



## Standard strategies for diagnosis and treatment of patients with newly diagnosed Parkinson disease

### COMMENTARY

**Richard L. Barbano, MD, PhD, FAAN, Department of Neurology, University of Rochester, and Department of Neurology, Rochester General Hospital, Rochester, NY:** Parkinson disease (PD) is one of the most common neurologic conditions in the United States, with an estimated prevalence of 500,000.<sup>1</sup> Prevalence estimates vary considerably between countries and worldwide estimates are approximate at best, but PD is clearly a relatively common disorder internationally as well.<sup>2</sup> Given that the incidence of PD increases with age, countries with aging populations will be especially challenged. This *Practice Across Borders* series explores several aspects of the standard strategies for diagnosis and treatment of patients with newly diagnosed PD, with an aim of highlighting similarities and differences among practitioners in various countries. International experts were queried as to what testing is used to help determine the diagnosis; the venue of care (who treats patients) and how frequently they are followed; whether established guidelines are used; which of the many treatments are preferred; and what role insurance or other factors plays in these decisions.

The classic signs and symptoms of PD are known to neurologists and internists alike. However, the classic signs are not always present in the early stages, leading to some degree of diagnostic uncertainty. DAT scanning has been developed as an adjunctive test to narrow the differential diagnosis. The penetration of such technologies is not uniform around the world.

As health care costs have risen in the United States, there has been a clamoring for “value-added” care. Some studies suggest that having care orchestrated by a specialist delivers on this promise.<sup>3</sup> The availability and accessibility of such specialists frequently varies widely even within the borders of a single country, let alone across many.

There is also an increasing trend toward development and implementation of guideline approaches to disease-specific care. Guidelines are used to counterbalance the lack of access to specialists with the hope of triaging limited expert resources toward more complex cases. Guidelines are also seen as a way to spread “best practices” more widely among care providers.

Research into the treatment of PD continues at unprecedented levels, and patients have benefitted from an increasing treatment armamentarium. Therapeutic options—noninvasive exercise programs, myriad medication choices, invasive procedures such as deep brain stimulation—have steadily increased over the last decades, yet the uptake of such therapies varies widely. How such choices are made, and what factors influence them, is explored.

Ultimately, in light of similarities and differences, we need to ask: how do patients fare under these systems? Large-scale international outcomes data might help to answer this and focus our attention on what makes a difference in patient care and what is simply local preference, i.e., what is substance and what is style? We hope this series adds to this important discussion.

**Study funding:** No targeted funding reported.

**Disclosures:** R. Barbano serves on a Scientific Advisory Board for Allergan; serves as an Associate Editor for *Neurology: Clinical Practice*; has served as an expert witness in legal proceedings including malpractice, but not involving



commercial entities; and has received research support from Allergan, and NIH, National Institute of Neurological Disorders and Stroke, ORDR: Dystonia Coalition Projects, Site PI. Full disclosure form information provided by the authors is available with the **full text of this article at [Neurology.org/cp](http://Neurology.org/cp)**.

**Correspondence to:** Richard\_barbano@urmc.rochester.edu

1. National Institute of Neurological Disorders and Stroke; website. 2004.
2. Dorsey ER, Constantinescu R, Thompson JP, et al. Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. *Neurology* 2007;68:384–386.
3. Cheng EM, Swarztrauber K, Siderowf AD, et al. Association of specialist involvement and quality of care for Parkinson's disease. *Mov Disord* 2007;22:515–522.



**Alberto Albanese, MD, Istituto di Neurologia, Università Cattolica del Sacro Cuore, Rome, and Fondazione Istituto Neurologico Carlo Besta, Milan, Italy:** The diagnosis of Parkinson disease (PD) is for the most part made by neurologists. A survey performed by an Italian patient association estimated that in Italy about 20% of patients with PD ask for a medical consultation 2 years after onset of symptoms. The delay from first consultation (usually with a general practitioner) to diagnosis is around 5–6 months. Up to 80% of patients are referred to a center specialized in movement disorders, either early in the disease course or later, when motor complications appear. PD is for the most part treated by neurologists and there is insufficient exchange of information between the treating neurologist and the patient's general practitioner.

