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Does This Patient Have Parkinson Disease?

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CLINICAL SCENARIO

A 68-year-old man presents with a 3-month history of right arm tremor at rest. His movements have been slower and he has difficulty getting out of a chair. Physical examination reveals rigidity in the upper limbs. He walks with small steps and has limited ability to swing his arms. His facial expressions are limited.

Why Answer This Question With a Clinical Examination?

With a prevalence estimated between 150 and 200 per 100,000, Parkinson disease (PD) is one of the most common neurological disorders.¹ It is more prevalent in older persons, affecting 1% of those older than 65 years and 2% of those older than 85 years.²

Although common, the diagnosis of PD is challenging. Laboratory tests are not available and conventional imaging studies are not helpful. The best reference standard is, unfortunately, neuropathologic (depletion of brain stem pigmented neurons and proliferation of Lewy bodies).³ Serial neurological evaluation with or without concomitant treatment can also be used.⁴ The response to an acute levodopa challenge has been used as a diagnostic tool. This test is problematic for a number of reasons. Its sensitivity and specificity are low. Acute levodopa adminis-

Context Diagnosis of Parkinson disease (PD) remains challenging. An accurate diagnosis is important because effective symptomatic treatment for PD is available.

Objective To systematically review the literature for information on the precision and accuracy of the clinical examination for diagnosing PD.

Data Sources MEDLINE database was searched for all English-language articles related to the diagnosis of PD published from January 1966 through April 2001. The reference lists of all articles retrieved were searched for additional relevant sources.

Study Selection Studies in which patients presented with 1 or more typical features of PD were included if the final diagnosis was confirmed by a suitable criterion standard and data could be extracted to determine the accuracy of 1 or more symptoms or signs. Variability in descriptions of symptoms and signs made it impossible to combine data across existing studies for most findings.

Data Synthesis We identified 6 studies that met our criteria. The positive (presence) likelihood ratios (LRs) for tremor as a symptom of PD ranged from 1.3 to 17 (range of negative [absence] LRs, 0.24 to 0.60). Tremor as a sign of PD produced a range of positive LRs from 1.3 to 1.5 (negative LRs, 0.47 to 0.61). Clinical features useful in the diagnosis of PD include a history of the combination of symptoms of rigidity and bradykinesia (positive LR, 4.5; negative LR, 0.12); a history of loss of balance (range of positive LRs, 1.6 to 6.6; range of negative LRs, 0.29 to 0.35), symptoms of micrographia (range of positive LRs, 2.8 to 5.9; range of negative LRs, 0.30 to 0.44), and a history of shuffling gait (range of positive LRs, 3.3 to 15; range of negative LRs, 0.32 to 0.50). Trouble with certain tasks such as turning in bed (positive LR, 13; negative LR, 0.56), opening jars (positive LR, 6.1; negative LR, 0.26), and rising from a chair (range of positive LRs, 1.9 to 5.2; range of negative LRs, 0.39 to 0.58). Useful signs include the glabella tap test (positive LR, 4.5; negative LR, 0.13), difficulty walking heel-to-toe (positive LR, 2.9; negative LR, 0.32), and rigidity (range of positive LRs, 0.53 to 2.8; range of negative LRs, 0.38 to 1.6). Significant selection bias was detected in all studies included for review.

Conclusions Symptoms of tremor, rigidity, bradykinesia, micrographia, shuffling gait, and difficulty with the tasks of turning in bed, opening jars, and rising from a chair should be carefully reviewed in all patients with suspected PD. The glabella tap and heel-to-toe tests also should be assessed.

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tration is associated with significant adverse effects. There is lack of agreement on what constitutes a threshold response. The test is expensive and inconvenient.⁵ The clinical examination, therefore, is the basis for initial

diagnosis. Classic clinical features of PD include tremor at rest, bradykinesia, rigidity, and postural instability.

There is evidence that the accuracy of diagnosis in some settings is improving. In a 1991 study by Rajput et al⁶ among

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Box 1. Typological Classification of Tremors

Rest Tremor: Tremor occurring in a body part that is not voluntarily activated and is supported completely against gravity.

