Overview

Parkinson’s disease (PD) is a progressive, neurodegenerative disorder characterized by bradykinesia with resting tremor and/or rigidity. Postural instability can be seen late in the disease. Symptoms are initially unilateral with gradual, bilateral progression though the side of onset continues to have more prominent symptoms. Prevalence increases with age with 65 being the mean age of onset.

Diagnostic Considerations

History & Examination

- Resting tremor: 4-6 Hz, unilateral onset in one extremity, resolves with use
- Bradykinesia: Slow movement, shuffling gait, delay in initiation of movements, freezing of gait, micrographia
- Rigidity: Increased resistance with passive movement of the joint – with a tremor present = “cogwheeling” → differentiate between “lead pipe” continuous rigidity in PD and “clasp knife” in UMN lesion
- Postural instability: imbalance or falling
- Others: masked facies, hypophonia, micrographia, shuffling gait, stooped posture, fatigue
- Screen for depression and ensure examination rules out differential diagnoses

Diagnostic tests

- Clinical diagnosis; autopsy confirmation is the only definitive diagnostic test, showing nigrostriatal degeneration and Lewy bodies
- Best clinical predictors of pathologic PD diagnosis: unilateral onset of tremor and bradykinesia and/or rigidity with good initial response to dopaminergic agent, leading to improvement in symptoms
- Imaging should not be routinely done for diagnosis → However, may help differentiate PD from disorder with similar characteristics

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Indication</th>
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<tr>
<td>I123-FP-CIT SPECT</td>
<td>When there is uncertainty between PD and non-degenerative parkinsonism/tremor disorders</td>
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<tr>
<td>CT or MRI</td>
<td>To identify the presence of a structural lesion(s) which may cause/contribute to parkinsonism/gait disorder/tremor</td>
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<td>MRI</td>
<td>To identify the degree and extent of cerebrovascular disease, to differentiate idiopathic PD from vascular Parkinsonism, OR the degree and distribution of brain atrophy in patients with features suggesting a Parkinson’s plus disorder</td>
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<td>Tests that are NOT recommended:</td>
<td>Routine structural or functional imaging, PET scanning, transcranial ultrasound, olfactory testing</td>
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Differential Diagnosis

1. Essential Tremor
   - Symmetrical tremor, worse with movement
   - Improves with alcohol and B-blockers

2. Drug induced Parkinsonism
   - Symmetrical symptoms, diagnosis via history
   - Possible drugs: Neuroleptics, Metoclopramide, Reserpine, Tetrabenzine, Lithium, Calcium channel blockers

3. Lewy Body Dementia
   - Dementia, visual hallucinations, fluctuating mental status
   - Diagnosis via history
4. Multiple system atrophy (Shy-Drager syndrome)¹
   - Autonomic dysfunction (e.g. symptomatic hypotension), speech or bulbar dysfunction, pyramidal or cerebellar dysfunction
   - Diagnosis via pontine and cerebellar atrophy on brain MRI (not definitive), EMG
5. Hereditary disorders¹
   - Huntington’s disease, Wilson’s disease, Juvenile PD, mitochondrial cytopathies

Management
- Treatment initiated when patient develops functional disability ²

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Examples</th>
<th>Mechanism of Action</th>
<th>Side Effects</th>
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<tr>
<td>Anticholinergics</td>
<td>Benztropine, Ethopropazine</td>
<td>Block ACh receptors</td>
<td>Dry mouth, eyes, urinary retention, exacerbates glaucoma &amp; cognitive impairment</td>
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<tr>
<td>NMDA receptor antagonists</td>
<td>Amantidine</td>
<td>Blocks NMDA receptors, Ach receptors, and promotes release of dopamine</td>
<td>Cognitive dysfunction, peripheral edema, skin rash</td>
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<td>Levodopa preparations</td>
<td>L-dopa/carbidopa, L-dopa/benserazide</td>
<td>Metabolism to dopamine in cells containing dopa decarboxylase</td>
<td>Nausea, hypotension, hallucinations/psychosis, dystonic &amp; choreiform dyskinesias</td>
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<tr>
<td>Dopamine agonists</td>
<td>Bromocriptine, Pergolide, Ropinirole, Pramipexole</td>
<td>Directly stimulate dopamine receptors</td>
<td>Nausea, hypotension, hallucinations/psychosis, peripheral edema, pulmonary fibrosis, sudden onset of sleep</td>
</tr>
<tr>
<td>MAO inhibitors</td>
<td>Selegiline</td>
<td>Block MAO B receptors to reduce dopamine metabolism</td>
<td>Nausea, dizziness, sleep disorder, impaired cognition</td>
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<td>COMT inhibitors</td>
<td>Entacapone</td>
<td>Block peripheral COMT activity to improve L dopa pharmacokinetics</td>
<td>L dopa related SE exacerbation, diarrhea, urine discoloration</td>
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Adapted from Guttman³. Treatment Algorithm adapted from Guttman³

When starting therapy, consider:

<table>
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<th>Pts level of disability</th>
<th>Drug side effects</th>
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<td>Age</td>
<td>Cost</td>
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<td>Risk of response fluctuations</td>
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Anticholinergics
- For minimal treatment
- Less ideal for elderly patients – can cause or worsen cognitive impairment³

Amantidine
- Good for refractory tremor¹
- Less ideal for elderly pts
- May exacerbate ankle

Dopamine agonist
- For mild to moderate symptoms
- Can be used as monotherapy or combination¹
- May reduce risk of response fluctuations
- Not ideal for elderly patients (hallucinations, orthostasis, drowsiness, cognitive impairment)³
- May worsen ankle oedema

L-dopa preparation
- For patients with significant symptoms
- Affordable

Add a dopamine agonist or L-dopa

Disease progression

Increase dose

Add L-dopa/ dopamine agonist

Disease progression

Prognosis
Treatment does not modify the underlying disease process. Therefore, patients continue to experience a decline in motor and cognitive function. Patients presenting at an older age with prominent bradykinesia and rigidity continue with a more rapid decline in motor function. In contrast, prominent tremor at diagnosis may predict a slower rate of progression. Dementia incidence increases with age and duration of PD, with 60% of patients developing dementia within 12 years of diagnosis.

Bottom line
The progressive, degenerative aspect of Parkinson's disease along with the risks to consider with therapy (side effects, response fluctuations) make the disease best when managed in the multi-disciplinary setting.

References can be found online at http://www.dfcm.utoronto.ca/programs/postgraduateprograme/One_Pager_Project_References.htm