Diagnosis and Management of Parkinson's Disease

Miguel Situ-Kcomt, MD
Assistant Professor
Movement Disorders Division
Department of Neurological Sciences

University of Nebraska Medical Center

Summary

Diagnosis:

- Clinical Features
- DaTScan (?)
- Skin Biopsy (?)
- Cerebrospinal fluid test (?)

Management:

- Medication Therapy
- New approved therapies

Diagnosis

Risk Factors

- Genetics
- Environmental Risk Factors
- Exposure to certain chemicals
- Gut flora & Diet (?)
- We are living longer!

Clinical Features

Our rationale is based on two scales:

1988-1992 - UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria (UKPDSBB)

1999 – Gelb's Diagnostic Criteria for PD

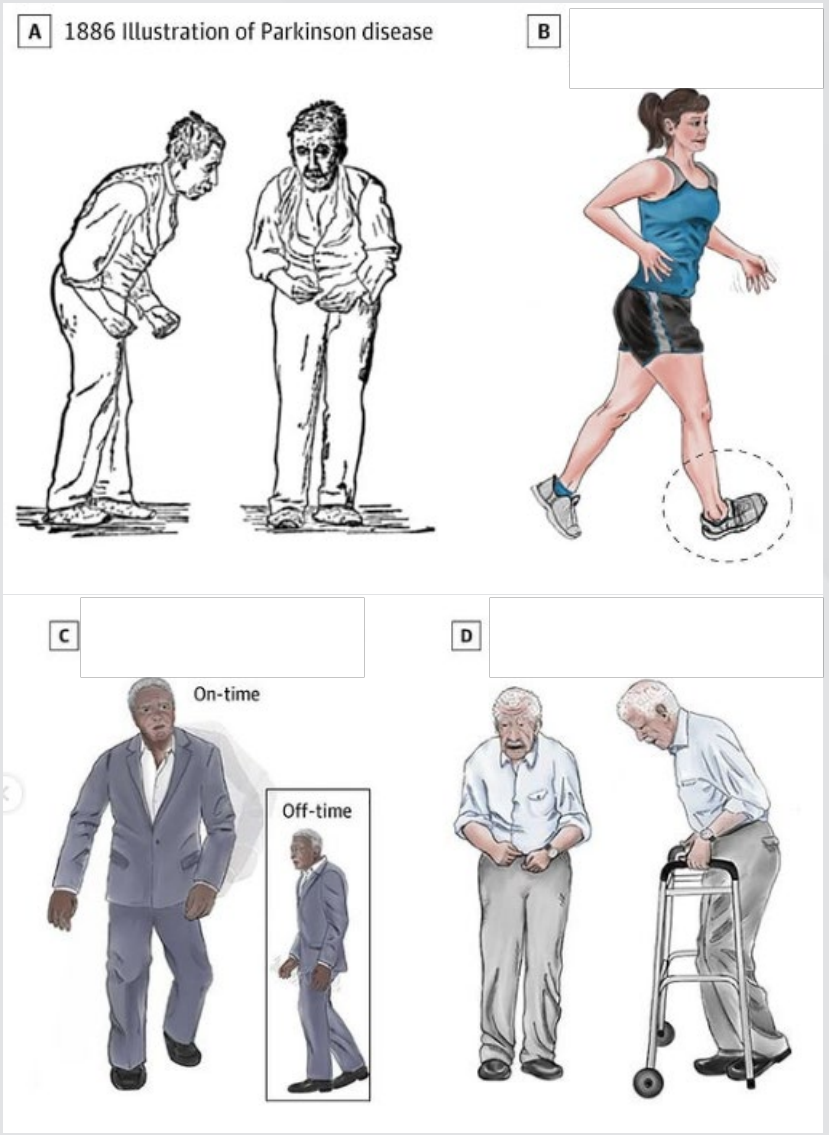
Calne DB, Snow BJ, Lee C. Criteria for diagnosing Parkinson's disease. Ann Neurol. 1992;32 Suppl:S125-7. doi: 10.1002/ana.410320721. PMID: 1510370.
Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson disease. Arch Neurol. 1999 Jan;56(1):33-9. doi: 10.1001/archneur.56.1.33. PMID: 9923759.

Clinical Features

Bradykinesia (slowness of movement)

AND at least one of the following

- Resting tremor (4-6 Hz in frequency)
- Muscular Rigidity
- Postural Instability



Taken from @jamanetwork IG

Step 2 Exclusion criteria for Parkinson's disease

- history of repeated strokes with stepwise progression of parkinsonian features
- history of repeated head injury
- history of definite encephalitis
- oculogyric crises
- neuroleptic treatment at onset of symptoms
- more than one affected relative
- sustained remission
- strictly unilateral features after 3 years
- supranuclear gaze palsy
- cerebellar signs
- early severe autonomic involvement
- early severe dementia with disturbances of memory, language, and praxis
- Babinski sign
- presence of cerebral tumor or communication hydrocephalus on imaging study
- negative response to large doses of levodopa in absence of malabsorption
- MPTP exposure

Step 3 supportive prospective positive criteria for Parkinson's disease

Three or more required for diagnosis of definite Parkinson's disease in combination with step one

- Unilateral onset
- Rest tremor present
- Progressive disorder
- Persistent asymmetry affecting side of onset most
- Excellent response (70-100%) to levodopa
- Severe levodopa-induced chorea
- Levodopa response for 5 years or more
- Clinical course of ten years or more

Clinical Features

Gelb's study contribution was describing a level of **diagnostic certainty**

BECAUSE ULTIMATELY A TRUE DIAGNOSIS IS NOT SET IN STONE

Table 2. Proposed Diagnostic Criteria for Parkinson Disease

Criteria for POSSIBLE diagnosis of Parkinson disease:

At least 2 of the 4 features in Group A* are present; at least 1 of these is tremor or bradykinesia

and

Either None of the features in Group B* is present

Or Symptoms have been present for less than 3 years, and none of the features in Group B* is present to date

and

Either Substantial and sustained response to levodopa or a dopamine agonist has been documented

Or Patient has not had an adequate trial of levodopa or dopamine agonist

Criteria for PROBABLE diagnosis of Parkinson disease:

At least 3 of the 4 features in Group A* are present

and

None of the features in Group B* is present (note: symptom duration of at least 3 years is necessary to meet this requirement)

and

Substantial and sustained response to levodopa or a dopamine agonist has been documented

Criteria for DEFINITE diagnosis of Parkinson disease:

All criteria for POSSIBLE Parkinson disease are met

and

Histopathologic confirmation of the diagnosis is obtained at autopsy (see Table 3)

**Group A and Group B are detailed in Table 1.*

Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson disease. Arch Neurol. 1999 Jan;56(1):33-9.

Clinical Features

Limitations:

- Too focused on motor criteria as cardinal features.
- Lack of depth in non-motor features, particularly cognition.
- No consideration for genetics.
- Does not address the question of prodromal symptoms.
- No **biological marker**.

Marsili L, Rizzo G, Colosimo C. Diagnostic Criteria for Parkinson's Disease: From James Parkinson to the Concept of Prodromal Disease. Front Neurol. 2018 Mar 23;9:156. doi: 10.3389/fneur.2018.00156. PMID: 29628907; PMCID: PMC5877503.

Can we test Parkinson's Disease?

