PARKINSONISM

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SYNOPSIS:

- Definition
- Incidence
- Etiology
- Pathophysiology
- Stages of Parkinson's Disease
- Clinical Presentation
- Diagnosis
- Differential Diagnosis
- Medical Management

DEFINITION

Parkinson's Disease is a progressive disorder of the central nervous system (CNS) that mainly affecting the basal ganglia and characterized by both motor and nonmotor symptoms.

Motor symptoms include the *cardinal features* of **rigidity**, **bradykinesia**, **tremor**, and, in later stages, **postural instability**.

Early symptoms can include loss of sense of smell, constipation, rapid eye movement (REM), sleep behaviour disorder, mood disorders, and orthostatic hypotension.

Other non-motor symptoms include altered bladder function, excessive saliva, difficulty speaking and swallowing, and cognitive problems (slowed thinking, confusion, and in some cases dementia).

Depression, are common in individuals with PD.

INCIDENCE

- More than 10 million people worldwide are living with PD.
- Annual incidence: 20 per 100 000. Prevalence: 190 per 100 000.
- Sex incidence: Male : female – 3:2
- Age of onset: 50 years upwards. Incidence peaks in mid-70s then declines.
- Familial incidence occurs in 5%.

ETIOLOGY

The causes of Parkinson's disease is unknown. Genetic and environmental influences have been identified.

- Parkinson's disease (PD), or idiopathic parkinsonism.
- Secondary parkinsonism
- Parkinsonism-plus syndromes

- **IDIOPATHIC PARKINSONISM:**

It is the most common form, affecting approximately 78% of patients.

Late-onset (>40 years; generally sporadic)

Early-onset (<40 years; often familial)

- Young-onset (>21 years)
- Juvenile (<21 years)

❑ Secondary parkinsonism:

It results from a number of different identifiable causes, including viruses, toxins, drugs, tumors.

- Virus (e.g., encephalitis lethargica)
- Toxins (e.g., carbon monoxide, manganese, methyl-phenyl-tetrahydropyridine [MPTP])
- Drugs (e.g., phenothiazines, reserpine, butyrophenones, metoclopramide)
- Vascular disease (multi-infarct)

- Tumors of basal ganglia
- Normal pressure hydrocephalus
- Hemiparkinsonism, hemiatrophy
- Metabolic
    - Wilson's disease
    - Hepatocerebral degeneration
    - Hallervorden-Spatz disease
    - Hypoparathyroidism

❑ Parkinsonism-plus syndromes:

This refers to those conditions that mimic PD in some respects, but the symptoms are caused by other neurodegenerative disorders.

- Progressive supranuclear palsy
- Cortical–basal ganglionic degeneration
- Disorders with prominent and often early dementia:
    - Diffuse cortical Lewy body disease
    - Alzheimer's disease with parkinsonism

- Disorders with cerebellar/autonomic/pyramidal manifestation:
  - Multiple-system atrophy
  - Striatonigral degeneration
  - Shy-Drager syndrome
  - Olivopontocerebellar atrophy
  - Machado-Joseph disease

PATHOPHYSIOLOGY

No specific, standard criteria exist for the neuropathologic diagnosis of Parkinson disease. The following are the 2 major neuropathologic findings in Parkinson disease:

- Loss of pigmented dopaminergic neurons of the substantia nigra pars compacta
- The presence of Lewy bodies and Lewy neurites

The loss of dopamine neurons occurs most prominently in the ventral lateral substantia nigra.

Approximately 60-80% of dopaminergic neurons are lost before the motor signs of Parkinson disease emerge.

NETWORK OF BASAL GANGLIA (BG)