Action Tremors:

Postural. Tremor that occurs while voluntarily maintaining a position against gravity.

Kinetic. Tremor occurring during any voluntary movement.

- (1) Simple. Tremor occurring during voluntary movements that are not target-directed.
- (2) Intention. Tremor whose amplitude increases during visually guided movements (eg, finger-to-nose test).
- (3) Task-Specific. Tremor that appears or is exacerbated by specific tasks (eg, writing).
- (4) Isometric. Tremor that occurs during voluntary muscle contraction against a rigid stationary object (eg, squeezing examiner's hand).

Box 2. Three Common Tremor Syndromes

Tremor of Parkinson Disease: Slow frequency (4-6/s) tremor at rest. Tremor inhibited during movement and sleep. Aggravated by emotional distress. "Pill rolling quality."

Classic Essential Tremor: Bilateral, usually symmetric postural or kinetic tremor. Family history of tremor is common. Attenuated by alcohol.

Physiological Tremor: Present to differing degrees in all subjects. Enhanced form is easily visible, mainly postural, and has a high frequency (8-12/s). No evidence of underlying neurological disease. Cause is usually reversible (eg, caffeine).

41 patients diagnosed clinically with PD by neurologists, the disease was confirmed neuropathologically at autopsy in 31 (positive predictive value [PPV] of 76%). Hughes et al⁷ recently evaluated the accuracy of clinical diagnosis among 100 patients with PD, 86 of whom were followed up by neurologists, 7 by geriatricians, and 7 by internists. The diagnosis was confirmed at autopsy in 90 persons (PPV=90%). An even more recent study confirmed PD at autopsy among 72 of 73 patients (PPV=98.6%) followed up by neurologists affiliated with a highly specialized movement disorders center.⁸ Despite these improvements and impressive results, it is important to keep in mind that the clinical diagnoses in these studies were often made over a long period and by physicians with a great deal of expertise and experience. The accuracy of clinical diagnosis in other settings is unclear. Parkinson disease is still mistaken for other

neurological disorders. The most frequent misdiagnoses include progressive supranuclear palsy, multisystem atrophy (MSA) (encompasses the diagnoses Shy-Drager syndrome, olivopontocerebellar atrophy, and striatonigral degeneration), and dementia with Lewy bodies.⁶ The differential diagnosis also includes essential tremor and vascular pseudoparkinsonism. Mistaking PD for other conditions can lead to inappropriate and ineffective treatment. While a patient with essential tremor, for example, may benefit from a β -blocker, this treatment would have no effect on the tremor of PD. Inappropriate treatment based on misdiagnosis also delays the use of dopaminergic medications, which can decrease the severity of symptoms and disability.⁹

Mistaking other disorders for PD is also harmful. Dyskinesias, for example, appear in 15% to 85% of persons within 5 years of treatment with

levodopa and hallucinations occur in 20% of patients.¹⁰ There is also evidence that levodopa causes damage to dopamine neurons leading to accelerated dopamine degeneration.⁵ Whether the initial diagnosis is correct or not, the disease has serious social and psychological consequences.^{11,12} In summary, the clinical examination is important in suspected PD because no laboratory or radiological tests are helpful diagnostically. Misdiagnosis of PD is associated with adverse effects.

Pathophysiological Characteristics

It is important to distinguish between PD and parkinsonism. *Parkinsonism* refers to any clinical syndrome in which 2 or more features are present such as tremor, rigidity, and bradykinesia. Parkinson disease is a form of primary or idiopathic parkinsonism. Viral infections, environmental toxins, oxidative stress, and heredity have all been suspected as causes.¹³ Secondary or acquired parkinsonism has a variety of causes including head trauma, cerebrovascular disease, and hydrocephalus.^{14,15} Secondary parkinsonism may persist for months after the drugs that caused it are discontinued. A thorough inquiry into past and current medication use, therefore, is essential when questioning patients presenting with parkinsonism. Parkinson disease manifests as neurons and dopamine are lost from the substantia nigra and intracytoplasmic inclusions (Lewy bodies) appear. Symptoms appear when 70% to 80% of dopamine is lost.¹⁶

Symptoms and Signs

Nonspecific insidious symptoms including generalized malaise, easy fatigability, and subtle personality changes mark the onset of PD. These may occur years prior to the appearance of tremor, limb rigidity, bradykinesia, and postural instability.¹⁶ Numerous secondary manifestations appear unpredictably and are as varied as disordered sleep (42% of patients),¹⁷ constipation (50%), pain (50%), depression (40%), and dementia (20%).^{16,18} Signs typically begin unilaterally and then progress asymmetrically.

