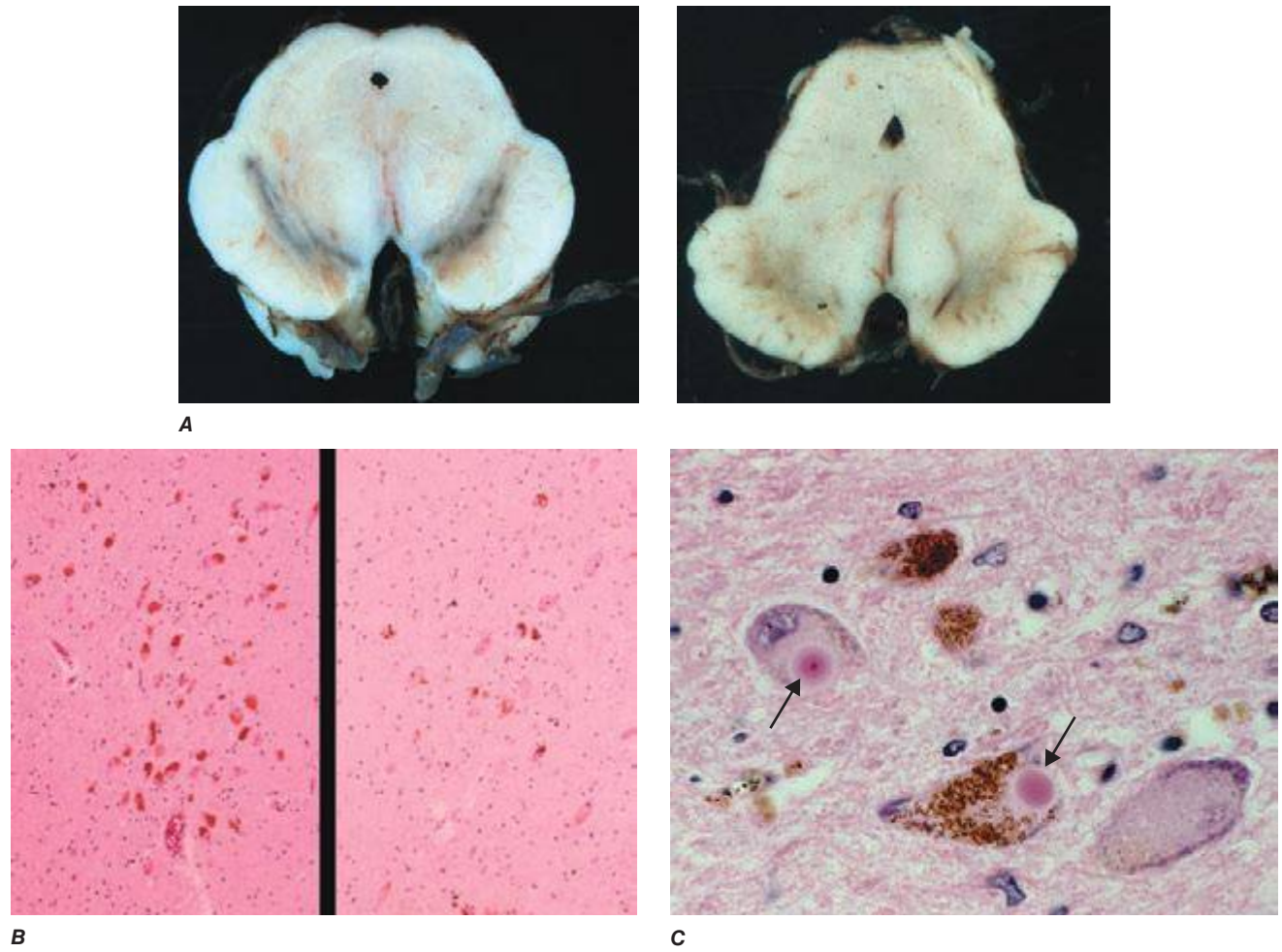

FIGURE 449-1 Pathologic specimens from a patient with Parkinson's disease (PD) compared to a normal control demonstrating (***A***) reduction of pigment in SNc in PD (*right*) versus control (*left*), (***B***) reduced numbers of cells in SNc in PD (*right*) compared to control (*left*), and (***C***) Lewy bodies (*arrows*) within melanized dopamine neurons in PD. SNc, substantia nigra pars compacta.

Multiple-system atrophy (MSA) manifests as a combination of parkinsonian, cerebellar, and autonomic features and can be divided into a predominant parkinsonian (MSA-p) or cerebellar (MSA-c) form. Clinically, MSA is suspected when a patient presents with atypical parkinsonism in conjunction with cerebellar signs and/or early and prominent autonomic dysfunction, usually orthostatic hypotension (Chap. 454). Pathologically, MSA is characterized by degeneration of the SNc, striatum, cerebellum, and inferior olivary nuclei coupled with characteristic glial cytoplasmic inclusions (GCIs) that stain for α-synuclein. Magnetic resonance imaging (MRI) can show pathologic iron accumulation in the striatum on T2-weighted scans, high signal change in the region of the external surface of the putamen (putaminal rim) in MSA-p, or cerebellar and brainstem atrophy (the pontine "hot cross buns" sign [Fig. 454-2]) in MSA-c. Mutations in the *CoQ2* gene encoding parahydroxybenzoate-polyprenyl transferase, an enzyme involved in the biosynthesis of coenzyme Q10 (CoQ10), a cofactor of the mitochondrial respiratory chain, have been identified in familial and sporadic forms of MSA.

Progressive supranuclear palsy (PSP) is a form of atypical parkinsonism that is characterized by slow ocular saccades, eyelid apraxia, and restricted eye movements with particular impairment of downward gaze. Patients frequently experience hyperextension of the neck with early gait disturbance and falls. In later stages, speech and swallowing difficulty and cognitive impairment become evident. MRI may reveal a characteristic atrophy of the midbrain with relative preservation of the pons, the "hummingbird sign" on midsagittal images. Pathologically,

TABLE 449-2 DIFFERENTIAL DIAGNOSIS OF PARKINSONISM

Parkinson's Disease	Atypical Parkinsonism	Secondary Parkinsonism	Other Neurodegenerative Disorders
Genetic	Multiple-system atrophy (MSA)	Drug-induced	Wilson's disease
Sporadic	Cerebellar type (MSA-c)	Tumor	Huntington's disease
Dementia with Lewy bodies	Parkinson type (MSA-p)	Infection	Neurodegeneration with brain iron accumulation
	Progressive supranuclear palsy	Vascular	SCA 3 (spinocerebellar ataxia)
	Corticobasal ganglionic degeneration	Normal-pressure hydrocephalus	Fragile X–associated ataxia-tremor-parkinsonism
	Frontotemporal dementia	Trauma	Prion disease
		Liver failure	Dystonia-parkinsonism (DYT3)
		Toxins (e.g., carbon monoxide, manganese, MPTP, cyanide, hexane, methanol, carbon disulfide)	Alzheimer's disease with parkinsonism

Abbreviations: MPTP, 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine.