# Clinical pearls for Parkinson's Disease and Related Movement Disorders

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### Case:

63 yo right handed taxi driver

Tremor in right hand x 2 months, painful right shoulder. Embarrassed by tremor. Wife says he is used to walk faster than her, but she is overtaking him now. More tired than usual. Good balance. Poor smell since Covid pandemic. Constipation. Vivid dreams, yells/kicks out in sleep x 20 years. Still driving. No dopamine blocking medications.

Examination: Normal face and voice. Gait shows moderate reduced right armswing, and overflow tremor. Resting tremor, increases with mental stress. Bradykinetic finger and hand taps. Right arm tone increased compared with left.

Is this Parkinson's disease? Would you treat him?



# Parkinsonism



Bradykinesia (slow/reduced movement)
Tremor
Rigidity (stiffness)
Imbalance

2 of 4





### Primary (neurodegenerative)

- Parkinson's disease (PD)\*
- Dementia with Lewy bodies (DLB)
- Multiple system atrophy (MSA)
- Corticobasal degeneration (CBD)
- Progressive supranuclear palsy (PSP)
- Frontotemporal dementia with parkinsonism
- chromosome 17 (FTDP-17)
- Huntington's disease
- Creutzfeldt-Jakob disease

### Secondary

- Medications\*
- Frontal gait disorder
  - Normal pressure hydrocephalus
  - Leukoariosis
- Wilson's disease
- Others



### Primary (neurodegenerative)

2. Most likely diagnosis

- Parkinson's disease (PD)\*
- Dementia with Lewy bodies (DLB)
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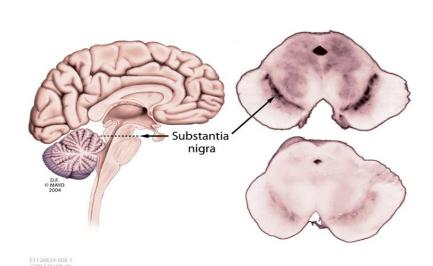
### **Secondary**

1. Any dopamine blocking drugs?

- Medications\*
- Frontal gait disorder
  - Normal pressure hydrocephalus
  - Leukoariosis
- Wilson's disease
- Others

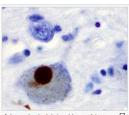


# #2 Parkinson's disease – loss of dopamine

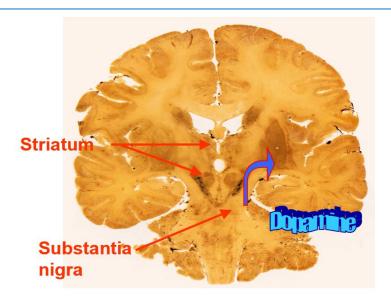


Loss of dopamine neurons in substantia nigra.

Hallmark is Lewy body pathology



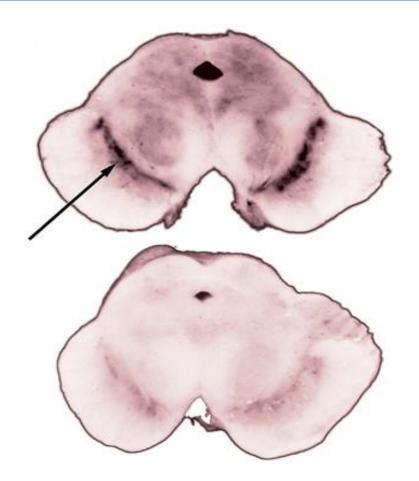
A <u>Lewy body</u> (stained brown) in a 5 brain cell of the substantia nigra in Parkinson's disease. The brown colour is positive immunohistochemistry staining for alpha-synuclein.



"Nigrostriatal degeneration"
Dopamine deficiency underlies
many PD symptoms
Basal ganglia role in movement
+ mood

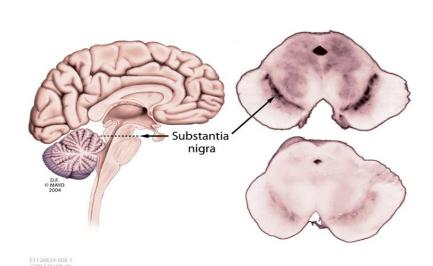


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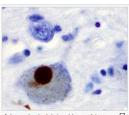


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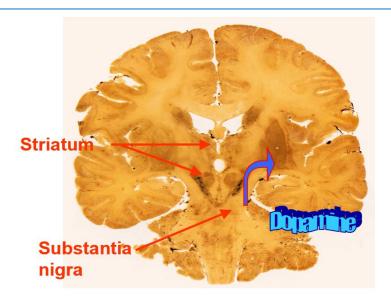


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Dopamine deficiency underlies
many PD symptoms
Basal ganglia role in movement
+ mood