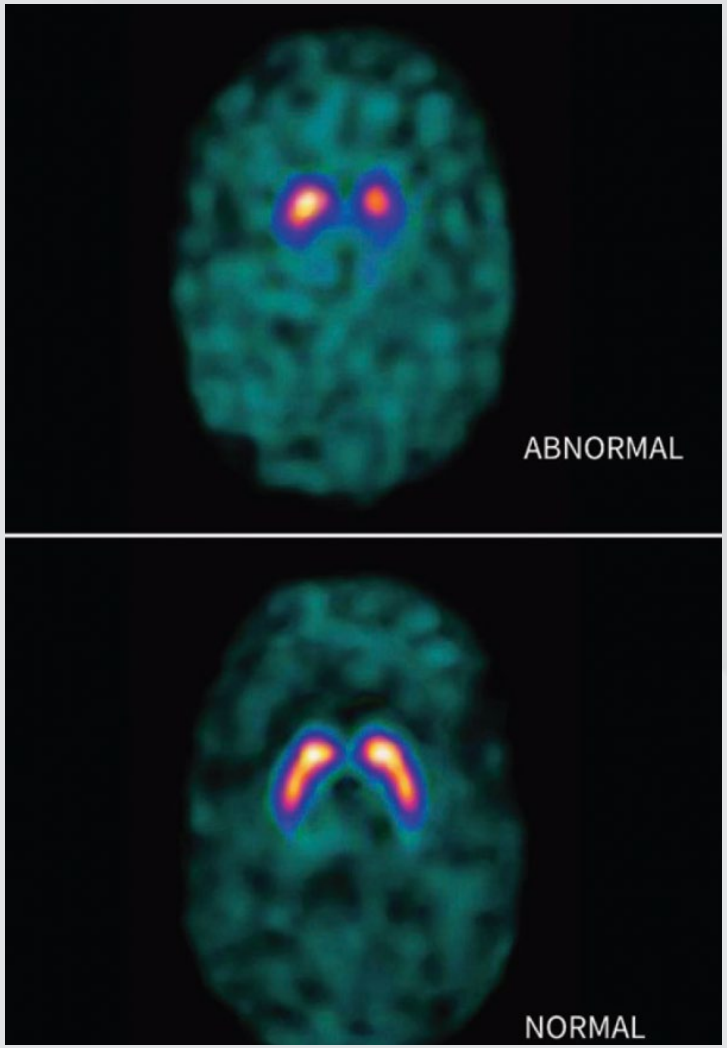
Dopamine Transporter Scan (DaT Scan)

Approved in the US since 2011

Checks for dopamine innervation in the brain – analyzed qualitatively

If positive – You have a primary deficit of dopamine.

DOES NOT DIAGNOSE PD



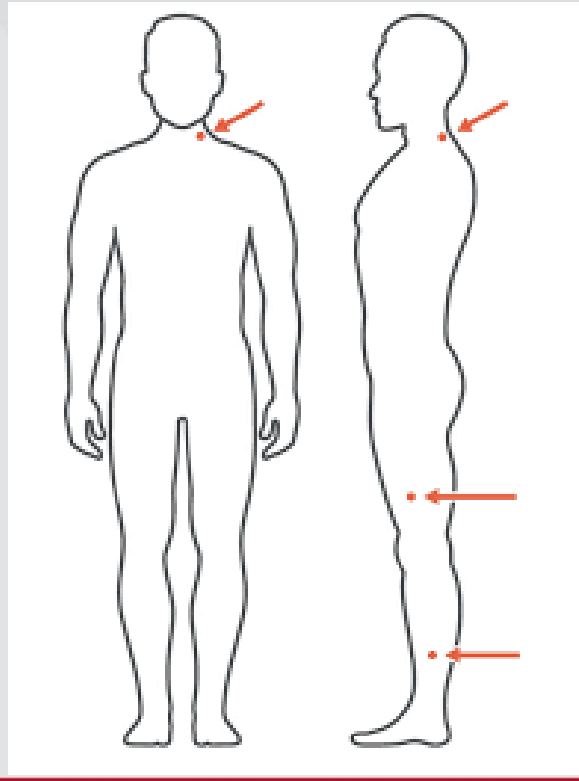
Skin Biopsy

The Syn-One Test® by CND Life Sciences (since 2022)

Detects phosphorylated alpha-synuclein (aSynP) deposition in the tissue.

- 92.7% in PD
- 98.2% in MSA
- 96% in DLB
- 100% in Pure Autonomic Failure
- 3.3% in healthy controls

IF POSITIVE – you have aSynP deposition… but not necessarily PD.



Gibbons CH, Levine T, Adler C, et al. Skin Biopsy Detection of Phosphorylated α-Synuclein in Patients With Synucleinopathies. Jama 2024;331(15):1298-1306, doi:10.1001/jama.2024.0792

