

PARKINSONISM

PARKINSONISM

akinetic-rigid
syndrome



PARKINSONISM

- Symptoms of Parkinson's disease: akinesia, bradykinesia, rigidity, postural instability, gait impairment, tremor
- A common, age-related syndrome

ATYPICAL PARKINSONISM

- Parkinson Plus Syndromes
- Secondary Parkinsonism
- Early falling, early dementia, early autonomic dysfunction

PARKINSON'S DISEASE

General Considerations

- The second most common progressive neurodegenerative disorder
- The most common neurodegenerative movement disorder
- It is a complex disease with variable symptoms
- Symptoms and neuropathology are well characterized
- Pathogenesis of PD is not clear
- May be multifactorial and heterogeneous in etiology
- Misdiagnosis rate of PD is about 10-25%



Parkinson's Disease

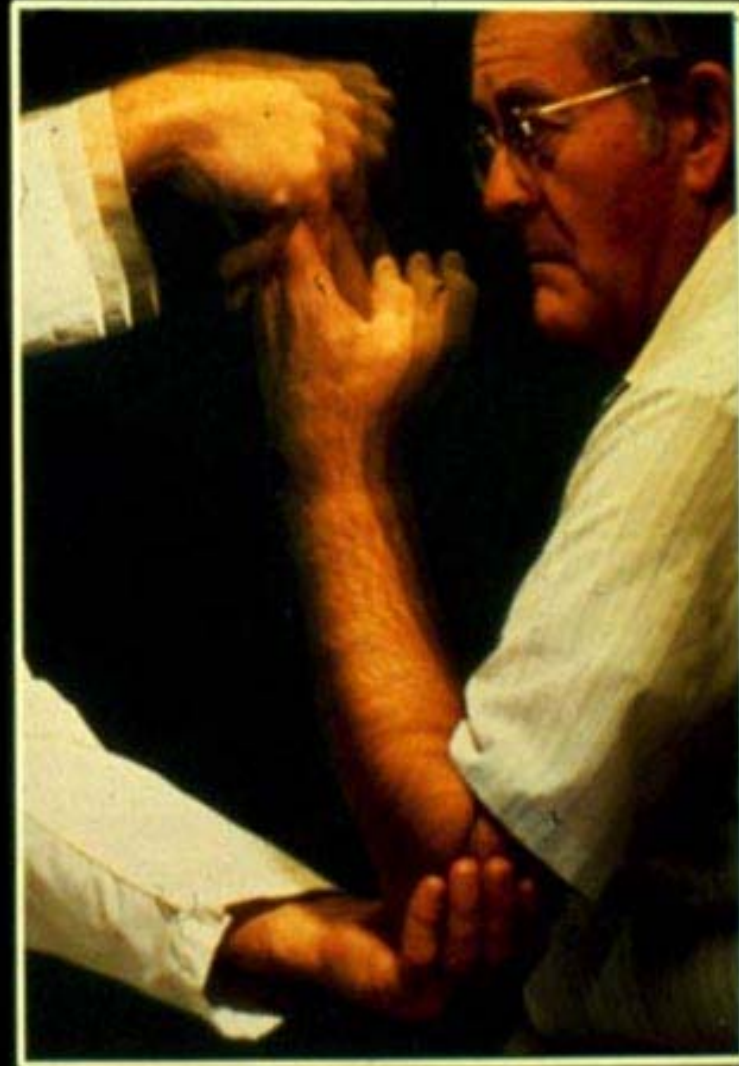
Tremor



Source: National Parkinson Foundation

Parkinson's Disease

Rigidity



Parkinson's Disease

Bradykinesia



PARKINSON'S DISEASE

Classical Clinical Features

- Tremor, resting
- Rigidity, cogwheel
- Akinesia, bradykinesia
- Postural Instability

PARKINSON'S DISEASE

Associated Clinical Features

- Micrographia
- Hypophonia
- Hypomimia
- Shuffling gait / festination
- Drooling
- Dysphagia
- Autonomic dysfunction
- Depression
- Dementia

