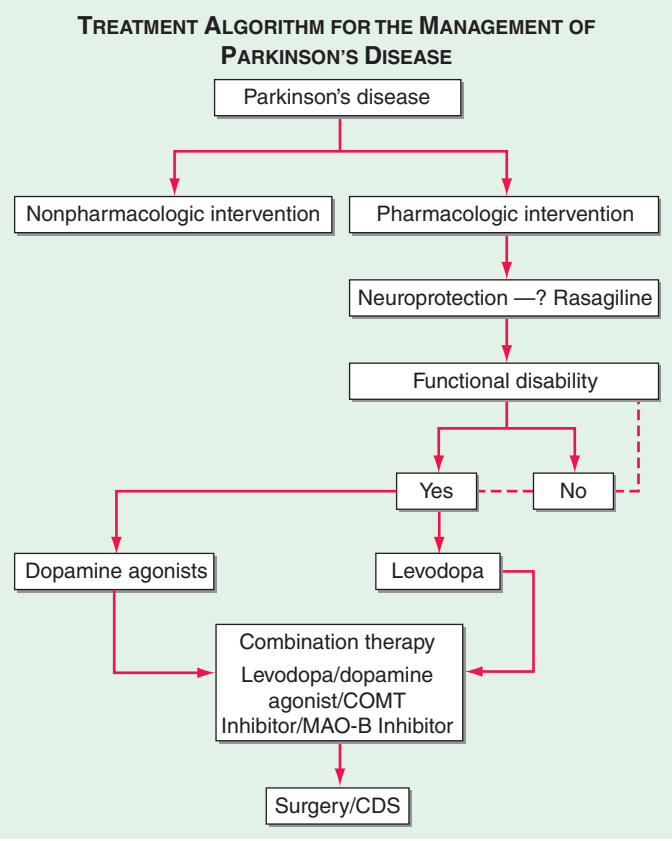

FIGURE 449-7 Treatment options for the management of Parkinson's disease (PD). Decision points include: (1) Introduction of a neuroprotective therapy: No drug has been established to have or is currently approved for neuroprotection or disease modification, but there are several agents that have this potential based on laboratory and preliminary clinical studies (e.g., rasagiline 1 mg/d, coenzyme Q10 1200 mg/d, the dopamine agonists ropinirole, and pramipexole). (2) When to initiate symptomatic therapy: There is a trend toward initiating therapy at the time of diagnosis or early in the course of the disease because patients may have some disability even at an early stage, and there is the possibility that early treatment may preserve beneficial compensatory mechanisms; however, some experts recommend waiting until there is functional disability before initiating therapy. (3) What therapy to initiate: Many experts favor starting with a monoamine oxidase type B (MAO-B) inhibitor in mildly affected patients because of the good safety profile of the drug and the potential for a disease-modifying effect; dopamine agonists for younger patients with functionally significant disability to reduce the risk of motor complications; and levodopa for patients with more advanced disease, the elderly, or those with cognitive impairment. Recent studies suggest the early employment of polypharmacy using low doses of multiple drugs to avoid side effects associated with high doses of any one agent. (4) Management of motor complications: Motor complications are typically approached with combination therapy to try and reduce dyskinesia and enhance the "on" time. When medical therapies cannot provide satisfactory control, surgical therapies such as DBS or continuous infusion of levodopa/carbidopa intestinal gel can be considered. (5) Nonpharmacologic approaches: Interventions such as exercise, education, and support should be considered throughout the course of the disease. CDS, continuous dopaminergic stimulation; COMT, catechol-*O*-methyltransferase. *(Adapted from CW Olanow et al: Neurology 72:S1, 2009.)*

ESSENTIAL TREMOR

ET is the commonest movement disorder, affecting approximately 5–10 million persons in the United States. It can present in childhood but dramatically increases in prevalence over the age of 70 years. ET is characterized by a high-frequency tremor (6–10 Hz) that predominantly affects the upper extremities. The tremor is most often manifest as a postural or action (kinetic) tremor and, in severe cases, can interfere with functions such as eating and drinking. It is typically bilateral and symmetric but may begin on one side and remain asymmetric. Patients with severe ET can have an intention tremor with overshoot and slowness of movement. Tremor involves the head in ~30% of cases, voice in ~20%, tongue in ~20%, face/jaw in ~10%, and lower limbs in ~10%. The tremor is characteristically improved by alcohol and worsened by stress. Subtle impairment of coordination or tandem walking may be present, and disturbances of hearing, cognition, personality, mood, and olfaction have also been described, but usually the neurologic examination is normal aside from tremor. The major differential is a dystonic tremor (see below) or PD. PD can usually be differentiated from ET based on the presence of bradykinesia, rigidity, micrographia, and other parkinsonian features. However, the examiner should be aware that PD patients may have a postural tremor and ET patients may develop a rest tremor. These typically begin after a latency of a few seconds (emergent tremor). The examiner must take care to differentiate the effect of tremor on measurement of tone in ET from the cogwheel rigidity found in PD.

TABLE 449-6 HYPERKINETIC MOVEMENT DISORDERS

Tremor	Rhythmic oscillation of a body part due to intermittent muscle contractions
Dystonia	Involuntary, patterned, sustained or repeated muscle contractions often associated with twisting movements and abnormal posture
Athetosis	Slow, distal, writhing, involuntary movements with a propensity to affect the arms and hands (this represents a form of dystonia with increased mobility)
Chorea	Rapid, semi-purposeful, graceful, dance-like nonpatterned involuntary movements involving distal or proximal muscle groups. When the movements are of large amplitude and predominant proximal distribution, the term *ballism* is used.
Myoclonus	Sudden, brief (<100 ms), jerk-like, arrhythmic muscle twitches
Tic	Brief, repeated, stereotyped muscle contractions that can often be suppressed for a short time. These can be simple and involve a single muscle group or complex and affect a range of motor activities.

ETIOLOGY AND PATHOPHYSIOLOGY

The etiology and pathophysiology of ET are not known. Approximately 50% of cases have a positive family history with an autosomal dominant pattern of inheritance. Linkage studies have detected loci at chromosomes 3q13 (ETM-1), 2p22-25 (ETM-2), and 6p23 (ETM-3), but no causative genes have been identified to date. GWAS demonstrated an association with the *LINGO1* gene, which is involved in oligodendrocyte differentiation and myelination, particularly in patients with young-onset ET. Recently, a nonsense mutation in the fused in sarcoma (*FUS*) gene was implicated as a cause of ET in a multigenerational family from Canada; this finding is of particular interest because different mutations in *FUS* are a known cause of familial amyotrophic lateral sclerosis (Chap. 452). It is likely that there are many other undiscovered genes for ET. The cerebellum and inferior olives have been implicated as possible sites of a "tremor pacemaker" based on the presence of cerebellar signs and increased metabolic activity and blood flow in these regions in some patients. Some pathologic studies have described cerebellar pathology with a loss of Purkinje cells and axonal torpedoes, but these findings are controversial and the precise pathologic correlate of ET remains to be defined.

TREATMENT

Many cases are mild and require no treatment other than reassurance. Occasionally, tremor can be severe and interfere with eating, writing, and activities of daily living. This is more likely to occur as the patient ages and is often associated with a reduction in tremor frequency. Beta blockers and primidone are the standard drug therapies for ET and help in about 50% of cases. Propranolol (20–120 mg daily, given in