Some medications can only be reimbursed if prescribed by a National Health System (NHS) specialist based on a written yearly treatment plan. The following drugs for PD and parkinsonian syndromes belong to this category: donepezil, clozapine, quetiapine, rasagiline, and rivastigmine. Patients taking these drugs therefore need to attend at least 1 yearly visit in an NHS specialized center to be granted renewal of treatment plan and reimbursement. Generic drugs are available for products containing levodopa and carbidopa and for oral dopamine agonists, either immediate release or prolonged release. Prescription of generics has been boosted by recent provisions stating that whenever a generic formulation is available it has to be proposed to patients as the first choice. If a generic is available, patients need to pay an additional fee to obtain the branded product.

Specialist visits for the NHS are carried out by NHS doctors during working time with no additional reimbursement and a short allotted time for each visit (around 20 minutes). There is no reimbursement for phone calls or e-mail requests made by the patients: these are usually carried out free of charge by specialist doctors and represent a sizable burden for their activity. The majority of doctors working in teaching and nonteaching hospitals see both NHS and private outpatients. There are no appreciable differences between urban and rural areas. Italy has a high density of urbanization and most patients living in rural areas have easy access to PD specialists in a nearby town.

The diagnosis of PD is clinical and based on the doctor's judgment. Levodopa products are typically used in later disease stages, an attitude shared by doctors and patients, as medical education and patient advocacy groups have repeatedly insisted on the need to delay levodopa prescriptions. Current national guidelines for PD treatment released in 2002 suggest prescribing dopamine agonists as the starting treatment in patients younger than 50 years old and levodopa in patients older than 70. New guidelines are expected to be issued next year. Usually a monoamine oxidase A inhibitor is prescribed as a first drug, followed by a dopamine agonist. Levodopa is typically added at later stages, when there is insufficient motor control. Concurrent prescription of 2 dopamine agonists in a patient is uncommon. A minority of centers prescribe levodopa in patients who have not tried dopamine agonists, also in early disease stages, based on the "oral pulse levodopa strategy" proposed some years ago.<sup>1</sup> The Italian

Medicines Agency has sponsored a multicenter trial aimed at testing the occurrence of dyskinesias in patients treated with the oral pulse levodopa strategy.

Most patients with PD undergo brain imaging, particularly DAT to confirm dopaminergic denervation and MRI to view brain morphology. DAT scan imaging is more frequently requested by general neurologists than by PD specialists. Clinimetric evaluations are typically based on the motor part of the Unified Parkinson's Disease Rating Scale (routinely performed only at specialized centers) and on cognitive assessment. Quality of life scales are not used in routine clinical practice.

There are specialized PD centers throughout Italy, with a higher density in Northern regions. Although the frequency of patient monitoring varies among centers, most propose follow-up visits every 6–9 months. Patient management is rather homogeneous throughout the country, also due to several medical educational programs on PD that have been run in recent years.

**Study funding:** No targeted funding reported.

**Disclosures:** A. Albanese serves as an Associate Editor for the *European Journal of Neurology* and as Editor-in-Chief of *Frontiers in Movement Disorders*; has received speaker honoraria from TEVA, Merz, Ipsen, and Medtronic; receives publishing royalties for *Botulinum Toxin: Clinical Practice and Science* (Saunders Elsevier, 2009); and has research support from Allergan, the Italian Ministry of Health, the Italian Ministry of Research, Catholic University, Beneficentia Stiftung, and the James and Gloria Grossweiler Foundation. Full disclosure form information provided by the authors is available with the **full text of this article at [Neurology.org/cp](http://Neurology.org/cp)**.

