Parkinsons Disease: Comprehensive Overview

1 Definition

Parkinsons disease (PD) is a progressive neurodegenerative disorder characterized by motor symptoms (tremor, rigidity, bradykinesia, and postural instability) and non-motor symptoms, resulting from the loss of dopaminergic neurons in the substantia nigra and other pathological changes in the brain.

2 Etiopathogenesis

Parkinsons disease arises from a combination of genetic, environmental, and cellular factors:

- **Genetic Factors**: Mutations in genes such as LRRK2, PARK7, PINK1, and SNCA (alpha-synuclein). Familial PD accounts for 10% of cases.
- **Environmental Factors**: Exposure to pesticides (e.g., paraquat), herbicides, or industrial toxins (e.g., MPTP). Rural living and head trauma increase risk.
- **Cellular Mechanisms**:
  - Alpha-synuclein misfolding and aggregation (Lewy bodies).
  - Mitochondrial dysfunction and oxidative stress.
  - Impaired protein degradation (ubiquitin-proteasome system).
- **Risk Factors**: Aging (most cases >60 years), male gender, and family history of PD.

3 Clinical Manifestations

PD presents with motor and non-motor symptoms:

- **Motor Symptoms**:
  - Resting tremor (pill-rolling, typically unilateral initially).
  - Bradykinesia (slowness of movement).
  - Rigidity (cogwheel or lead-pipe).
  - Postural instability (later stages).
- **Non-Motor Symptoms**:

  - Autonomic: Constipation, orthostatic hypotension, urinary dysfunction.
  - Neuropsychiatric: Depression, anxiety, cognitive impairment, dementia (late stages).
  - Sleep disorders: REM sleep behavior disorder, insomnia.
  - Sensory: Anosmia (loss of smell), pain.
- **Complications**: Falls, aspiration pneumonia, and reduced quality of life.

4 Pathophysiology

PD involves the progressive degeneration of dopaminergic neurons and Lewy body formation, disrupting basal ganglia function. The flowchart below illustrates the key mechanisms.

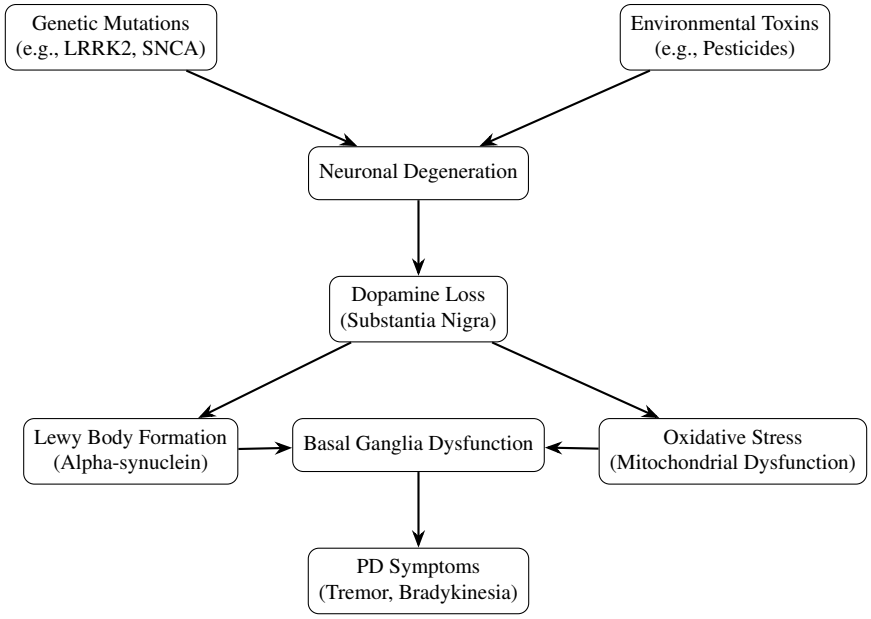

Figure 1: Pathophysiology of Parkinsons Disease

5 Symptoms

- **Motor Symptoms**:
  - Resting tremor (4–6 Hz, often in hands or legs).
  - Bradykinesia (difficulty initiating or slowing movements).
  - Rigidity (stiffness in limbs or trunk).
  - Postural instability (impaired balance, falls in later stages).
  - Shuffling gait, reduced arm swing.
- **Non-Motor Symptoms**:
  - Constipation, drooling, or dysphagia.
  - Depression, anxiety, or apathy.

  - Cognitive decline, hallucinations (late stages).
  - Sleep disturbances (e.g., vivid dreams, acting out dreams).
  - Loss of smell, fatigue, or chronic pain.

6 Diagnosis

Diagnosis is primarily clinical, supported by imaging and tests:

- **Clinical Criteria (UK Brain Bank)**: Bradykinesia plus at least one of resting tremor, rigidity, or postural instability. Asymmetry and levodopa response support diagnosis.
- **Neuroimaging**:
  - DaTSCAN (SPECT) to assess dopamine transporter loss.
  - MRI to rule out atypical parkinsonism (e.g., PSP, MSA).
- **Exclusion**: Rule out secondary causes (e.g., drug-induced parkinsonism, vascular parkinsonism) and atypical parkinsonism.
- **Supporting Features**: Anosmia, REM sleep behavior disorder, or unilateral onset.
- **Laboratory Tests**: To exclude metabolic causes (e.g., thyroid dysfunction, Wilsons disease).

7 Nonpharmacological Management

Nonpharmacological strategies aim to improve function and quality of life:

- **Physical Therapy**: Tailored exercise programs (e.g., tai chi, dance) to improve mobility, balance, and strength.
- **Occupational Therapy**: Adaptive strategies for daily activities (e.g., dressing, eating).
- **Speech Therapy**: Address dysphagia and speech difficulties (e.g., Lee Silverman Voice Treatment).
- **Exercise**: Regular aerobic exercise (150 minutes/week) and resistance training to reduce motor symptoms.
- **Diet**: Balanced diet with adequate fiber to manage constipation; hydration to prevent orthostatic hypotension.
- **Psychosocial Support**: Counseling or support groups for depression, anxiety, and social isolation.
- **Patient Education**: Teach fall prevention, medication timing, and disease progression awareness.
- **Surgical Options**: Deep brain stimulation (DBS) of subthalamic nucleus or globus pallidus for drug-resistant symptoms.

8 Pharmacological Management

Medications aim to restore dopamine levels or manage symptoms:

- **Levodopa**: First-line, combined with carbidopa (e.g., 100/25 mg 3–6 times/day). Improves motor symptoms but may cause dyskinesias.
- **Dopamine Agonists**: E.g., pramipexole (0.375–4.5 mg/day) or ropinirole (0.75–24 mg/day). Used in early PD or as adjunct.
- **MAO-B Inhibitors**: E.g., rasagiline (1 mg/day) or selegiline (5–10 mg/day). Slows dopamine breakdown.
- **COMT Inhibitors**: E.g., entacapone (200 mg with each levodopa dose). Extends levodopa effect.
- **Amantadine**: 100–300 mg/day for dyskinesias or tremor.
- **Anticholinergics**: E.g., trihexyphenidyl (2–6 mg/day) for tremor in younger patients; caution in elderly due to cognitive side effects.
- **Non-Motor Symptom Management**:
  - SSRIs (e.g., sertraline 50–200 mg/day) for depression.
  - Rivastigmine (3–12 mg/day) for dementia.
  - Midodrine or fludrocortisone for orthostatic hypotension.
- **Monitoring**: Adjust doses based on symptom control, side effects (e.g., dyskinesias, hallucinations), and disease progression.