James Parkinson described the combination of tremor and bradykinesia as a shaking palsy.¹⁸ Seventy-five percent of patients complain initially of a tremor that usually occurs at rest in an upper extremity and is characterized by visible oscillations with a frequency of 4 to 6 per second. Tremor appears intermittently, disappearing during sleep and increasing in severity during times of emotional distress or anxiety. It is often described as pill-rolling, because a rhythmic movement is observed in the hand as the index finger flexes and extends against the thumb repetitively.¹⁹

Some basic features distinguish the tremor of PD from physiological and essential tremors (BOX 1 and BOX 2).^{20,21}

Rigidity, an involuntary stiffness of the skeletal muscles, is a common sign. Electromyogram assessment of parkinsonian patients reveals an alternating discharge pattern in opposing muscle groups, even at rest (eg, triceps and biceps). Resistance to movement of limbs may be smooth or interrupted. *Cog wheeling* refers to the jerky motion of limbs as constant force is applied across a joint, which is similar to the ratcheting of the cogs of gears as they click.²² Unlike rigidity, *spasticity* refers to a selective increase of tone of flexor muscles in the arms and extensor muscles in the legs²³ and suggests a diagnosis other than PD.

Bradykinesia refers to the overall slowing of active movement or slowness in initiating movement. The initial surge of motor activity is inadequate and movements are fragmented into a series of incremental steps. Postural instability in patients with PD presents as changes in gait and balance. Short and shuffling steps are often accompanied by festination. Loss of arm movements commonly appears. The patient may walk with the arms straight down, rather than swinging them back and forth. Gait disturbance is the major cause of disability in many patients. As postural reflex mechanisms are lost, patients become stooped over and have a tendency to fall. Those with severe deficits are sometimes confined to a wheelchair or bed.

How to Elicit Signs

Tremor. Tremor can be defined as any rhythmical, involuntary oscillatory movement of a body part. The tremor classification is complex and has overlapping features in different disease syndromes. Nevertheless, the Movement Disorder Society has developed a classification system to help clinicians distinguish tremor types.²⁴ Tremors can be classified as *rest* or *action*.

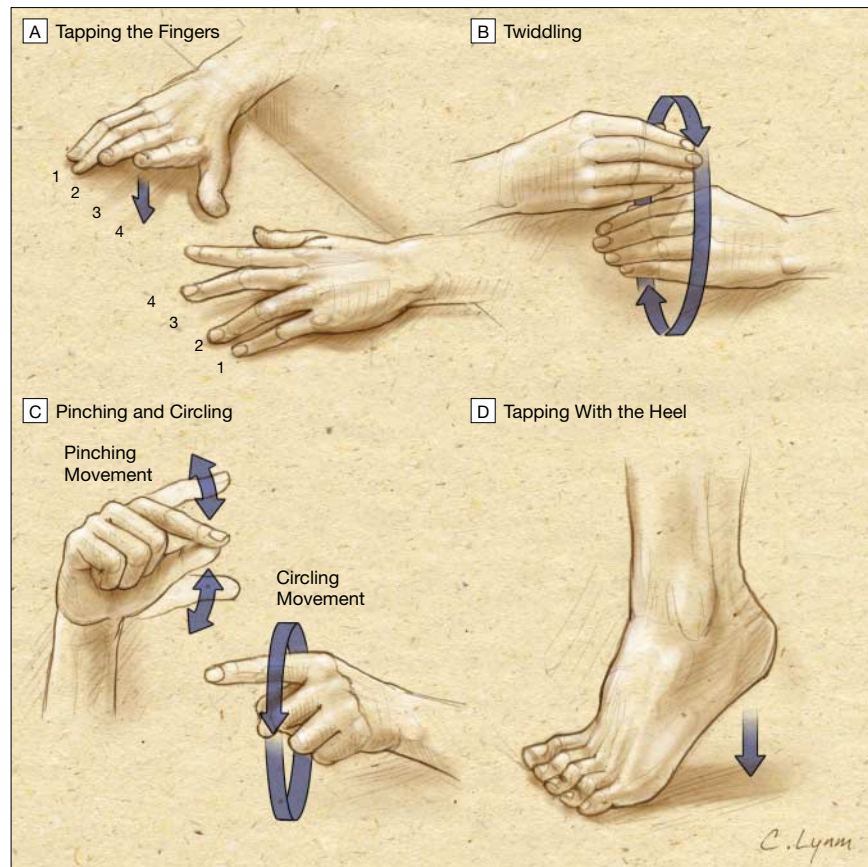
The classification system divides tremors into 11 syndromes. Patients with PD typically have a slow (frequency of about 4-6/s) tremor at rest. It is easily observed by having the patient position his/her hands on his/her lap. Clinicians should be aware of the key features of this and classic essential tremor and physiological tremor (Box 2).