PARKINSON'S DISEASE

Features supporting diagnosis

- Unilateral symptom onset
- Characteristic resting tremor
- Narrow-based gait with flexed/
stooped posture
- Reduced arm swing with
tremor
- Sustained and significant
levodopa effect

DISEASES ASSOCIATED WITH PARKINSONISM

Sporadic Disorders

- Parkinson's disease
- Multiple system atrophy
- Dementia with Lewy bodies
- Progressive supranuclear palsy
- Corticobasal degeneration
- Prion diseases
- Amyotrophic-parkinson-dementia complex of Guam
- Pallidal degeneration
- Hemiatrophy hemiparkinsonism

DISEASES ASSOCIATED WITH PARKINSONISM

Hereditary Disorders

- Huntington's disease
- Wilson's disease
- Juvenile onset parkinsonism
- Hallervorden-Spatz disease
- Dentatorubropallidoluysian atrophy (DRPLA)
- Frontotemporal dementia with parkinsonism
- Hereditary prion diseases
- Lubag
- Machado-Joseph disease (SCA 3)
- Neuroacanthocytosis
- Type 3 GM1 gangliosidosis

DISEASES ASSOCIATED WITH PARKINSONISM

Acquired Disorders

- Drug-induced parkinsonism
- Vascular parkinsonism
- Toxic parkinsonism
- Post-traumatic parkinsonism
- Post-encephalitic parkinsonism
- Prion diseases
- Extrapontine myelinolysis
- Space occupying lesions
- Hydrocephalus

PARKINSONISM

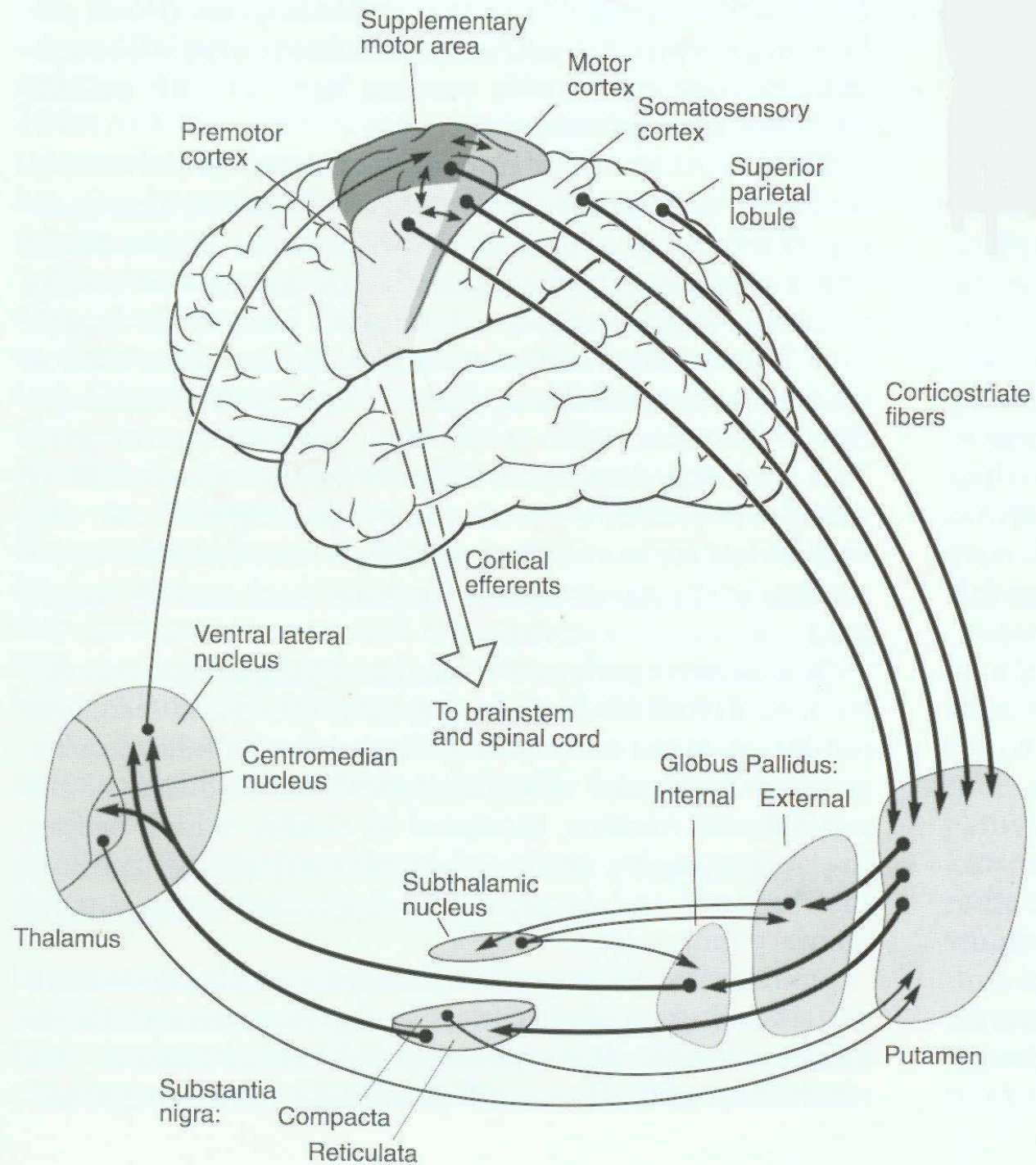
AAN Practice Parameter Recommendations:

