movement phenomenon, or may be used to describe a syndromic disorder in which involuntary or abnormalities of movement are cardinal features of the disease. In contrast to most seizures, the involuntary movements occur when the patient is conscious, but are absent during sleep.

Movement disorders can be classified as either hyperkinetic or hypokinetic. Hyperkinetic phenomena include tremor, chorea, dystonia, tics, myoclonus, and other involuntary movements. Hypokinetic disorders encompass the Parkinsonian disorders characterized by a paucity of spontaneous movement (akinesia) and low amplitude slow movements (bradykinesia). While this classification strategy is a valuable means for approaching the patient with abnormal movements, many movement disorders include both hyperkinetic and hypokinetic phenomena. Idiopathic Parkinson's disease is the prototypical hypokinetic movement disorder, but it is associated with the hyperkinetic phenomenon of tremor in over 60% of patients. Similarly, Huntington disease, a traditionally hyperkinetic disorder, is associated with bradykinetic voluntary movements.

Parkinsonism

Parkinsonism is the most common of the extrapyramidal disorders and is characterized by akinesia, rigidity, tremor, and postural instability. Parkinsonism is caused by a wide variety of degenerative disorders, medication and toxins, and systemic diseases. Table 114-2 summarizes the differential diagnosis of Parkinsonism.

Idiopathic Parkinson's Disease

Idiopathic Parkinson's disease (PD) accounts for most individuals with Parkinsonism and is the second most common adult onset neurodegenerative disease after Alzheimer's disease. The average age of onset is around 60 years with an increasing prevalence associated with aging and a slight male preponderance. The motor symptoms of PD result from the selective loss of dopaminergic neurons in the substantia nigra-pars compacta that project to the striatum. The pathological hallmark of PD is the presence of eosinophilic cytoplasmic neuronal inclusions known as Lewy bodies containing α-synuclein.

TABLE 114-2 DIFFERENTIAL DIAGNOSIS OF PARKINSONISM

DEGENERATIVE/ INHERITED CAUSES	Idiopathic Parkinson's disease
	Multiple system atrophy
	Progressive supranuclear palsy
	Dementia with Lewy body
	Corticobasal degeneration
	Frontotemporal dementia with Parkinsonism
	Huntington's disease
	Wilson's disease
	Dopa-responsive dystonia
	Pantothenate kinase–associated neurodegeneration
SECONDARY CAUSES	Dopamine receptor blocking medications (e.g. antipsychotics, metoclopramide, prochlorperazine)
	Presynaptic dopamine depleting medications (tetrabenazine)
	Cerebrovascular disease
	Toxins (MPTP, manganese, carbon monoxide)

MPTP, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine.

Clinically, PD is characterized by its motor phenomenon with asymmetric rigidity, bradykinesia, rest tremor, and postural instability. However, PD is also characterized by secondary, non-motor manifestations (facial hypomimia, hypophonia, dysphagia, micrographia, and flexed posture), autonomic dysfunction (orthostatic hypotension, constipation, hyperactive bladder, and impaired temperature regulation), behavioral symptoms (depression, anxiety, psychosis), cognitive impairment and dementia, sleep disorders (impaired sleep architecture, restless legs syndrome, REM sleep behavior disorder), and sensory phenomena.

Until recently the diagnosis of PD was made based on the findings of an adult onset disorder of unilateral onset, persistent asymmetry of motor findings, and responsiveness of motor features to levodopa therapy. In addition, a number of "red flags" on history or examination might suggest an atypical or secondary cause of Parkinsonism (Table 114-3). However, Dopamine Transporter (DAT) SPECT imaging has recently been approved to assist in distinguishing PD from PD mimics, notably drug-induced Parkinsonism and essential tremor with parkinsonian features. The dopamine transporter is responsible for re-uptake of dopamine into presynaptic terminals and is, therefore, an indirect measure of nigro-striatal neuronal density. In PD, nigrostriatal neurons are lost asymmetrically; on dopamine transporter imaging, this is characterized by asymmetric reduction in dopamine transporter signal in the striatum. Unfortunately, this imaging method does not distinguish atypical Parkinsonism from PD.

A number of monogenic causes of Parkinsonism have been identified. Mutations in α-synuclein *(SNCA),* leucine-rich repeat kinase 2 *(LRRK2),* vacuolar protein sorting 35 *(VPS35),* and eukaryotic translation initiation factor 4-γ *(EIF4G1)* are associated with autosomal dominant Parkinsonism. Autosomal dominant causes account for less than 2% of all adult onset Parkinson's disease cases with higher frequencies in certain populations due to founder effects. Autosomal recessive monogenic causes include parkin, PTEN-induced kinase 1 *(PINK1),* and Parkinson protein 7 *(DJ-1)* and are relatively common in familial cases with onset before the age of 45. An improved understanding of these genetic causes suggests an important role of impairment in lysosomal pathways and protein degradation in PD pathogenesis.

PD is a slowly progressive disorder associated with accumulating disability. No treatments have been proven to slow progression; however, ongoing efforts continue to identify putative

TABLE 114-3 "RED FLAGS" IN THE DIAGNOSIS OF PARKINSON'S DISEASE

CLINICAL OR HISTORICAL "RED FLAG"	SUGGESTED DIAGNOSIS
Early postural instability and falls	PSP, MSA, CBD, DLB, Vascular
Early dysphagia	PSP, CBD
Early or spontaneous hallucinations	DLB
Early dementia or dementia predating PD	DLB
Early or severe dysautonomia	MSA
Pyramidal tract and/or Cerebellar signs	MSA
Antipsychotic exposure	Tardive or drug-induced
Acute onset and/or non-progressive	Vascular

CBD, Corticobasal degeneration; DLB, dementia with Lewy body; MSA, multiple system atrophy; PSP, progressive supranuclear palsy.