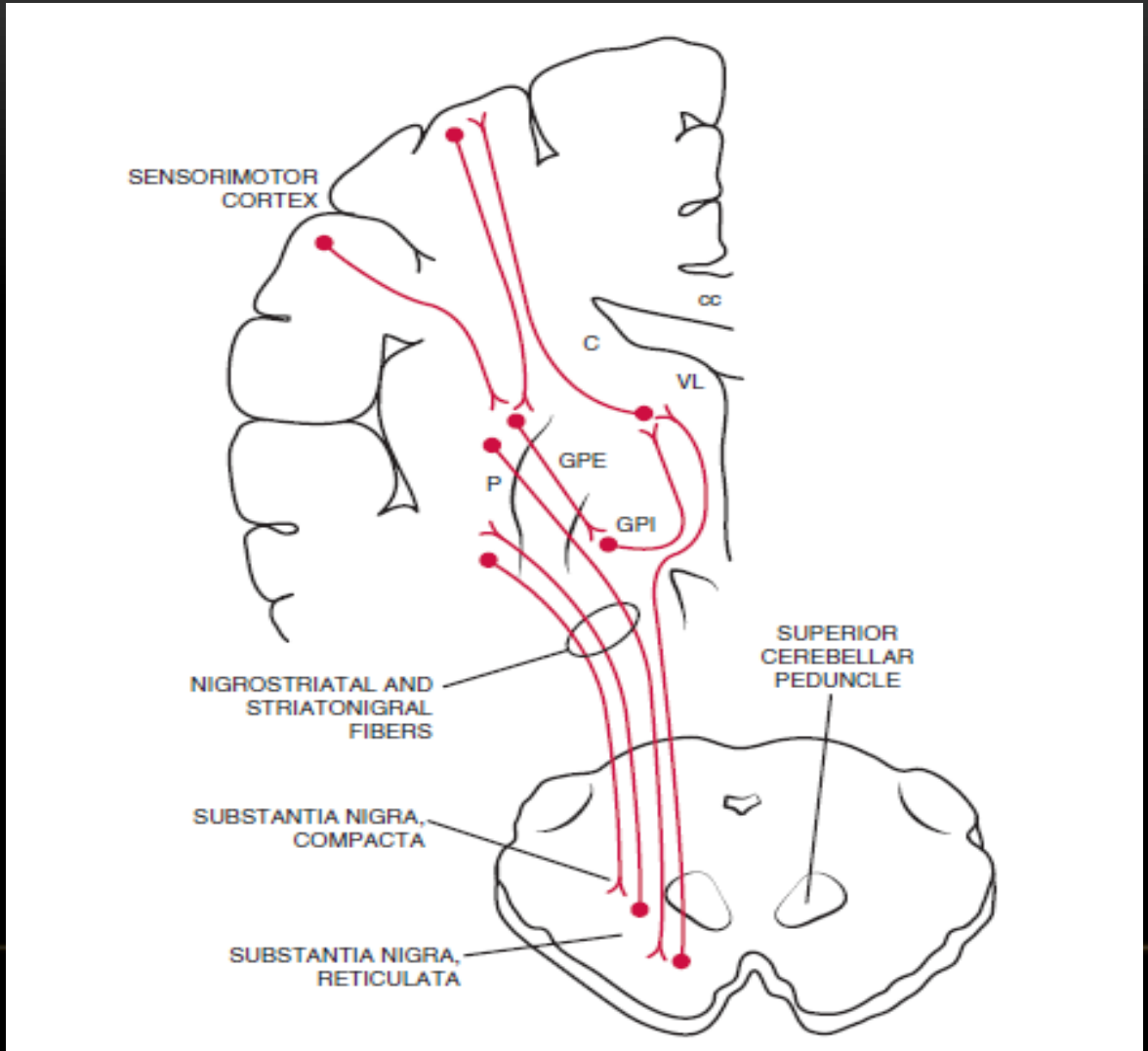
The BG is a network of subcortical nuclei consisting of the caudate nucleus, the putamen, the globus pallidus, and the subthalamic nucleus along with the substantia nigra.

The BG engages in a number of parallel circuits or loops. They are as follows:

i. Direct motor loop
ii. Indirect loop

Direct motor loop:

The *direct motor loop* through the BG consists of signals transmitted from the cortex to putamen to globus pallidus, to ventrolateral (VL) nucleus of the thalamus, and back to cortex (supplementary motor area [SMA])


SENSORIMOTOR CORTEX
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NIGROSTRIATAL AND STRIATONIGRAL FIBERS
SUPERIOR CEREBELLAR PEDUNCLE
SUBSTANTIA NIGRA, COMPACTA
SUBSTANTIA NIGRA, RETICULATA

This VL-SMA connection is excitatory and facilitates discharge of cells in the SMA.

The BG thus serves to activate the cortex via a positive-feedback loop and assists in the initiation of voluntary movement.

Inhibition of the thalamus by the BG is thought to underlie the hypokinesia seen in PD.

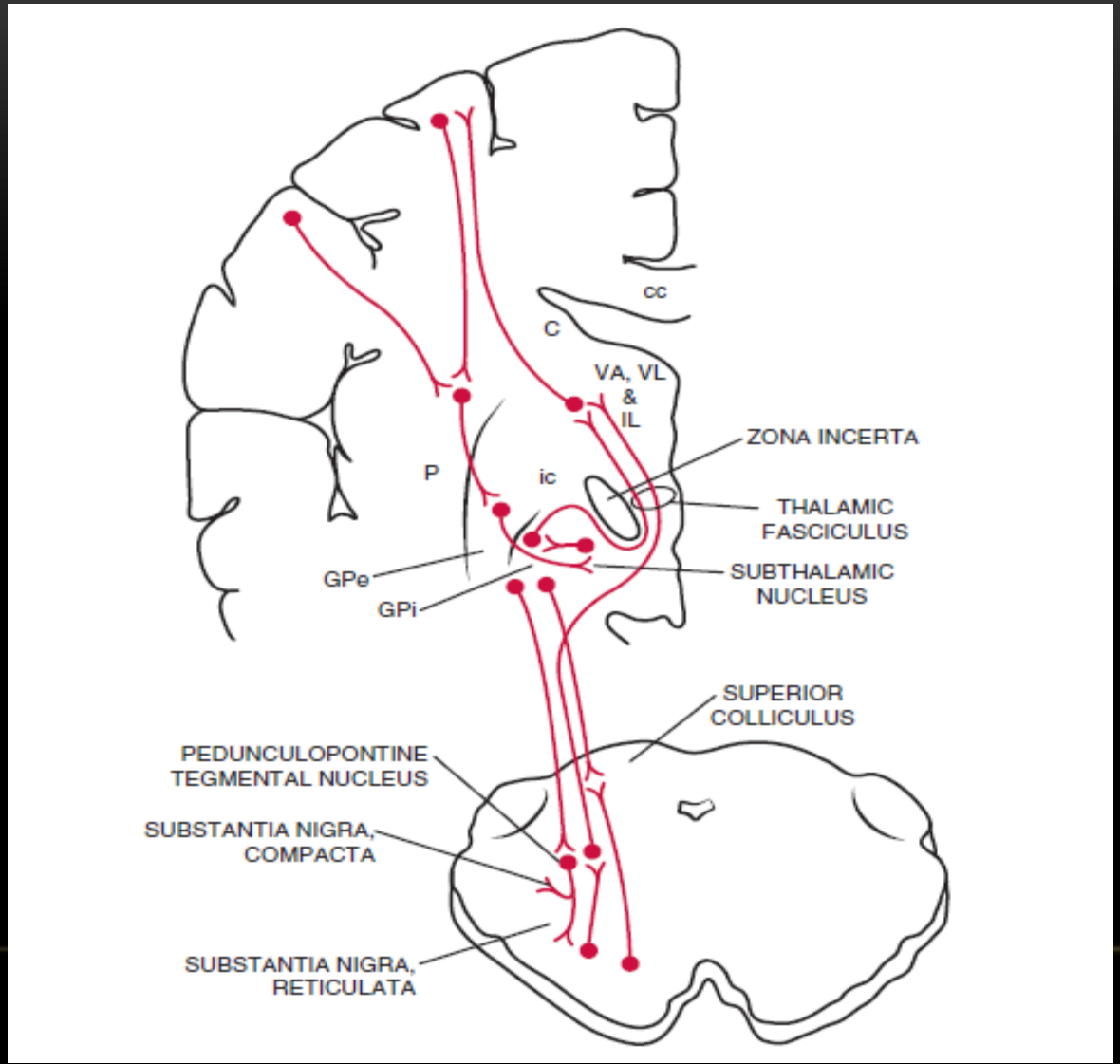
Indirect loop:

An indirect loop through the BG involves the subthalamic nucleus, the globus pallidus interna, and substantia nigra pars reticulata to the superior colliculus and midbrain tegmentum.

This indirect loop serves to decrease thalamocortical activation. The BG projection to the superior colliculus assists in regulation of saccadic eye movements.

The BG projection to the reticular formation assists in the regulation of trunk and limb musculature (via extrapyramidal pathways), sleep and wakefulness, and arousal.

Other circuits in the BG are involved with memory and cognitive functions.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PEDUNCULOPONTINE
TEGMENTAL NUCLEUS
SUBSTANTIA NIGRA,
COMPACTA
SUBSTANTIA NIGRA,
RETICULATA

So the Parkinson's disease is defined by

(1) degeneration of dopaminergic neurons in the BG in the pars compactus of the substantia nigra that produce *dopamine* and

(2) As the disease progresses and neurons degenerate, the presence of cytoplasmic inclusion bodies, called Lewy bodies.

Substantial neurodegeneration occurs in PD before the onset of motor symptoms with clinical signs emerging at 30% to 60% degeneration of neurons.

Loss of the melanin-containing neurons produces characteristic changes in depigmentation in the substantia nigra with a characteristic pallor.

STAGES OF PD

Stage 1: Lesions are found in the medulla oblongata (dorsal IX/X nucleus or intermediate reticular zone).

Stage 2: pathology is expanded to involve lesions of the caudal raphe nuclei, reticular nucleus.

Stage 3: involvement of the nigrostriatal system is apparent (pars compacta of the substantia nigra).

Stage 4: lesions are also found in the cortex (temporal mesocortex and allocortex).

