Table 114-4 MEDICATIONS FOR PARKINSON'S DISEASE

ANTICHOLINERGIC AGENTS
Trihexyphenidyl (Artane) Benztropine (Cogentin)
DOPAMINE PRECURSORS (COMBINED WITH PERIPHERAL AROMATIC AMINO ACID DECARBOXYLASE INHIBITORS)
Carbidopa-levodopa (Sinemet, Sinemet-CR, Parcopa) (regular, controlled-release, and orally disintegrating) Benserazide-levodopa (Madopar) (marketed in Europe)
DOPAMINE AGONISTS
Apomorphine (Apokyn) (injectable short acting), bromocriptine (Parlodel) Pramipexole (Mirapex) Rotigotine (Neupro) (transdermal patch) Ropinirole (Requip, Requip XR)
MONOAMINE OXIDASE TYPE B (MAO-B) INHIBITORS
Selegiline (deprenyl) (Carbex, Eldepryl, Zelapar) Rasagiline (Azilect)
CATECHOL *O*-METHYLTRANSFERASE (COMT) INHIBITORS
Tolcapone (Tasmar) Entacapone (Comtan)
CATECHOL *O*-METHYLTRANSFERASE (COMT) INHIBITORS COMBINED WITH CARBIDOPA-LEVODOPA
Entacapone-carbidopa-levodopa (Stalevo)

disease modifying therapies. Treatments of the motor symptoms can reduce disability and improve function (Table 114-4). The mainstay of treatment is levodopa, the precursor to dopamine, given with a dopa-decarboxylase inhibitor to maximize CNS penetration of levodopa and minimize systemic side effects. Other symptomatic treatments stimulate dopamine receptors in the brain or inhibit the breakdown of levodopa and dopamine (Table 114-4). This approach to symptom management is effective early in the course of the disease; however, as the disease continues to progress, it may be complicated by the development of motor fluctuations, drug-induced dyskinesias, and psychosis.

Atypical Parkinsonism

Atypical Parkinsonism or "Parkinson plus" disorders refer to a heterogeneous group of inherited and sporadic neurodegenerative disorders characterized by Parkinsonism and a reduced or absent response to dopaminergic therapy. The most common are multiple system atrophy (MSA), progressive supranuclear palsy (PSP), dementia with Lewy bodies (DLB), and corticobasal degeneration (CBD).

MSA is a sporadic neurodegenerative disorder characterized clinically by the variable combination of Parkinsonism, autonomic dysfunction, cerebellar dysfunction, and extrapyramidal motor signs. The term MSA was coined to encompass three previously distinct clinical entities: striatonigral degeneration with prominent parkinsonism, olivopontocerebellar atrophy with prominent cerebellar dysfunction, and Shy-Drager syndrome with prominent autonomic dysfunction, particularly profound orthostatic hypotension. The identification of a shared neuropathological correlate of neuronal inclusions consisting of α-synuclein bolstered the shared nomenclature of these disorders. Currently, the preferred classification refers to either MSA-parkinsonism type or MSA-cerebellar type depending on the predominant clinical symptoms and signs. An MSA-autonomic type is proposed for those with an overwhelmingly autonomic presentation. Although relatively rare, MSA is among the most frequently encountered of the atypical Parkinsonisms with an overall incidence of 0.6/100,000 and an increasing incidence with age. It is universally fatal with a mean survival of 7 to 9 years, though longer disease duration is sometimes seen. Treatment is challenging and largely symptomatic. Some patients may be partially responsive to dopaminergic therapy and levodopa is recommended for individuals with prominent parkinsonism. Autonomic manifestations can be managed with symptomatic treatments to address orthostatic hypotension, constipation, and bladder symptoms (see Chapter 110).

Progressive supranuclear palsy is a relentlessly progressive disorder characterized by early gait instability and falls, prominent and early dysphagia, early speech difficulties progressing to a non-fluent aphasia, dementia, and supranuclear gaze palsy; death occurs on average 5 years after diagnosis. Supranuclear gaze palsy, in its fully realized form, is characterized by vertical greater than horizontal gaze palsy with preserved oculocephalic reflexes. Early, the gaze palsy may manifest by the presence of square wave jerks, difficulty initiating saccades, and loss of the fast phase on optokinetic nystagmus testing. Patients have a wide-eyed stare and lid lag may be present. Opposed to the flexed posture and asymmetry of PD, individuals with progressive supranuclear palsy have extensor trunk posturing and greater axial rigidity with relatively appendicular symmetry. Up to 20% of patients may have a modest response to levodopa therapy.

Dementia with Lewy bodies is the second most common degenerative cause of dementia after Alzheimer's disease. It is characterized clinically by Parkinsonism, dementia preceding or within 1 year of the motor symptoms, propensity for psychosis, early falls, and fluctuations in cognition and arousal. Motorically, it may be indistinguishable from Parkinson's disease. Patients have a high risk for psychosis associated with dopaminergic therapy and antipsychotics may cause worsening of Parkinsonism and even death making management of these patients challenging.

Corticobasal degeneration is a rare and heterogenous disorder. The characteristic Parkinsonian disorder presents with marked asymmetric Parkinsonism, focal limb dystonia, cortical sensory findings, alien limb phenomenon, and myoclonus. However, it may present with primary cortical cognitive symptoms and have features of progressive supranuclear palsy. It is a relentlessly progressive and fatal illness. Treatment is symptomatic.

Secondary Parkinsonism

There are many causes of secondary Parkinsonism, including medications, toxins, and cerebrovascular disease. Medications associated with Parkinsonism include any medication that reduces dopaminergic tone in the brain, either through direct blockade of post-synaptic dopamine receptors (e.g. antipsychotics) or through depletion of pre-synaptic dopamine stores (e.g. tetrabenazine). Metoclopramide, a medication commonly used to treat gastroparesis, is a frequent cause because its dopamine blocking effects may be overlooked. Drug-induced Parkinsonism can be indistinguishable from Parkinson's disease and is frequently asymmetric. Treatment consists of withholding the