**Correspondence to:** alberto.albanese@unicatt.it

1. Quattrone A, Zappia M. Oral pulse levodopa therapy in mild Parkinson's disease. *Neurology* 1993;43:1161–1166.



## JAPAN

**Shin-ichiro Kubo, MD, PhD, Taku Hatano, MD, PhD, Genko Oyama, MD, PhD, Nobutaka Hattori, MD, PhD, Department of Neurology, Juntendo University School of Medicine, Bunkyo, Tokyo, Japan:** In Japan, diagnosis of Parkinson disease (PD) is based on the United Kingdom PD brain bank criteria,<sup>1</sup> including comprehensive physical examination and additional ancillary investigation, routinely a cerebral MRI. 99mTc hexamethyl-propyleneamine oxime SPECT analysis is optional with attending neurologists. Striatal dopamine transporter binding measured using  $\beta$ -carboxymethoxy-3- $\beta$ -(4-iodophenyl) tropane (CIT) SPECT is not available on a practical basis. Instead, an examination using <sup>123</sup>I-metaiodobenzylguanidine myocardial scintigraphy has been available even at local hospitals, which is useful in differentiating PD from parkinsonian variants with high sensitivity and specificity.<sup>2</sup>

In 2002, PD therapeutic guidelines were published in Japan and later revised in 2011 (<http://www.neurology-jp.org/guidelinem/parkinson.html>). The standard approach to assessment and therapies for newly diagnosed PD includes the following:

- Make sure diagnosis is made correctly
- Consider the necessity of starting symptomatic therapies that are withheld for patients with no functional disability who are followed up conservatively with rehabilitation
- Initiate symptomatic therapy with levodopa for functionally disabled patients who are advanced in age (older than 70–75 years), cognitively impaired, or at high risk of falls or unemployment
- Initiate with a dopamine agonist for patients who are relatively young without cognitive dysfunction; although monoamine oxidase B inhibitor (only selegiline available in Japan) had been approved as an adjunct to levodopa, it has just become available for monotherapy
- Add on levodopa when dopamine agonist therapy can no longer exhibit adequate efficacy to control motor symptoms

The approach to assessment and therapies for patients with PD generally is not affected by socioeconomic reasons because a national system of public health insurance has been

established in Japan. In addition, patients with advanced PD (Hoehn and Yahr stage III or higher) are able to be subsidized by the Japanese government.

Issues concerning driving, indispensable to rural life and maintaining employment, may affect decision making regarding the use of dopamine agonists because of their serious side effect of sedation with excessive daytime sleepiness, including sudden onset of sleep. Factors associated with impulse control disorders, including younger age, being unmarried, current cigarette smoking, and a family history of gambling problems, also need to be included in decision making regarding the use of dopamine agonists.

From a global point of view, there are some aspects of PD medications unique to Japan. A mixture tablet of levodopa/dopa decarboxylase inhibitor (DCI) is composed of 100 mg levodopa/10 mg carbidopa or 25 mg benserazide. The choice of the mixture tablet of levodopa/DCI depends on a physician's preference. Some patients respond well to the former and others to the latter. Some specialists take advantage of each of the properties: the carbidopa mixture may be suspended easily in liquid (liquefied oral levodopa is not available) and absorbed effectively through the gut, while the benserazide mixture may exhibit more potent DCI activity resulting in possible reduction of incidence of gastrointestinal symptoms and higher concentration of levodopa in the CNS. While Stalevo, a combination medication containing levodopa, carbidopa, and entacapone, is not available, a 100- or 200-mg tablet of entacapone can be chosen to control motor fluctuations. A considerable number of Japanese patients enjoy the benefits of a 100-mg tablet added to each dose of levodopa/DCI. Interestingly, the major gastrointestinal side effect of entacapone in Japan is constipation, in contrast to diarrhea in Western countries. Zonisamide (ZNS), known as an anticonvulsant, is approved as an adjunct to levodopa to control motor fluctuations in patients with advanced PD.<sup>3</sup> ZNS may induce fewer hallucinations and dyskinesias and be a good option to manage patients having motor complications accompanied with hallucinations. It is intriguing that ZNS is effective for controlling tremor in essential tremor as well as in PD.<sup>4</sup>