# #3 Loss of dopamine underlies many PD symptoms

### **MOTOR**

- Bradykinesia (slowness)
- Tremor
- Rigidity (stiffness)
- Imbalance



# #4 Parkinson's disease is not just a movement disorder





# #5 Motor and non-motor symptoms

### **MOTOR**

- Tremor
- Rigidity
- Bradykinesia
- Gait difficulty

### **SECONDARY MOTOR**

- Hypokinetic speech
- Facial masking
- Decreased blinking
- Drooling
- Micrographia

### NON-MOTOR

### Cognitive

- Bradyphrenia
- Cognitive impairment
- Dementia (late)

### **Psychiatric**

- Depression, Anxiety, Apathy
- Hallucinations / Psychosis

#### **Autonomic**

- Orthostatic hypotension
- Impotence
- Constipation\*
- Urinary frequency

### **Sleep disorders**

- REM sleep behavior disorder\*
- Restless legs, periodic limb movements of sleep
- Obstructive sleep apnea

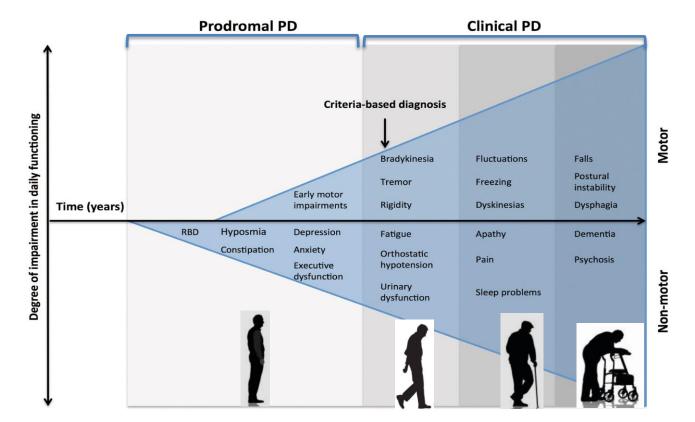
### **Sensory**

- Pain
- Numbness or tingling
- Decreased sense of smell\*
- Fatigue



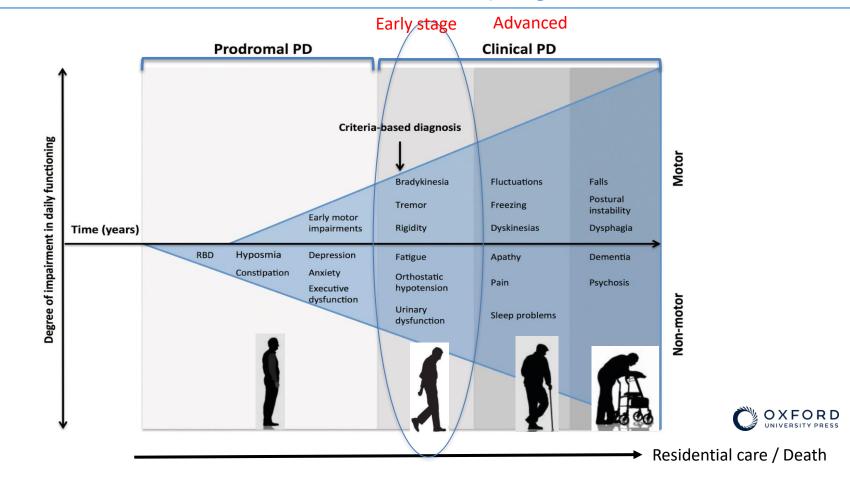
<sup>\*</sup> May occur decades before motor signs