Precise measurement of tremor frequency and amplitude are sometimes used in diagnostic evaluation. This re-

quires special devices and is beyond the scope of the clinical examination.

Rigidity. Involuntary muscle stiffness or rigidity can be shown if resistance to passive movement of the limbs is detected. With the patient relaxed, the examiner places his/her thumb across the antecubital fossa with one hand while passively flexing and extending the elbow several times with the other hand. Rigidity often increases with repeated flexion and extension movements. With cog wheeling, the examiner feels alternate periods of resistance and relaxation. With lead-pipe rigidity, the examiner feels smooth but increased muscle tone throughout passive flexion and extension.²⁵ Rigidity and cog wheeling may be felt in other large joints, but if detected in the arms, there is no need to confirm their presence elsewhere. Many patients with essential tremor manifest a rhythmical resistance to passive movements of a limb

Figure 1. Maneuvers to Detect Bradykinesia



while there is voluntary action of another body part. This is not true cog wheeling but is known as Froment sign, which also appears in PD patients.²⁶

Bradykinesia. Bradykinesia refers to a decrease in the speed and amplitude of complex movements. Jobbagy et al²⁷ describe 4 maneuvers designed to detect bradykinesia: tapping the fingers, twiddling, pinching and circling, and tapping with the heel. *Twiddling* refers to repeated rotation of the hands

in front of the body. The *pinching and circling* test is a sequence of 6 movements: pinching (opposing thumb and index finger) with the right hand and then with the left hand; circling (rotating the hand in a circle) with the right hand and then with the left hand; pinching with the right hand while simultaneously circling with the left; and pinching with the left hand while simultaneously circling with the right (FIGURE 1). Jobbagy et al²⁷ were able to quantify the performance of patients on these tasks using a motion analyzer, although a specific threshold “score” to define bradykinesia was not determined. However, poor performance of these maneuvers is easily detectable and clinicians can use them to confirm the presence of bradykinesia subjectively.

Glabella Tap Reflex. This reflex is tested by percussion of the forehead with the examiner’s index finger or by pulling a fold of skin between the thumb and index finger on the temple lateral to the external canthus and tapping with the thumb. The orbicularis oculi muscle reflexively contracts causing both eyes to blink. The reflex blink-

ing normally stops after tapping is repeated 5 to 10 times. Persistent blinking is a positive response sometimes referred to as Myerson sign.²⁸ Care should be taken to keep the examiner’s finger above the patient’s eyes to avoid blinking in response to visual threat (FIGURE 2).

Are These Features Found in Other Diseases?

The symptoms and signs of idiopathic PD overlap with those of other neurological diseases including MSA and progressive supranuclear palsy.