With the chronically progressive course of PD, the major issue is how to monitor patients over time. It is important to pay attention to nonmotor symptoms, which frequently have more harmful effects upon quality of life (QOL) than motor symptoms. For instance, impulse control disorders are of concern to patients' families as well as patients themselves. Detailed history taking from family members is necessary, since patients are often unwilling to admit their abnormal behaviors. Our experience shows that patients, especially females, can exhibit compulsive shopping when they become more flashily dressed than before. Autonomic dysfunction may also be problematic in the course of the disease. L-threo-dihydroxyphenylserine (L-DOPS) has been used for orthostatic hypotension (OH) as well as freezing of gait (FOG) over the past few decades in Japan. Evidence is lacking to draw a conclusion that L-DOPS is effective against OH or FOG in PD. Managing patients with PD properly for a long period of time requires an adept understanding of all aspects of the disease, and further studies will provide better QOL for patients.

**Study funding:** No targeted funding reported.

**Disclosures:** S-i. Kubo, T. Hatano, and G. Oyama report no disclosures. N. Hattori serves on the editorial boards of *Movement Disorders* and the *Journal of Neural Transmission*. Full disclosure form information provided by the authors is available with the **full text of this article at [Neurology.org/cp](http://Neurology.org/cp)**.

**Correspondence to:** skubo@juntendo.ac.jp

1. Hughes AJ, Daniel SE, Kilford L, et al. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatry* 1992;55:181–184.
2. Orimo S, Suzuki M, Inaba A, Mizusawa H. 123I-MIBG myocardial scintigraphy for differentiating Parkinson's disease from other neurodegenerative parkinsonism: a systematic review and meta-analysis. *Parkinsonism Relat Disord* 2012;18:494–500.
3. Murata M, Hasegawa K, Kanazawa I. Zonisamide improves motor function in Parkinson disease: a randomized, double-blind study. *Neurology* 2007;68:45–50.
4. Mochio S, Sengoku R, Kono Y, et al. Actigraphic study of tremor before and after treatment with zonisamide in patients with Parkinson's disease. *Parkinsonism Relat Disord* 2012;18:906–908.



## BRAZIL

**Francisco Cardoso, MD, PhD, Neurology Service, Internal Medicine Department, The Federal University of Minas Gerais, Belo Horizonte, MG, Brazil:** Drug-induced parkinsonism (DIP) is a substantial public health problem in Brazil. According to an epidemiologic study, DIP accounts for 37% of parkinsonian patients in the community.<sup>1</sup> As the clinical picture of DIP and Parkinson disease (PD) are virtually identical,<sup>2</sup> the most important item in the assessment of a patient suspected of having de novo PD is to check on the list of medications. Interestingly, in addition to the usual suspects, i.e., neuroleptics, agents commonly causing DIP in Brazil are calcium channel antagonists (cinnarizine and flunarizine) as well as the antiarrhythmic amiodarone.<sup>1</sup> Most neurologists order imaging of these patients. The majority of Brazilians receive medical care from the public health system, where access to MRI can be limited whereas CT scan is widely available. Of course there is the understanding that CT scan and even MRI brain are not usually contributory to the differential diagnosis of the early stages of PD.<sup>3,4</sup> However, as vascular parkinsonism is the third most common cause of parkinsonian syndrome in the country,<sup>1</sup> abnormalities on neuroimaging may help to support this diagnosis. The use of SPECT imaging of the dopamine transporter with [<sup>99m</sup>Tc]TRODAT, which recently became available in the country, is on the rise as a tool to differentiate PD from nondegenerative conditions such as DIP and essential tremor.<sup>5</sup> However, TRODAT is not provided by the public health system, remaining an expensive test. The majority of Brazilian PD patients are followed up by neurologists, although geriatricians and neurosurgeons also take care of a substantial number of these individuals. The frequency of visits to the office depends on the severity of the illness, but in general patients return every 6 months.