Stage 5: pathology is extended to involve the sensory association areas of the neocortex and prefrontal neocortex.

Stage 6: pathology is extended to involve the sensory association areas of the neocortex and premotor areas.

CLINICAL PRESENTATION

Cardinal Features:

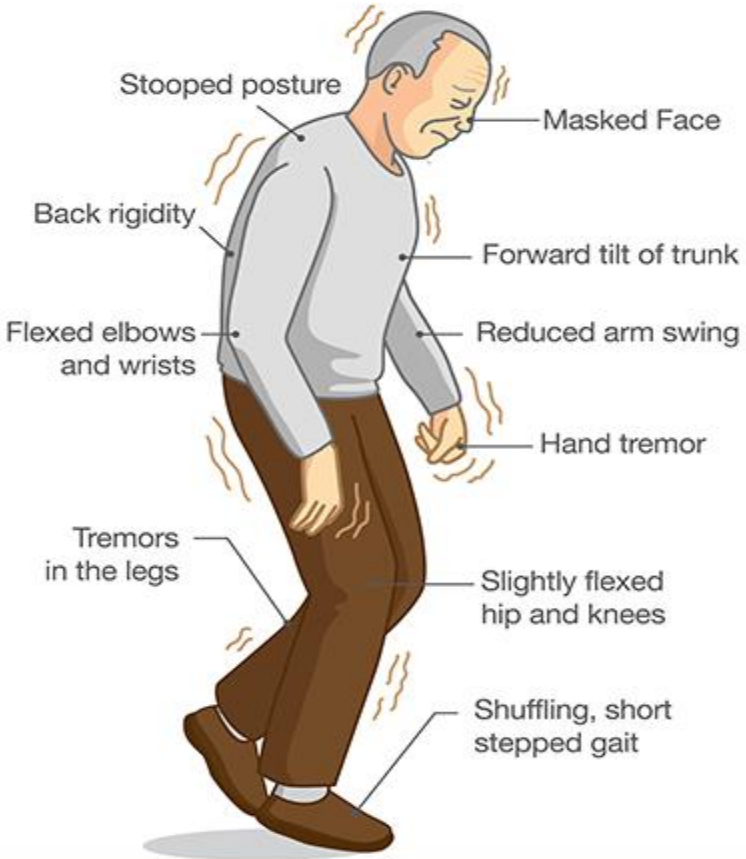
(Primary Motor Symptoms)

- Rigidity (Cogwheel rigidity, Lead pipe rigidity)
- Bradykinesia
- Tremor (Resting tremor, Action tremor)
- Postural Instability

Secondary Motor Symptoms:

- **Motor Performance:**
  - Decreased torque production
  - Fatigue
  - Contractures and deformity
  - Masked face
  - Micrographia
  - Start hesitation
  - Freezing episodes
  - Festination gait or Freezing gait
  - Kyphosis posture with forward head

PARKINSON DISEASE SYMPTOMS



Non-Motor Symptoms:

- **Sensory Symptoms:**
  - Paresthesias
  - Pain
  - Akathisia
- **Speech & swallowing disorder:**
  - Hypokinetic dysarthria
  - Dysphagia
- **Cognitive function:**
  - Dementia, Bradyphrenia
  - Visuospatial deficits
  - Depression, Dysphoric mood

- **Autonomic nervous system:**
  - Excessive sweating
  - Abnormal sensations of heat and cold
  - Seborrhea
  - Sialorrhea
  - Constipation
  - Urinary bladder dysfunction
- **Cardio pulmonary system:**
  - Low resting blood pressure (BP)
  - Compromised cardiovascular response to exercise
  - Impaired respiratory function

DIAGNOSIS

There is no single definitive test or group of tests used to diagnose the disease. The diagnosis is made on the basis of history and clinical examination.

Handwriting samples, speech analysis, interview questions that focus on developing symptoms, and physical examination are used.

A diagnosis of PD is typically made if at least two of the four cardinal motor features are present.

DIFFERENTIAL DIAGNOSIS

- Essential tremor
- Huntington chorea
- Dementia with Lewy bodies
- Progressive supranuclear palsy
- Neuroacanthocytosis
- Normal pressure hydrocephalus

MEDICAL MANAGEMENT

- Levodopa/Carbidopa (Dopamine precursor)
- Dopamine Agonists (stimulate postsynaptic dopamine receptors)
  - Ropinirole (Requip)
  - Pramipexole (Mirapex); bromocriptine (Parlodel)
- Anticholinergics (tremor and the dystonia)
  - Trihexyphenidyl (Artane)
  - Benztropine mesylate (Cogentin).
- Monoamine Oxidase B Inhibitors (to enhance levels of dopamine)