Like PD, MSA often presents with asymmetric rigidity and akinesia, but only a minority of patients has resting tremor.²⁹ Half of patients with MSA present with autonomic dysfunction and cerebellar symptoms and one quarter demonstrate a transient response to levodopa.^{25,29} Similarly, patients with progressive supranuclear palsy seldom present with tremor. Rigidity and postural instability, however, are common.³⁰

Parkinsonism is sometimes also a feature of Alzheimer disease.¹⁴ However, Alzheimer disease is easy to distin-

Figure 2. Glabella Tap Test

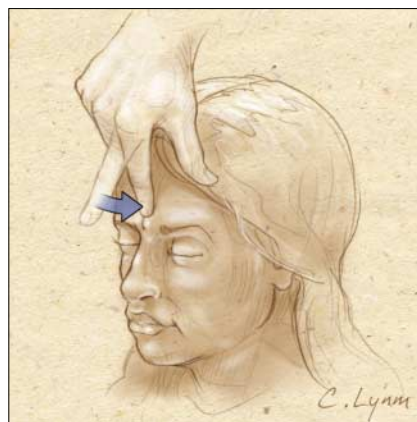


Table 1. Grade C Studies Included for Review

Source	No. of Subjects	Age, Mean (Range), y	Patient Population	Reference Standard for Diagnosis of PD	Reason Study Not Grade A
Hughes et al, ³⁴ 1992	100	64.5 (31-85)	Diagnosed clinically as having PD	Autopsy findings of depletion of nigral pigmented neurons and proliferation of Lewy bodies	Significant selection bias because patients studied were clinically diagnosed as having PD
Wenning et al, ³⁵ 2000	138	60.6 (NA)	Diagnosed clinically as having PD or MSA	Autopsy findings consistent with PD or MSA	Significant selection bias because patients studied were clinically diagnosed as having PD or MSA
Pearce et al, ³⁶ 1968	100	47.8 (NA)	Unselected inpatients and outpatients diagnosed as having PD and controls without known neurological disease	Detailed neurological examination	Samples of patients who obviously have the condition; comparisons nonindependent; small sample size
Duarte et al, ³⁷ 1995	128	66.3 (30-89)*	Patients attending a movement disorders polyclinic for the first time	Detailed neurological evaluation	Convenience sample including many individuals likely to have PD; small sample size
Mutch et al, ³⁸ 1991	123				Nonindependent comparisons with unclear standard; samples of patients who obviously have the condition; small sample size
		75 (57-89)	35 Diagnosed as having PD	Unclear standard used	
		73 (71-76)	88 From general practices	Neurological evaluation	
Meneghini et al, ³⁹ 1992	108	NA	87 Inpatients with neurological disorders and 21 patients without known neurological disease	Detailed neurological evaluation	Samples of patients who obviously have the condition (including many individuals likely to have PD and controls); small sample size; prone to observer bias

Abbreviations: PD, Parkinson disease; MSA, multisystem atrophy; NA, not available.

*For 37 patients diagnosed as having PD only.

guish from PD because other features are much more prominent. Furthermore, unlike in PD, cognitive impairment is present at the onset of Alzheimer disease.

METHODS

Four of the authors (G.R., L.F., T.O., and C.E.) performed independent searches of the MEDLINE database (1966-2001), using a number of Medical Subject Headings (*exp tremor*, *exp PD*, *essential tremor*) combined with the search terms and strategy used for the Rational Clinical Examination series.³¹

All relevant articles were retrieved. The resulting set of articles was divided into 3 parts, each of which was reviewed by a pair of authors. The reference lists of all articles were also carefully searched for additional articles. Articles were included for study if they met the following criteria: dealt primarily with the diagnosis of PD; included patients presenting with 1 or more typical parkinsonian symptoms or signs (eg, tremor, rigidity); final diagnosis confirmed by a suitable criterion standard, such as serial or detailed neurological evaluation or pathological confirmation at autopsy; and contained original data from which 2 × 2 tables could be extracted to calculate the sensitivity, specificity, and positive and negative likelihood ratios (LRs) for different signs and symptoms. As the number of suitable articles was small, additional inclusion criteria such as a minimum sample size or publication after a certain year were not used. However, the quality of articles included was assessed according to criteria previously developed for this series.³¹

The LRs for different diagnostic features were calculated when not available in the original articles. Corresponding 95% confidence intervals (CIs) were determined by the method of Greenland and Robins.³² All values were rounded to 2 significant digits. When identical or similar diagnostic features appeared in more than 1 article and the patients were similar across studies in

terms of demographics and illness characteristics, weighted summary LRs (pooled LRs) and the corresponding 95% CIs were calculated using the DerSimonian-Laird random effects method.³³ We used MetaWin statistical software (version 2; Sinauer Associates, Sunderland, Mass).