### Therapeutic strategies

Neuroprotection in PD remains an elusive goal. The possibility, though unproved, that rasagiline may have a disease-modifying effect<sup>6</sup> has led many neurologists to prescribe it. As rasagiline is not available in Brazil, its use remains confined to a small number of patients who can afford to import it. Of note, Brazilian regulation allows patients to import medications unavailable in the country as long as they are prescribed by a licensed doctor. After the rasagiline studies came out, the prescription of selegiline for de novo PD patients has grown substantially. Although an off-label indication not supported by scientific evidence, such use is based on the biochemical and pharmacologic similarities between rasagiline and selegiline. Moreover, the latter is available free of charge in the Brazilian public health system.

Patients with mild parkinsonism, particularly those with tremor-dominant forms, used to be treated with anticholinergics, especially biperiden. This practice was based on the wide availability and low cost of these agents as well as the unproven notion that anticholinergics are the most effective drugs for parkinsonian tremor. With the realization that these drugs have the potential of inducing a wide range of peripheral (constipation and urinary retention, for instance) and central (cognitive and behavioral changes) side effects, this situation has changed. Nowadays Brazilian neurologists rarely prescribe anticholinergics for patients with PD, preferring agents with better tolerability that are effective for tremor as well as other parkinsonian signs.<sup>7,8</sup> Amantadine is another drug occasionally prescribed for patients with mild early PD, improving, although modestly, tremor, bradykinesia, and rigidity.<sup>8</sup> Its use has increased in the context of managing levodopa-induced dyskinesias in later stages of the disease.

The big dilemma faced by Brazilian neurologists when starting treatment of early PD patients is the same as in other geographic regions: levodopa vs dopamine agonists. In Brazil bromocriptine and pramipexole are the available dopamine agonists with indications for use in PD. In the recent past, neurologists were inclined to postpone introduction of levodopa on the grounds that it could hasten the progression of the disease. After the demonstration that this is not true<sup>9</sup> there

has been a substantial decline in the use of agonists. This trend was reinforced by the findings that agonists may cause severe behavioral problems, particularly impulse control disorders, in up to 1/5 of treated patients.<sup>10</sup> Economic aspects, especially in a developing country, remain a consideration since levodopa is less expensive than agonists. Although both drugs are available free of charge for all patients in the public health system, doctors need not forget that all these medications are covered with money generated from taxes paid by citizens.

Nonmotor findings are common even in the early stages of PD. One of the first and most disabling manifestations of PD is often depression.<sup>11,12</sup> There is growing awareness among Brazilian neurologists of the need to manage depression in early PD patients. Nortriptyline and paroxetine are antidepressants frequently prescribed based on the limited evidence showing they are efficacious in PD.<sup>13</sup> However, the choice of antidepressants is tailored by the clinical features of the patients.

**Study funding:** No targeted funding reported.

**Disclosures:** F. Cardoso has received funding for travel from Roche; serves on the editorial boards of *Arquivos de Neuropsiquiatria*, *Parkinsonism and Related Disorders*, *Tremor and Other Hyperkinetic Movements*, and *Current Treatment Options in Neurology*; receives research support from FAPEMIG; and received a donation from Andrade Valladares to support the Movement Disorders Unit of UFMG. Full disclosure form information provided by the author is available with the **full text of this article at [Neurology.org/cp](http://Neurology.org/cp)**.

