Guidelines

for the Management of

Parkinson`s Disease & Movement Disorders

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Movement is produced and coordinated by several interacting brain structures, such as the motor cortex, the cerebellum, and the basal ganglia (BG), disruption of this complex circuitry within the BG causes movement disorders, such as Parkinson's disease (PD), essential tremor (ET) and dystonia.
Movement disorders are neurological conditions that affect the speed, fluency, quality, and ease of movement. There may be either an excess or a paucity of voluntary and automatic movements, unrelated to weakness or spasticity.

Movement disorders can be classified as:
Hyperkinesias (excess of movements). Dyskinesias (unnatural movements and abnormal involuntary movements). Hypokinesia (decreased amplitude of movement). Bradykinesia (slowness of movement). Akinesia (loss of movement).
Movement disorders can develop acutely or over time. Acute morbidities encountered in movement disorders include those related to Parkinson's disease, acute drug reactions (acute dystonia, neuroleptic malignant syndrome, serotonergic syndrome, and malignant hyperthermia), acute exacerbation of chronic movement disorders (status dystonicus), hemiballism, and stiff-person syndrome.

Parkinson's disease PD
Parkinson's disease is a complex disorder that can be difficult to diagnose clinically, especially in the early stages.
The disorder is constellation of clinical manifestations involving not only motor difficulty (*the 6 cardinal features of parkinsonism are tremor-at-rest, bradykinesia, rigidity, loss of postural reflexes, flexed posture, and freezing of gait*) but also by the presence of non-motor features; which include (*Sleep Problems, Fatigue, Sensory Issues, Autonomic Issues, Personality and Behavior issues, Cognition and Mental Issues).* Some of these non-motor features occur several years before the first motor symptom; this is especially true of reduced sense of smell, constipation, and acting out one's dreams (also known as rapid eye movement [REM] sleep behavior disorder [RBD]).
Diagnosis based on etiology or neuropathology is impractical and to date, no single test (whether pharmacological, radiological or neuro-physiological) has any advantage over the clinical diagnostic criteria of PD nor has been shown to have sufficient sensitivity and specificity to reliably diagnose PD or distinguish PD from other forms of Parkinsonism.

PD should be differentiated from other forms of parkinsonism, including multiple system atrophy (MSA), progressive supra-nuclear palsy (PSP), cortico-basal degeneration (CBD) & from secondary causes of parkinsonism such as drugs, neurotoxins, and structural brain lesions as well as other causes of tremor.
In early stages; the following clinical features should be considered to distinguish PD from other parkinsonian syndromes:
1) falls at presentation and early in the disease course;
2) poor response to levodopa;
3) symmetry at onset;
4) rapid progression (to Hoehn and Yahr stage 3 in three years);
5) lack of tremor;
6) dysautonomia (urinary urgency/incontinence and fecal incontinence, urinary retention requiring catheterization, persistent erectile failure or symptomatic orthostatic hypotension).

In newly diagnosed PD; the followings predict more rapid rate of motor progression:
male sex, older age at onset, co-morbidities (stroke, auditory deficits, visual impairments), poor levodopa response, rigidity/hypokinesia &/or Postural Instability/Gait difficulty (PIGD) as an initial symptom; while younger age & tremor as a presenting symptom may predict a more benign course and longer therapeutic benefit to levodopa.

General Treatment Considerations

▪ These include medications, surgical procedures, physiotherapy, occupational therapy and other support services.

▪ Despite the increase in non-pharmacological treatments, an individual with Parkinson's becomes more reliant on their medication to maintain their ability to function as the disease progresses. A balance between the side effects of the medication and the benefit often becomes more difficult with time.

▪ Currently, there is no evidence to suggest any of the medications, in particular levodopa, are toxic and that treatment should be initiated earlier rather than later for dopaminergic neuronal"sparing".

▪ Anti-parkinsonian medication should not be withdrawn abruptly or allowed to fail suddenly due to poor absorption (for example gastroenteritis, abdominal surgery) to avoid the potential for acute akinesia or neuroleptic malignant syndrome.

▪ The practice of withdrawing patients from their antiparkinsonian drugs (so-called 'drug holidays') to reduce motor complications should not be undertaken because of the risk of neuroleptic malignant syndrome.

▪ In view of the risks of sudden changes in anti-parkinsonian medication, people with PD who are admitted to hospital or care homes should have their medication:
A) given at the appropriate times, which in some cases may mean allowing self-medication;
B) adjusted by, or adjusted only after discussion with, a specialist in the management of PD.