RESULTS

Quality of the Evidence

A total of 185 articles were reviewed. All authors agreed about which articles met our selection criteria. We chose 6 articles. Two articles^{34,35} included independent blind comparisons of symptoms and signs of a small number of patients who had been diagnosed as having PD or MSA based on

comparison of clinical records to pathological results at autopsy. Because the patients studied had already been diagnosed clinically as having PD or MSA, selection bias was a serious problem. These 2 articles provided level 3 evidence, leading to grade C recommendations.

The remaining 4 articles³⁶⁻³⁹ had numerous methodological biases. Although of lower methodological quality, they can still be classified as containing level 3 evidence and providing grade C recommendations (TABLE 1). Selection bias was a major problem in all 4 articles since many of the patients evaluated had either been diagnosed as having PD on initial clinical examination or had obvious par-

Table 2. Symptoms Evaluated in Patients With Possible Parkinson Disease

Symptom	Positive LR (95% CI)	Negative LR (95% CI)
Tremor		
Arms or legs shake		
Duarte et al, ³⁷ 1995	1.4 (1.2-1.6)	0.25 (0.08-0.78)
Pearce et al, ³⁶ 1968	17 (6.3-44)	0.24 (0.13-0.44)
Tremor as initial symptom ³⁴	1.3 (0.90-2.0)	0.60 (0.34-1.1)
Tremor of head or limbs ³⁹	11 (4.8-24)	0.26 (0.12-0.55)
Rigidity		
Muscle stiffness ³⁸	2.3 (1.3-4.3)	0.73 (0.54-0.97)
Paralysis or weakness ³⁹	1.3 (0.60-2.8)	0.93 (0.75-1.2)
Rigidity and bradykinesia ³⁹	4.5 (2.9-7.1)	0.12 (0.03-0.45)
Facies and general symptoms or historical findings		
Face less expressive ³⁷	2.1 (1.4-3.2)	0.54 (0.35-0.84)
Feet freeze ³⁷	3.7 (2.1-6.7)	0.55 (0.39-0.79)
Impaired consciousness ³⁹	0.31 (0.08-1.20)	1.3 (1.1-1.6)
Symmetric onset ³⁵	1.01 (0.53-1.90)	1.00 (0.78-1.28)
Bradykinesia		
Difficulty rising from chair		
Duarte et al, ³⁷ 1995	1.9 (1.3-2.7)	0.58 (0.38-0.90)
Mutch et al, ³⁸ 1991	5.2 (2.9-9.5)	0.39 (0.25-0.63)
Posture and motor tasks		
Loss of balance		
Duarte et al, ³⁷ 1995	1.6 (1.3-2.2)	0.29 (0.13-0.68)
Mutch et al, ³⁸ 1991	6.6 (3.4-12.8)	0.35 (0.21-0.57)
Shuffling gait		
Duarte et al, ³⁷ 1995	3.3 (2.1-5.0)	0.32 (0.18-0.58)
Mutch et al, ³⁸ 1991	15 (4.7-47)	0.50 (0.36-0.71)
Trouble turning in bed ³⁸	13 (4.1-43)	0.56 (0.41-0.76)
Trouble buttoning ³⁷	3.0 (2.0-4.4)	0.33 (0.19-0.60)
Trouble opening jars ³⁸	6.1 (3.4-11)	0.26 (0.14-0.48)
Uncontrolled limbs ³⁹	1.30 (0.53-3.10)	0.93 (0.72-1.20)
History of falls ³⁵	0.65 (0.52-0.81)	3.19 (1.37-7.42)
Fine motor		
Micrographia		
Duarte et al, ³⁷ 1995	2.8 (1.8-4.2)	0.44 (0.27-0.71)
Mutch et al, ³⁸ 1991	5.9 (3.1-9.4)	0.30 (0.17-0.53)