**Correspondence to:** cardosofo@terra.com.br

1. Barbosa MT, Caramelli P, Maia DP, et al. Parkinsonism and Parkinson's disease in the elderly: a community-based survey in Brazil (the Bambuí study). *Mov Disord* 2006;21:800–808.
2. Hardie RJ, Lees AJ. Neuroleptic-induced Parkinson's syndrome: clinical features and results of treatment with levodopa. *J Neurol Neurosurg Psychiatry* 1988;51:850–854.
3. Suchowersky O, Reich S, Perlmutter J, et al. Practice parameter: diagnosis and prognosis of new onset Parkinson disease (an evidence-based review). *Neurology* 2006;66:968–975.
4. Berardelli A, Wenning GK, Antonini A, et al. EFNS/MDS-ES/ENS recommendations for the diagnosis of Parkinson's disease. *Eur J Neurol* 2013;20:16–34.
5. Shih MC, Hoexter MQ, Andrade LA, Bressan RA. Parkinson's disease and dopamine transporter neuroimaging: a critical review. *Sao Paulo Med J* 2006;124:168–175.
6. Olanow CW, Rascol O, Hauser R, et al. A double-blind, delayed-start trial of rasagiline in Parkinson's disease. *N Engl J Med* 2009;361:1268–1278.
7. Schrag A, Schelosky L, Scholz U, Poewe W. Reduction of Parkinsonian signs in patients with Parkinson's disease by dopaminergic versus anticholinergic single-dose challenges. *Mov Disord* 1999;14:252–255.
8. Fox SH, Katzenschlager R, Lim SY, et al. The Movement disorder society evidence-based medicine review update: treatments for the motor symptoms of Parkinson's disease. *Mov Disord* 2011;26 (Suppl 3):S2–S41.
9. Fahn S, Oakes D, Shoulson I, et al. Levodopa and the progression of Parkinson's disease. *N Engl J Med* 2004;351:2498–2508.
10. Weintraub D, Koester J, Potenza MN, et al. Impulse control disorders in Parkinson disease: a cross-sectional study of 3090 patients. *Arch Neurol* 2010;67:589–595.
11. Khoo TK, Yarnall AJ, Duncan GW, et al. The spectrum of nonmotor symptoms in early Parkinson disease. *Neurology* 2013;80:276–281.
12. Noyce AJ, Bestwick JP, Silveira-Moriyama L, et al. Meta-analysis of early nonmotor features and risk factors for Parkinson disease. *Ann Neurol* 2012;72:893–901.
13. Seppi K, Weintraub D, Coelho M, et al. The Movement disorder society evidence-based medicine review update: treatments for the non-motor symptoms of Parkinson's disease. *Mov Disord* 2011;26 (Suppl 3):S42–S80.



**FRANCE**

**François Tison, MD, PhD, Wassilios G. Meissner, MD, PhD, for the French Parkinson's Disease Expert Centers; Service de Neurologie, CHU de Bordeaux, Pessac, France; Université de Bordeaux, Institut des Maladies Neurodégénératives, Bordeaux, France:**  
In France, newly diagnosed patients with Parkinson disease (PD) are mostly referred by a

general practitioner (GP) to a public (hospital-based) or private practice neurologist for confirmation of the diagnosis and treatment initiation. Most neurologists rely on a clinical evaluation according to National Health Authority (HAS) recommendations and guidelines.<sup>1</sup> MRI scans and dopamine transporter imaging are increasingly being performed for the differential diagnosis of atypical parkinsonism, for drug-induced parkinsonism and tremor, in early-onset patients, or to deal with the anxiety of patients and their families. Clinical scales such as the Unified Parkinson's Disease Rating Scale are scarcely used in routine practice. Therapeutic strategies are not or little affected by who is covering the cost of treatment or by how medical facilities and professionals are reimbursed, ensuring that health care guidelines are usually respected. Indeed, the expenses for drugs and other inpatient and ambulatory health care are almost fully covered by the health insurance within the frame of chronic diseases ("*Affection de longue durée n°16*"), providing that the parkinsonian syndrome is irreversible and requires the administration of antiparkinsonian drugs for at least 6 months. Some newly diagnosed patients, before being registered by the free care system for chronic diseases, may only have partial coverage of costs (65%). However, most of them have complementary private insurance allowing full reimbursement of their expenses.

There may be some disparities between patients living in urban vs rural areas regarding the ease or delay of being referred to a neurologist or tertiary center, particularly in remote rural areas. Treatment initiation by French neurologists depends upon age, severity, comorbidities, and the neurologist's own experience and beliefs. A direct influence of the marketing of drug companies may exist, but things are changing with new laws emerging that regulate the relationship between the industry and doctors. Most neurologists follow national guidelines (HAS 2000, 2012) recommending that young patients (<60–65 years old) be started with dopamine agonists or monoamine oxidase B inhibitors and older patients be started with standard levodopa + dopa decarboxylase inhibitor. Recent concerns about behavioral side effects of dopamine agonists and the broadcasting of related medicolegal issues have certainly had an effect on the neurologist's choice for treatment initiation.

