prostate problems. Anticholinergic agents, such as oxybutynin (Ditropan), may be helpful. Constipation can be a very important problem for PD patients. Mild laxatives or enemas can be useful, but physicians should first ensure that patients are drinking adequate amounts of fluid and consuming a diet rich in bulk with green leafy vegetables and bran. Agents that promote gastrointestinal (GI) motility can also be helpful.

Sleep disturbances are common in PD patients, with many experiencing fragmented sleep with excess daytime sleepiness. Restless leg syndrome, sleep apnea, and other sleep disorders should be treated as appropriate. REM behavior disorder (RBD) is a syndrome comprised of violent movements and vocalizations during REM sleep, possibly representing acting out of dreams due to a failure of the normal inhibition of motor movements that typically accompanies REM sleep. Many PD patients have a history of antecedent RBD preceding the onset of the classic motor features of PD, and most cases of RBD go on to develop an α-synucleinopathy (PD or MSA). Low doses of clonazepam (0.5–1 mg at bedtime) are usually effective in controlling this problem. Consultation with a sleep specialist and polysomnography may be necessary to identify and optimally treat sleep problems.

NONPHARMACOLOGIC THERAPY

Gait dysfunction with falling is an important cause of disability in PD. Dopaminergic therapies can help patients whose gait is worse in "off" time, but there are currently no specific therapies available. Canes and walkers may become necessary to increase stability and reduce the risk of falling.

Freezing, where patients suddenly become stuck in place for seconds to minutes as if their feet were glued to the ground, is a major cause of falling. Freezing may occur during "on" or "off" periods. Freezing during "off" periods may respond to dopaminergic therapies, but there are no specific treatments for "on" period freezing. Some patients will respond to sensory cues such as marching in place, singing a song, or stepping over an imaginary line.

Exercise, with a full range of active and passive movements, has been shown to maintain and even improve function for PD patients, and active and passive exercises with full range of motion reduce the risk of arthritis and frozen joints. Some laboratory studies suggest the possibility that exercise might also have neuroprotective effects, but this has not been confirmed in PD. Exercise is generally recommended for all PD patients. It is less clear that physical therapy or specific exercises such as tai chi are required. It is important for patients to maintain social and intellectual activities to the extent possible. Education, assistance with financial planning, social services, and attention to home safety are important elements of the overall care plan. Information is available through numerous PD foundations and on the web, but should be reviewed with physicians to ensure accuracy. The needs of the caregiver should not be neglected. Caring for a person with PD involves a substantial work effort and there is an increased incidence of depression among caregivers. Support groups for patients and caregivers may be useful.

CURRENT MANAGEMENT OF PD

The management of PD should be tailored to the needs of the individual patient, and there is no single treatment approach that is universally accepted and applicable to all individuals. Clearly, if an agent could be demonstrated to have disease-modifying effects, it should be initiated at the time of diagnosis. Indeed, constipation, RBD, and anosmia may represent premotor features of PD and could permit the initiation of a disease-modifying therapy prior to the onset of the classical motor features of the disease. However, no therapy has yet been proved to be disease modifying. For now, physicians must use their judgment in deciding whether or not to introduce rasagiline (see above) or other drugs for their possible disease-modifying effects.

The next important issue to address is when to initiate symptomatic therapy. Several studies now suggest that it may be best to start therapy at the time of diagnosis (or soon after) in order to preserve beneficial compensatory mechanisms and possibly provide functional benefits even in the early stage of the disease. Levodopa remains the most effective symptomatic therapy for PD, and some recommend starting it immediately using low doses (≤400 mg/d), but others prefer to delay levodopa treatment, particularly in younger patients, in order to reduce the risk of inducing motor complications. An alternate approach is to begin with an MAO-B inhibitor and/or a dopamine agonist, and reserve levodopa for later stages when these drugs can no longer provide satisfactory control. In making this decision, the age, degree of disability, and side effect profile of the drug must all be considered. In patients with more severe disability, the elderly, those with cognitive impairment, or those in whom the diagnosis is uncertain, most physicians would initiate therapy with levodopa. Regardless of initial choice, it is important not to deny patients levodopa when they cannot be adequately controlled with alternative medications.

If motor complications develop, patients can initially be treated by manipulating the frequency and dose of levodopa or by combining lower doses of levodopa with a dopamine agonist, a COMT inhibitor, or an MAO-B inhibitor. Amantadine is the only drug that has been demonstrated to treat dyskinesia without worsening parkinsonism, but benefits may be short-lasting, and there are important side effects related to cognitive function. In advanced cases, it may be necessary to consider a surgical therapy such as DBS if the patient is a suitable candidate, but as described above, these procedures have their own set of complications. Continuous intraintestinal infusion of levodopa/carbidopa intestinal gel (Duodopa) appears to offer similar benefits to DBS, but also requires a surgical intervention with potentially serious complications. Continuous infusion of apomorphine is another treatment option and does not require surgery but is associated with potentially troublesome skin nodules. Comparative studies of these approaches in more advanced patients are awaited. There are ongoing efforts aimed at developing a long-acting oral or transdermal formulation of levodopa that mirrors the pharmacokinetic properties of a levodopa infusion. Such a formulation might provide all of the benefits of levodopa without motor complications and avoid the need for polypharmacy and surgical intervention.

A decision tree that considers the various treatment options and decision points for the management of PD is provided in **Fig. 449-7**.

HYPERKINETIC MOVEMENT DISORDERS

Hyperkinetic movement disorders are characterized by involuntary movements unaccompanied by weakness and occurring in isolation or in combination **(Table 449-6)**. The major hyperkinetic movement disorders and the diseases with which they are associated are considered in this section.

TREMOR

CLINICAL FEATURES

Tremor consists of alternating contractions of agonist and antagonist muscles in an oscillating, rhythmic manner. It can be most prominent at rest (rest tremor), on assuming a posture (postural tremor), or on actively reaching for a target (kinetic tremor). Tremor is also assessed based on distribution, frequency, and related neurologic dysfunction.

PD is characterized by a resting tremor, essential tremor (ET) by a postural tremor (trying to sustain a posture), and cerebellar disease by an intention or kinetic tremor (on reaching to touch a target). Normal individuals can have a physiologic tremor that typically manifests as a mild, high-frequency (10–12 Hz), postural or action tremor that is usually of no clinical consequence and often is only appreciated with an accelerometer. An enhanced physiologic tremor (EPT) can be seen in up to 10% of the population, often in association with anxiety, fatigue, a metabolic disturbance (e.g., hyperthyroidism, electrolyte abnormalities), drugs (e.g., valproate, lithium), or toxins (e.g., alcohol). Treatment is initially directed to the control of any underlying disorder and, if necessary, can often be improved with a beta blocker.