Clinical features distinguishing other parkinsonian syndromes from PD

- Falls at presentation and early in the disease course
- Poor response to levodopa
- Symmetry at onset
- Rapid progression (to H&Y stage 3 in 3 years)
- Lack of tremor
- Early dysautonomia

THE BASAL GANGLIA

- Consists of a group of nuclei in the deep part of the cerebrum and upper brain stem: caudate, putamen, globus pallidus, subthalamic nucleus, substantia nigra
- Coordinates muscle actions and voluntary movements
- Controls the higher-order, cognitive aspects of voluntary movement: the planning and execution of complex motor strategies
- Cognitive functions (procedural memory - skills & habits)
- Structural defects and neurotransmitter imbalance cause movement disorders: hypokinesia or hyperkinesia



ATYPICAL PARKINSONIAN DISORDERS

- Multiple system atrophy
- Dementia with Lewy bodies
- Progressive supranuclear palsy
- Cortical basal degeneration
- Vascular parkinsonism
- Drug-induced parkinsonism
- Normal pressure hydrocephalus

NEURODEGENERATIVE PARKINSONIAN DISORDERS

ALPHA-SYNUCLEINOPATHIES

- Parkinson's disease (PD)
- Dementia with Lewy bodies (DLB)
- Multiple system atrophy (MSA)

TAUOPATHIES

- Progressive supranuclear palsy (PSP)
- Corticobasal degeneration (CBD)

ACQUIRED PARKINSONIAN DISORDERS

- Vascular parkinsonism
- Normal pressure hydrocephalus
- Drug-induced parkinsonism

DEMENTIA WITH LEWY BODIES

Clinical Features

- Second most common form of degenerative dementia in old age
- Early psychotic symptoms: hallucinations/delusions
- Mild extrapyramidal dysfunction
- Fluctuations in attention or level of arousal
- Orthostatic hypotension, syncope
- Depression
- Diurnal variations in behavior
- Neuroleptic sensitivity
- REM sleep behavior disorder

DEMENTIA WITH LEWY BODIES

(McKeith Criteria, 2005)

- Probable DLB
 - Dementia
 - Two or more: marked fluctuations, typical visual hallucinations, parkinsonism
- Possible DLB
 - Dementia
 - One of the following: marked fluctuations, typical visual hallucinations, parkinsonism
- Specificity is high (>85%), but sensitivity is low