Follow-up is usually performed every 3 to 6 months in outpatient hospital-based or private practice neurology clinics depending on the therapeutic strategy, the drug response, and side effects. When a patient with PD is followed by a neurologist, the GP usually does not interfere too much with the antiparkinsonian treatment besides minor adjustments or emergencies.

The landscape of medico-social care for PD is currently changing in France with the recent funding of 24 regional expert and 7 interregional coordinating centers that cover the entire national territory. The mission of the expert centers is to organize and coordinate multidisciplinary and personalized care, to implement patient education, and to disseminate good practice tools for improving the care of PD beyond the expert centers and their networks.

**Study funding:** No targeted funding reported.

**Disclosures:** F. Tison has served on scientific advisory boards for Novartis, UCB, Boehringer-Ingelheim, GlaxoSmithKline, and ABBOTT; has received funding for travel from GlaxoSmithKline, Lundbeck, Novartis, TEVA, and UCB; serves as a consultant for ADDEX Pharma; and receives research support from Novartis, the French Ministry of Health, the University Hospital Bordeaux, and the Michael J. Fox Foundation. W. G. Meissner has served on scientific advisory boards for ANM GmbH and Novartis; has served on speakers bureaus for and received funding for travel and/or speaker honoraria from GSK, Expression Santé, Lundbeck, Novartis, TEVA, and UCB; serves on the editorial board of the *Journal of Neural Transmission*; and has received research funding from the Michael J. Fox Foundation, the University Hospital Bordeaux, the French Health Ministry, APTEs (French patient association for essential tremor), and PSP-France, as well as unrestricted research grants from Novartis and TEVA/Lundbeck. Full disclosure form information provided by the authors is available with the **full text of this article at [Neurology.org/cp](http://www.neurology.org/cp)**.

**Correspondence to:** francois.tison@chu-bordeaux.fr

1. Haute Autorité de Santé, 2000 and 2012. Guide du parcours de soins: maladie de Parkinson. Available at: [http://www.has-sante.fr/portail/upload/docs/application/pdf/2012-04/guide\\_parcours\\_de\\_soins\\_parkinson.pdf](http://www.has-sante.fr/portail/upload/docs/application/pdf/2012-04/guide_parcours_de_soins_parkinson.pdf). Accessed September 30, 2013.



## UNITED STATES

**Daniel Tarsy, MD, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA:**

### Assessment

Special clues to diagnosis of idiopathic Parkinson disease (PD) are asymmetric onset, resting tremor, and an objective, robust response to treatment with L-dopa. Brain MRI is used to exclude rare structural causes of parkinsonism. Ceruloplasmin levels to exclude Wilson disease and thyroid function tests are appropriate in some patients. Dopamine uptake scans, or DaTscans, are now available in the US for diagnosis of PD. Currently DaTscan technology in the US is not able to estimate duration or severity of PD. These tests also do not differentiate idiopathic PD from atypical parkinsonism and are used mainly when there is uncertainty concerning diagnosis, for example, in patients in whom drug-induced or arteriosclerotic parkinsonism may simulate PD.

### Therapeutic strategies

**Education and support** The diagnosis of PD is frightening and proper education is essential to provide the patient and family with some feeling of control over the disorder. Incorrect and misleading information is sometimes found on the Internet and must be countered by accurate information concerning symptoms, expected clinical course, and available treatments. Web sites of national PD organizations such as the Parkinson's Disease Foundation ([www.pdf.org](http://www.pdf.org)), the National Parkinson Foundation ([www.parkinson.org](http://www.parkinson.org)), the American Parkinson Disease Association ([www.apdaparkinson.org](http://www.apdaparkinson.org)), and the Michael J. Fox Foundation ([www.michaeljfox.org](http://www.michaeljfox.org)) are good sources of basic clinical information and information concerning research into the causes and treatment of PD.