Abbreviations: CI, confidence interval; LR, likelihood ratio.

kinsonian features. In one study,³⁹ a screening instrument was administered to patients with either an initial diagnosis of PD, peripheral neuropathy, stroke, or epilepsy. The instrument included both a self-administered questionnaire and a set of physical

tasks, performance of which was graded subjectively. Neurologists confirming the presence of PD were aware of each patient's initial diagnosis and responses to the screening instrument. This obviously makes the study prone to observer bias. Like most studies with

low methodological quality, these 4 articles³⁶⁻³⁹ reported optimistic LRs.

Precision

Interclinician and intraclinician reliability of symptoms and signs was documented only for the glabella tap sign.³⁶ Precision could not be quantified in the clinicopathological studies since symptom histories were obtained retrospectively from charts.

Interclinician reliability in eliciting the glabella tap sign was found to be 88% among patients with intracranial disease and 100% in controls.³⁶ A κ coefficient for interclinician agreement could not be calculated because data about how each clinician scored each patient was not included. No causes for imprecision in assessing symptoms or signs were documented in the selected articles.

Accuracy

Several symptoms, collected by patient self-report in a questionnaire,³⁸ significantly increase the likelihood of PD when present and decrease it when absent. The symptoms are: trouble turning in bed; shuffling while walking; micrographia; difficulty rising from a chair; loss of balance; and trouble opening jars. The diagnostic value of tremor as a symptom varied widely among the selected articles, with a range in positive LRs of 1.3 to 1.4 in the studies of higher quality (TABLE 2 and TABLE 3).

The lack of tremor as a symptom makes PD less likely (range of negative LRs, 0.24 to 0.60). However, the usefulness of the lack of tremor as a symptom is limited by verification bias in the corresponding studies. Verification bias occurs when confirmatory or criterion standards are selectively applied to patients depending on the results of their preliminary screening test.⁴⁰

The value of a tremor detected on physical examination approximates that tremor as a sign (range of positive LRs, 1.3 to 1.5). The 95% CIs around the LR for the absence of tremor on physical examination are also similar to those for the lack of tremor as a sign (LR, 0.27-1.03). Rigidity as a symptom or

Table 3. Signs Evaluated in Patients With Possible Parkinson Disease

Sign	Positive LR (95% CI)	Negative LR (95% CI)
Tremor		
Hughes et al, ³⁴ 1992	1.5 (1.0-2.3)	0.47 (0.27-0.84)
Wenning et al, ³⁵ 2000	1.3 (0.95-1.7)	0.61 (0.36-1.03)
Tremor, rigidity, and bradykinesia ³⁴	2.2 (1.2-4.2)	0.50 (0.34-0.75)
Rigidity		
Initial ^{35*}		
	0.53 (0.35-0.80)	1.6 (1.1-2.4)
Throughout		
Wenning et al, ³⁵ 2000	0.99 (0.92-1.10)	1.5 (0.18-13)
Meneghini et al, ³⁹ 1992	2.8 (1.8-4.4)	0.38 (0.19-0.76)
Bradykinesia also	4.5 (2.9-7.1)	0.12 (0.03-0.45)
Facies and general findings		
Glabella tap ³⁵		
	4.5 (2.8-7.4)	0.13 (0.03-0.47)
Asymmetric disease ³⁴	1.80 (0.98-3.20)	0.61 (0.41-0.91)
Dementia ³⁵	3.2 (1.5-6.8)	0.55 (0.42-0.71)
Depression ³⁵	1.20 (0.84-1.80)	0.74 (0.46-1.20)
Bradykinesia		
Akinetic/rigid disease ³⁴		
	0.44 (0.25-0.75)	1.67 (1.1-2.6)
Wenning et al, ³⁵ 2000	0.93 (0.85-1.00)	3.7 (0.49-28)
Posture and motor tasks		
Difficulty or inability to walk heel to toe ³⁹		
	2.9 (1.9-4.5)	0.32 (0.15-0.70)
Central/autonomic nervous system findings		
Autonomic signs ³⁵		
	0.31 (0.21-0.44)	4.7 (2.2-9.9)
Cerebellar signs ³⁵	0.03 (0-0.23)	1.5 (1.2-1.8)
Pyramidal signs ³⁵	0.14 (0.06-0.31)	1.9 (1.3-2.6)
Speech/bulbar disturbance ³⁵	0.24 (0.16-0.36)	6.0 (2.6-13.6)