DEMENTIA WITH LEWY BODIES

Pharmacological Management

- Cholinesterase inhibitors: rivastigmine, donepezil
 - Multicenter, controlled, 20-week study of rivastigmine (6-12 mg/d)
 - No worsening of motor function
 - Improvement of total Neuropsychiatric Inventory (NPI) score
 - Improvement of 4-item (delusion, hallucination, apathy, depression) subscore
 - Open-label study of donepezil
- Antipsychotic agents:
 - Neuroleptic sensitivity to typical antipsychotics
 - Low dose atypical antipsychotics are tolerated. Consider quetiapine
- Dopaminergic therapy:
 - Carbidopa/levodopa

MULTIPLE SYSTEM ATROPHY

Clinical Features

- Prevalence of 2-4 per 100,000 population (may be underestimated)
- Median age of onset is 55 years (range 33-76)
- Men : women = 1.3 : 1
- Mean survival 6-9 years; half of pts disabled or WC bound within 5 years of onset of motor symptoms
- Autonomic dysfunction, cerebellar signs, parkinsonism, poorly or transiently responsive to levodopa therapy, sleep apnea or RBD, stimulus sensitive myoclonus
- Dysarthria, laryngeal stridor, anterocollis
- Not compatible with MSA: asymmetric sx, rest tremor, early dementia, prominent ophthalmoplegia, apraxia, cortical sensory loss
- Subtypes: Shy-Drager syndrome (MSA-A), striatonigral degeneration (MSA-P), olivopontocerebellar atrophy (MSA-C)

MULTIPLE SYSTEM ATROPHY

Symptomatic Treatments

- Levodopa for parkinsonian features
- Sodium, fluid intake, pressure stockings, midodrine, fludrocortisone for orthostatic hypotension
- Oxybutinin or tolterodine for urinary frequency or incontinence
- Sildenafil for impotence
- Selective serotonin reuptake inhibitors for depression
- No good treatment of ataxia or dementia

PROGRESSIVE SUPRANUCLEAR PALSY

Clinical Features

- Prevalence of about 6 per 100,000 population
- Median age of onset is mid-60s, gradual sx onset
- Mean survival 5-9 years; half of pts disabled or WC bound within 3-4 years of onset of motor symptoms
- Parkinsonism, early instability with falls, poorly or transiently responsive to levodopa therapy, marked slowing of vertical gaze (esp. downward), eyelid apraxia, axial rigidity, retrocollis, motor perseveration
- Dysarthria, dysphagia, stuttering/palilalia early, laryngeal stridor
- Not compatible with PSP: asymmetric sx, rest tremor, early dementia, cortical sensory loss

PROGRESSIVE SUPRANUCLEAR PALSY

(NINDS-SPSP CRITERIA)

- PROBABLE PSP

- a) Presence of a gradually progressive disorder
- b) Onset at age 40 or older
- c) Supranuclear limitation of vertical gaze AND a hx of prominent postural instability and falls in the first year of onset
- d) No evidence of other diseases that can explain the above features

- POSSIBLE PSP

- a), b), and d) as above
- c) Supranuclear limitation of vertical gaze OR a hx of prominent postural instability and falls in the first year of onset

CORTICAL BASAL DEGENERATION

Clinical Features

- Prevalence of about 5-7 / 100,000 population
- Median age of onset is 60s-70s
- Mean survival about 7 years
- Insidious onset and progression of asymmetric cortical and basal ganglionic features
- Akinetic, rigid syndrome; hyperkinetic movement disorder (e.g. tremor, dystonia, myoclonus); alien limb phenomenon; speech impairment; gait disorder with postural instability; eye movement abn (slow horizontal saccades)
- Cortical dysfunction including dementia, apraxia, cortical sensory disturbance
- Not compatible with CBD - prominent ocular impairment, axial rigidity or dystonia out of proportion to limb involvement, rest tremor, autonomic failure, aphasia

PSP and CBD

Clinical Features

SIMILARITIES:

- Relatively rapid disease progression
- Speech and gait disturbance
- Poorly or transiently responsive to levodopa therapy

DIFFERENCES:

- PSP - symmetric parkinsonism, vertical supranuclear gaze palsy, postural instability at onset and early falls, axial rigidity, wide-based/slow/unsteady gait
- CBD - asymmetric parkinsonism, asymmetric cortical signs, dystonic posturing of unilateral limb, alien limb syndrome

PSP and CBD

Pharmacological Treatments

- Levodopa for parkinsonian features
- Clonazepam for action tremor, myoclonus, and RBD
- Baclofen and tizanidine for rigidity, muscle spasms
- Botulinum toxin injection for limb dystonia and blepharospasm
- SSRI for depression, anxiety, pseudobulbar palsy
- Six-week, placebo-controlled, double-blind study of donepezil for PSP: modest improvement in memory test scores were offset by deterioration in functional mobility

CLINICAL DIFFERENTIATING OF PARKINSONIAN DISORDERS

	PD	MSA	PSP	CBD
Symmetry of deficits	+	+++	+++	--
Axial rigidity	++	++	+++	++
Limb dystonia	+	+	+	+++
Postural instability	++	++	+++	+
Vertical gaze restriction	+	++	+++	++
Frontal behavior	+	+	+++	++
Dysautonomia	+	++	--	--
L-dopa response early	+++	+	+	--
L-dopa response late	++	+	--	--
Asym cortical atrophy on MRI	--	--	--	++

VASCULAR PARKINSONISM

Clinical Features

- Acute or subacute onset with stepwise evolution of akinesia and rigidity
- Presence of risk factors for cerebrovascular disease
- Two or more basal ganglia infarcts OR more widespread subcortical white matter lesions evident on neuroimaging
- No rest tremor
- Prominent postural instability and gait disorder
- Unresponsive to levodopa treatment

VASCULAR PARKINSONISM

Symptomatic Treatments

- Control stroke risk factors
- Keep active, stretching exercises
- Physical therapy for leg strengthening and gait training
- Assistive devices
- Safety-proof living environment

NORMAL PRESSURE HYDROCEPHALUS

- Syndrome of gait disturbance, urinary incontinence, and a dementing process
- CT/MRI: ventricular enlargement disproportionate to cortical atrophy and small-vessel ischemic changes
- Confirmed by beneficial response to large-volume cerebrospinal fluid drainage (30-50 ml)

NORMAL PRESSURE HYDROCEPHALUS

- Surgical treatment by CSF shunting procedure
- Good prognosis is associated with presence of full triad, short duration of symptoms, mild dementia, lack of cerebral atrophy in combination with enlarged ventricles and intermittent CSF pressure elevations
- Complications of shunt procedures include shunt malfunction, subdural hematoma, infection, seizure
- Proper selection of patients and use of appropriate techniques are important for successful treatment

DRUG-INDUCED PARKINSONISM

- Bradykinesia, rigidity, mild tremor, rabbit syndrome
- Caused by exposure to a dopamine-receptor blocking agent within 6 months of the onset of symptoms
- Offending drugs include: antipsychotics, anti-emetics, metoclopramide
- Mild cases can frequently remit after cessation of the offending drug
- Usually unresponsive to dopaminergic therapy
- Elderly patients are most susceptible
- Treatment may include: tetrabenazine, reserpine, vitamin E, benzodiazepines

ATYPICAL PARKINSONIAN DISORDERS

The differential diagnosis of atypical parkinsonian disorders is difficult because there are abundant overlapping features of the many disorders. Clinicians should be familiar with the less common but distinctive features of these disorders and have a high index of suspicion in order to tackle the diagnostic challenge, particularly in the early stages of disease. There is no reliable diagnostic markers available for the majority of the disorders.