dopamine agonists have similar efficacy. One potential advantage of these agents is that, as compared with levodopa, their use is associated with a lower risk by a factor of two or three of dyskinesia and motor fluctuations in the first four to five years of treatment, particularly among patients receiving dopamine-agonist monotherapy.\textsuperscript{6,24,25} However, it is common for levodopa to be needed in addition to dopamine-agonist therapy within a few years after diagnosis to control advancing symptoms; it is unknown how long the risk of motor complications remains lower when levodopa is added to a dopamine agonist.\textsuperscript{6} Dopamine agonists are avoided in the treatment of patients with dementia because of the drugs’ propensity to produce hallucinations.

The older dopamine agonists, bromocriptine and pergolide, are ergot derivatives that can rarely induce retroperitoneal, pleural, and pericardial fi-

\textbf{Surgical Therapy}

Thalamotomy and thalamic stimulation — deep-brain stimulation with the use of implanted electrodes — can be efficacious in treating the tremor of Parkinson’s disease when it is severe and unresponsive to medication. Pallidotomy, pallidal deep-brain stimulation, and subthalamic deep-brain stimulation can improve all features of Parkinson’s disease in patients in whom the response to antiparkinsonian medications is complicated by severe motor fluctuations and dyskinesia. Because this indication is absent in the early stage of the disease, and because of the risks and expense, surgical therapy has no role in early Parkinson’s disease.

\textbf{Areas of Uncertainty}

\textbf{Possible Neuroprotective Therapies}

At present, there are no proven neuroprotective therapies. There are, however, clinical trials suggesting that selective MAO-B inhibitors,\textsuperscript{32,33} do-
Pramine agonists, and coenzyme Q10 may slow the progression of Parkinson’s disease. Data are needed to clarify the neuroprotective effects of these agents as well as of other putative neuroprotective therapies.

**Timing of the Initiation of Levodopa**

The optimal time for initiating levodopa therapy is uncertain. Limited in vitro data have aroused concern that levodopa may be toxic to dopamine neurons and may actually accelerate the disease process, suggesting that its use should be delayed as long as possible. However, there is little evidence of in vivo toxicity in animals and none in humans. In a randomized trial involving patients with early Parkinson’s disease, those studied after 40 weeks of levodopa therapy (followed by 2 weeks of withdrawal), as compared with those treated with placebo, had better motor function, suggesting that levodopa was not toxic. Neuroimaging, however, showed a reduction in dopamine transporters in the patients treated with levodopa; these results suggest the possibility of some toxic effect but alternatively, may reflect pharmacologic down-regulation of the transporters.

**Choice of Initial Therapy**

It is uncertain whether levodopa therapy or dopamine-agonist therapy is the better choice for initial treatment for Parkinson’s disease. The trade-off for reduced motor complications with the use of dopamine agonists is that the agonists are less efficacious antiparkinsonian agents and have a different spectrum of adverse events — namely, an increase in the rate of somnolence, hallucinations, freezing of gait, and ankle edema. Measures of the quality of life do not differentiate between patients treated with dopamine agonists as initial therapy and those treated with levodopa as initial therapy. Guidelines from the American Academy of Neurology suggest that initiating dopaminergic therapy with either levodopa or dopamine agonists is reasonable.

It is also uncertain whether reducing pulsatile dopaminergic stimulation, as occurs with immediate-release oral preparations of levodopa, will decrease the risk of motor fluctuations and dyskinesia. There is currently no evidence that controlled-release preparations of levodopa decrease this risk. Ongoing studies are examining the effects of carbidopa, levodopa, and entacapone in combined preparations as initial therapy.

**Guidelines**

The American Academy of Neurology has issued clinical-practice guidelines for initial therapy in Parkinson’s disease, and the Movement Disorder Society has published evidence-based recommendations for Parkinson’s disease therapy. The recommendations in the present review are consistent with these guidelines.

**Summary and Recommendations**

The presence of an asymmetric rest tremor, rigidity, and bradykinesia, as in the patient in the vignette, are classic features of early Parkinson’s disease. If there are no other neurologic signs inconsistent with the diagnosis, and if the patient is not taking drugs that may cause parkinsonism, the diagnosis of Parkinson’s disease can be made with confidence without further testing. We would educate the patient about the disease, suggest useful Web sites (e.g., www.apdaparkinson.org, www.michaeljfox.org, and www.parkinson.org), and encourage regular exercise (although its efficacy in slowing disease progression is unclear). His mild symptoms do not necessarily require treatment. Patients who do not require pharmacologic therapy might be encouraged to enter trials of neuroprotective therapies. Were his symptoms interfering with function, we would discuss the pros and cons of various therapies. If the patient had no preference, and given that he is younger than 70 years and his cognitive ability is intact, we would start therapy with a non-ergot dopamine agonist because of the low risk of motor complications during the first five years of treatment. Levodopa would be a reasonable, and more potent, alternative. If there were an inadequate response to the agonist at the maximal tolerated dose, levodopa could be added to the regimen.

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REFERENCES