Abbreviations: CI, confidence interval; LR, likelihood ratio.
*Appearing only within 5 years of disease onset.

Table 4. Pooled Estimates

Source	Clinical Feature	Positive LR (95% CI)	Negative LR (95% CI)
Speech/Voice Quality			
Meneghini et al, ³⁹ 1992	Change in speech	2.6 (1.2-5.3)	0.73 (0.53-1.00)
Duarte et al, ³⁷ 1995	Voice softer	3.7 (2.4-5.6)	0.25 (0.13-0.49)
Pooled estimate		3.4 (2.6-3.7)	0.45 (0.25-0.73)
Asymmetry			
Hughes et al, ³⁴ 1992	Tremor	1.9 (1.1-3.0)	0.38 (0.22-0.66)
Wenning et al, ³⁵ 2000	Disease	1.60 (0.99-2.60)	0.69 (0.50-0.95)
Pooled estimate		1.7 (1.6-1.9)	0.53 (0.38-0.69)
Medication Response			
Hughes et al, ³⁴ 1992	Levodopa	1.20 (0.87-1.60)	0.63 (0.31-1.30)
Wenning et al, ³⁵ 2000	Levodopa	1.8 (1.1-2.8)	0.40 (0.25-0.64)
Pooled estimate*		1.4 (1.0-1.8)	0.46 (0.31-0.68)

Abbreviations: CI, confidence interval; LR, likelihood ratio.
*The response to levodopa is not ideal for the clinical examination.

sign has limited usefulness because the 95% CIs include 1.

The glabella tap sign is useful with a positive LR of 4.5 (95% CI, 2.8-7.4) and a negative LR of 0.13 (95% CI, 0.03-0.47).³⁶ Pooling the results for "change in speech" and "voice softer"^{37,39} provides a positive LR of 3.4 (95% CI, 2.6-3.7) and a negative LR of 0.45 (95% CI, 0.25-0.73) (TABLE 4). The results confirm the limited usefulness of a positive response to levodopa, as the pooled positive LR is 1.4 (95% CI, 1.0-1.8). The negative LR, however, is 0.46 (95% CI, 0.39-0.68) making PD less likely in patients who do not respond.

SCENARIO RESOLUTION

This patient presents with many common features of PD. We would question him about the tasks of turning in bed and opening jars. A sample of his writing may reveal micrographia. A glabella tap test should be performed. Additional positive symptoms or signs

would justify empiric treatment with dopaminergic medication with careful follow-up by a physician experienced in the treatment of this condition.

BOTTOM LINE

Few studies address the clinical diagnosis of PD rigorously. Nearly 200 years after it was first described, the accurate clinical diagnosis of PD remains a significant challenge. There is a great need for diagnostic studies involving larger numbers of patients in which presenting symptoms and signs are prospectively compared with the final diagnosis, established through a suitable criterion standard, such as autopsy or serial neurological evaluation.

A number of classic features of PD, when present, do help establish the diagnosis. These include the symptoms of tremor, the combination of rigidity and bradykinesia, loss of balance, micrographia, and shuffling gait. Difficulty with the tasks of turning in bed, open-

ing jars, and rising from a chair should also raise the suspicion of PD. It is difficult to gauge the usefulness of the absence of tremor as a symptom in ruling out PD because of verification bias in the studies in which it was evaluated.

The diagnostic value of the classic combination of tremor, rigidity, and bradykinesia on examination is modest at best. Useful signs include the glabella tap, difficulty walking heel to toe, and the presence of rigidity on examination.

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