**Diet** There is no specific diet recommended for patients with early PD. Large high-fat meals that slow gastric emptying should be avoided and fiber should be encouraged to prevent the constipation that often accompanies PD. Poor nutrition and weight loss should be avoided with appropriate diet. Avoiding protein, which competes with L-dopa absorption, is recommended later in the disease for patients with motor fluctuations. Coenzyme Q10 is not ineffective in slowing the progression of PD.

**Exercise and lifestyle** Regular exercise promotes a feeling of physical and mental well-being for patients with PD. Aerobic exercise and muscle stretching are particularly useful. There is recent evidence that some forms of exercise may relieve symptoms of PD or possibly even slow its progression. Tai chi has been shown to improve balance and reduce falls in patients with mild-moderate PD and is often recommended for patients with PD. Physical and occupational therapy become important in more advanced stages of PD.

**Medications** To date no medications with definite disease-modifying effects are available for treatment of PD. Symptomatic medications are introduced when motor symptoms become intrusive enough to warrant therapy. Selective monoamine oxidase B inhibitors such as selegiline and rasagiline have appeared to show mild disease-modifying effects, likely due to the modest therapeutic benefits they provide for some patients with early PD. A hierarchy of medications with symptomatic benefit is available for treatment of PD. In the United States, rasagiline is often used for treatment of patients with mild symptoms and signs, particularly when patients desire early therapeutic intervention. Amantadine appears to have mild therapeutic effects in early PD and is also often used for initial monotherapy in patients with early PD. Anticholinergic drugs benefit some patients with resting tremor or the foot dystonias that accompany PD in younger patients. Patients with more intrusive motor symptoms are usually first treated with dopamine agonists such as pramipexole and ropinirole, which are available as oral agents in immediate- or extended-release formulations. Rotigotine is a transdermally applied, slowly released dopamine

agonist applied daily as a skin patch that is useful for patients with mild motor fluctuations. This formulation is appealing to some patients who prefer it to orally administered medications. L-dopa remains the gold standard treatment for patients with PD, especially in patients older than age 60 with substantial bradykinesia. Extended-release formulations of L-dopa are less commonly used than in the past and currently are largely used before sleep in patients experiencing nocturnal akinesia. Levodopa-carbidopa intestinal gel is currently used in Europe in patients with motor fluctuations but is not currently available in the US. Catechol-O-methyltransferase inhibitors such as entacapone and tolcapone increase the half-life of L-dopa by slowing its metabolism and produce more stable plasma L-dopa concentrations with longer therapeutic effect. They are ineffective if given alone to patients with early PD without motor fluctuations. Treatment of nonmotor symptoms with standard medications used for depression, anxiety, sleep disorders, autonomic disorders, dementia, and psychosis is common when required at any stage in the disease.

**Patient monitoring** Ideally, the effects and potential side effects of these medications should be monitored by regular follow-up visits to a neurologist experienced in the management of PD. However, in practice, most patients with PD in the US are followed by general neurologists or primary care providers together with occasional consultation with movement disorders specialists.

**Influence of insurance and health care systems** Routine diagnostic testing in patients with PD is adequately covered in the US. Medications are generally covered as well with the exception of some more expensive extended-release dopamine agonist preparations in which failure to respond to standard-release preparations must be documented before extended-release preparations are covered. Some antiparkinson medications are very expensive. Since many PD patients in the US are covered by Medicare and often require other medications, coverage for expensive antiparkinson medications is often limited, resulting in a considerable burden for the patient.

**Study funding:** No targeted funding reported.

**Disclosures:** D. Tarsy has received speaker honoraria from UCB Pharma and the International Movement Disorders Society; receives publishing royalties from *UpToDate* and for *Movement Disorders: A Video Atlas* (Springer 2012); serves as a consultant for Genzyme and Neurocrine Biosciences; receives research support from Phytopharm PLC and the National Parkinson Foundation; and has participated in medicolegal proceedings. Full disclosure form information provided by the author is available with the **full text of this article at [Neurology.org/cp](http://Neurology.org/cp)**.

**Correspondence to:** dtarsy@bidmc.harvard.edu