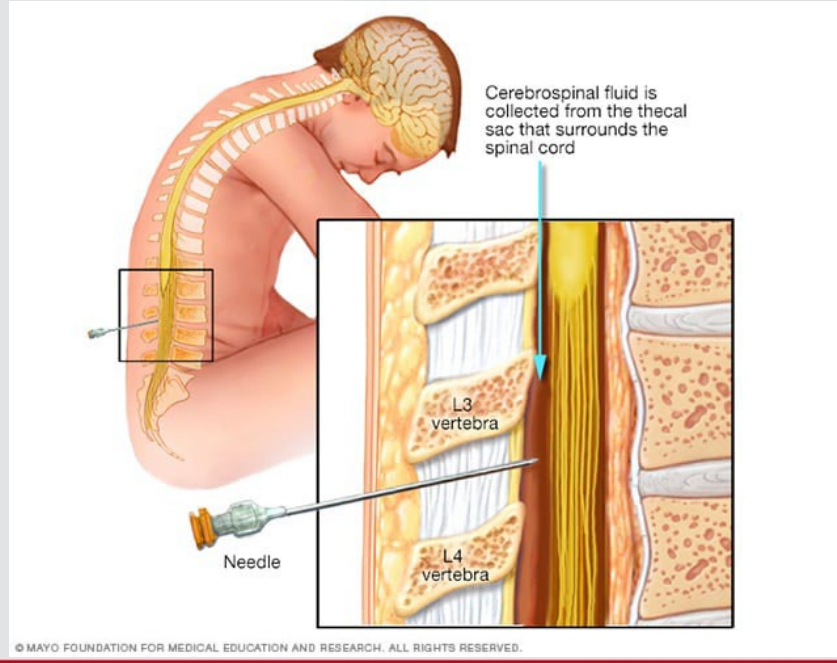
Lumbar Puncture Testing

Cerebrospinal Fluid (CSF) Alpha-Synuclein Testing by Seed Amplification Assay (since 2021)

Takes a sample of CSF, checks for the misfolded protein and if present, amplifies it to detect it

Results are qualitative: **Present or Absent**

IF POSITIVE – You have misfolded protein… but not necessarily PD.



Pros & Cons

- All may aid in diagnosing a primary parkinsonism.
- Skin and CSF testing may aid in detecting alpha-synuclein, which is commonly found in PD but also in other diseases (DLB, MSA, PAF).
- **NONE OF THEM CONFIRM PD**
- **NONE OF THEM HELP US STAGE PD (how far advanced)**

Management of PD

Initial Management

Levodopa therapy

Other medications:

- Dopamine agonists
- Rasagiline

PT/OT/SLP – Afternoon presentations!

Exercise if able!

Levodopa

Sinemet 25/100 (or Sinemet IR 25/100)
Sinemet 25/250
Sinemet CR 25/100 or 50/200
Rytary (carbidopa-levodopa ER)
Duopa (Intestinal Gel)
Inbrija (On-demand Inhaler)

Discontinued:
Parcopa (since December 2022)

Other medications

Dopamine Agonists:

- Pramipexole (Mirapex)
- Ropinirole (Requip)
- Rotigotine (Neupro patch)
- Apomorphine [on-demand] (Apokyn)

COMT Inhibitors:

- Entacapone (Comtan)
- Tolcapone (Tasmar)
- Opicapone (Ongentys)

MAO Inhibitors:

- Rasagiline (Azilect)
- Selegiline (Eldepryl)

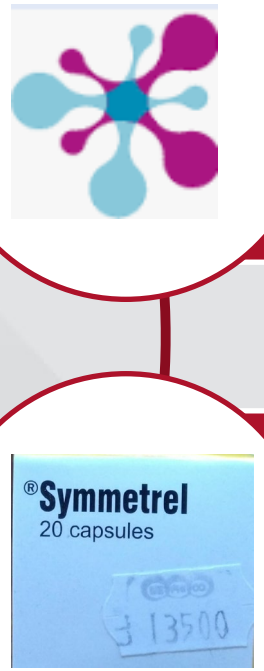
Anti-cholinergics:

- Trihexyphenidyl (Artane)
- Benztropine (Cogentin)

Other medications

Istradefylline (Nourianz)

- Helps with OFF periods



Amantadine (Symmetrel, Gocovri, Osmolex ER)

- Has been used as monotherapy before
- Mainly used for dyskinesias

New kids on the block

…More levodopa!

Crexont – New version of extended-release levodopa.

New kids on the block

Vyalev – Subcutaneous levodopa pump

- Can deliver up to 2500mg daily of levodopa in 24 hours
- Reversible procedure
- Needs to be refilled daily

THANK YOU!

University of Nebraska Medical Center