# #6 Clinical timeline of Parkinson's disease progression

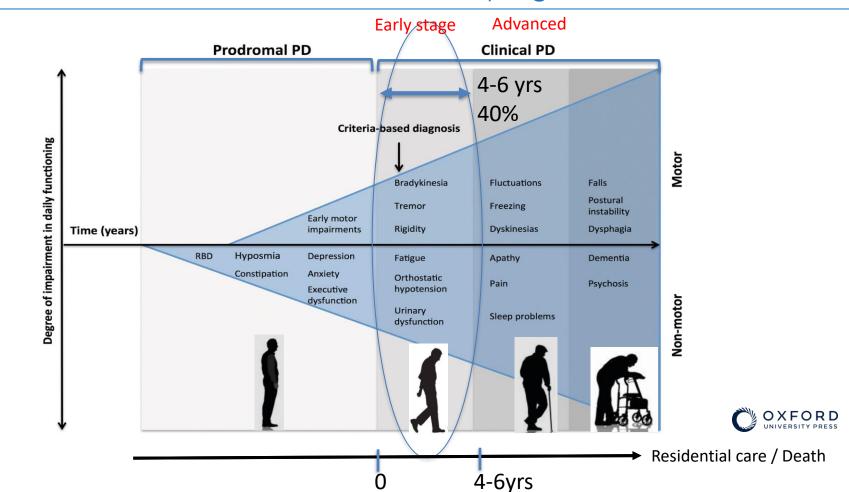




# #6 Clinical timeline of Parkinson's disease progression



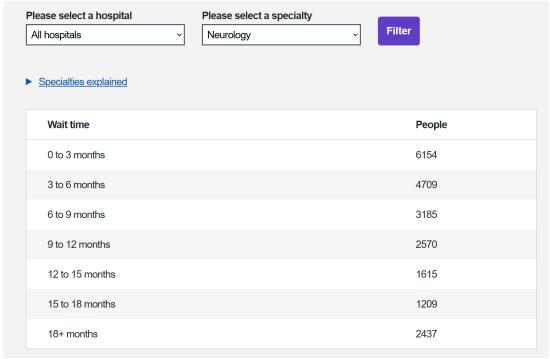
# #6 Clinical timeline of Parkinson's disease progression



# **Outpatient waiting lists**



31/3/2025



# #7 Treating Parkinson's disease



Medications Exercise



# Levodopa first-line treatment

- Therapeutic
- Diagnostic
- May benefit parkinsonian conditions other than PD

- MAOb inhibitors (rasagiline, selegiline)
- Dopamine agonists (pramipexole, ropinirole, rotigotine patch)
- Amantadine
- COMT inhibitors (entacapone, opicapone)



# #6 Replacing dopamine improves PD symptoms

### **MOTOR**

- Tremor
- Rigidity
- Bradykinesia
- Gait difficulty

### SECONDARY MOTOR

- Hypokinetic speech
- Facial masking
- Decreased blinking
- Drooling
- Micrographia

### **NON-MOTOR**

### Cognitive

- Bradyphrenia
- Cognitive impairment
- Dementia (late)

### **Psychiatric**

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### Sensory

- Pain
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# #7 Levodopa trial

Sinemet 25/100 (carbidopa/levodopa)

Starting dose 1/2 tab TDS (or 12.5/50 TDS) (1 hour before meals)

Increase dose every 1-2 weeks until benefit

25/100 1 tab TDS 25/100 1.5 tabs TDS 25/100 2 tabs TDS 25/100 2.5 tabs TDS

Patient picks lowest effective dose

Reassess patient in 2 months



# #8 Trouble-shooting Levodopa issues

Nausea? – take with crackers/plain toast

Severe nausea? – start ¼ tablet, increase by ¼ tablet increments

Lightheaded? – ensure standing SBP > 90mmHg, drink 1 glass water with meds

No response? Levodopa full challenge



# #8 Exercise is (the only) neuroprotective treatment

- Animal PD models: Exercise slows progression
- Human studies: Moderate-high intensity exercise appears to have a neuroprotective effect

### Advice:

- Aerobic exercise (ideally moderate-high intensity, most days, 30 mins+)
- Balance training
- Stretching program / improve postures

Ahlskog JE. Does vigorous exercise have a neuroprotective effect in Parkinson disease? Neurology. 2011 Jul 19;77(3. Corcos DM et al. Advice to People with Parkinson's in My Clinic: Exercise. J.Parkinsons Dis. 2024;14(3):609-617



### Back to Case:

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Examination: Normal face and voice. Gait shows moderate reduced right armswing, and overflow tremor. Resting tremor, increases with mental stress. Bradykinetic finger and hand taps, with reduced amplitude of taps. Right arm tone increased compared with left.

Ils this Parkinson's disease? Yes, most likely Would you treat him?



# Treating the patient – Outcome 1

Levodopa 25/100 prescribed Patient self-uptitrated to 25/100 1.5 TDS.

### 2 months later:

Tremor lessened, shoulder pain improved, faster gait speed, less tired. Brighter and less moody. Still acting out dreams. Constipation a bit worse.

Exam: Improved. Gait shows mild reduced right armswing, hint of overflow tremor. Mild decrement finger and hand taps. Minor rigidity right arm.

Responded to levodopa – confirms likely Parkinson disease Exercise program / physiotherapy Education Parkinson foundations/charity supports LTI scheme



# Treating the patient – Outcome 2

Levodopa 25/100 prescribed and patient uptitrated to 25/100 1 TDS.

2 months later:

Minimal subjective and objective clinical improvement

Taking medication on an empty stomach? Titrate up to maximum 2.5 or 3 tabs TDS

2 months later:

Subjective and objective improvement at 2 tabs TDS.

Continue TDS

Long duration response in early PD



### #9 Clues this is not Parkinson's disease

Poor response to levodopa

Dementia (early or prominent)

Early falls

Severe autonomic symptoms (low BP, bladder)

Rapidly worsening course

Dopamine antagonist medications

Vertical gaze palsy

Cerebellar signs

Wide-based gait



# Take home points

- Suspect Parkinson's disease?
- Start dopamine replacement (Levodopa trial) for therapeutic and diagnostic response
- 3. Start exercise program/physiotherapy
- 4. Refer to Neurology



# Time is precious!







# Thank You