▪ Clinicians should be aware of dopamine dysregulation syndrome (impulse control disorders), an uncommon disorder in which dopaminergic medication misuse is associated with abnormal behaviours.

Pharmacological Therapy for Motor Symptoms in Early PD

The goal of treatment:
reducing motor symptoms, and improving quality of life without causing side effects.
Factors which influence treatment decision include:
symptom severity, whether the symptoms affect the dominant hand, embarrassment, ability to continue working and/or participate in activities such as hobbies, cost, and patient preference. If symptoms are very mild, the patient may choose not to begin therapy.

▪ Levodopa remains the most effective medication for the treatment of motor symptoms.
It is always given in combination with carbidopa ("Sinemet") or benserazide ("Prolopa") to prevent decarboxylation in the periphery.
As it is associated with a higher risk for the development of motor complications (fluctuations and dyskinesia), keeping the dose as low as possible to provide symptomatic benefit is generally recommended.

▪ Dopamine agonists are the second most potent class of medication (after levodopa) for control of motor symptoms in PD and can be used in early PD with success as having less likelihood of producing fluctuations in early disease, but are less effective, associated with a higher prevalence of side effects and they are also more expensive than levodopa.
In older patients, over the age of 70, dopamine agonists should be used with caution, if not avoided.

When using an ergot-derived agonist (bromocriptine); baseline ESR, renal function, cardiac echocardiogram and chest X-ray are recommended prior to starting treatment and annually as long as the patient remains on the medication due to the risk of pleura-pulmonary and cardiac valve fibrosis.
As non-ergot derived agonists (pramipexole, ropinirole) do not carry this risk nor require this monitoring, they are preferred to an ergot-derived agonist.
As there is no good evidence that one dopamine agonist is superior to another regarding control of motor symptoms in PD, thus, if one results in side effects, another could be substituted but the side effect profiles are similar.
▪ Monoamine-oxidase B inhibitors (selegiline, rasagiline) prevent the breakdown of dopamine in the brain. Each has been shown to have mild but definite symptomatic benefit as monotherapy in early PD.
▪ Amantadine may be used as monotherapy, but should not be a drug of first choice.
Side effects such as livedo reticularis and leg edema need to be monitored & used with caution in patients with renal dysfunction.
▪ Anticholinergics (trihexyphenidyl and benztropine) are used primarily in young patients with early PD and prominent tremor. They are not recommended in the elderly, as they tend to cause confusion and memory difficulties.
▪ While the classical tremor seen in PD is a resting tremor, some patients have an associated postural tremor. Beta-blockers may be considered in this situation.

Pharmacological Therapy for Motor Symptoms in Later PD
▪ After years, the duration of benefit from treatment especially levodopa may become progressively shorter. This phenomenon is referred to as "*end of dose deterioration*" or "*wearing-off*" and eventually patients may experience more unpredictable fluctuations including: *on-off responses*, *freezing* & *involuntary movements* (*dyskinesias*).
COMT inhibitor (entacapone), MAO-B inhibitor (rasagiline) and Dopamine agonists (pramipexole, ropinirole, bromocriptine) can reduce this off time.
▪ Modified-release levodopa preparations may be used in people with later PD to reduce motor fluctuations especially most useful in addressing overnight wearing off, however, they should not be considered as drugs of first choice.
▪ With advancing disease, dyskinesias become more frequent and more severe resulting in a considerable source of disability to many patients. The therapeutic window of levodopa becomes narrower so that small increases in dose to improve clinical effect result in dyskinesias. To date, only amantadine has been shown in clinical studies to improve dyskinesia without worsening parkinsonism but is associated with cognitive side-effects & edema which may necessitate discontinuation of the drug.

Surgery
▪ The surgical treatment for PD is considered in advanced disease and the optimized medical treatment has failed in treating motor symptoms (e,g motor fluctuations and/or dyskinesia).
▪ In considering the type of surgery, account should be taken of:
○ Clinical and lifestyle characteristics of the person with PD
○ Patient preference after the patient has been informed of the potential benefits and drawbacks of the different surgical procedures.
▪ Surgical procedures of the basal ganglia such as thalamotomy for treating tremor and pallidotomy for levodopa-induced dyskinesias were initially employed.
▪ Deep brain stimulation (DBS) is currently the surgical treatment of choice in advanced PD patients. Compared to ablative surgery, DBS can decrease disease progression, has reversible effects, and can be used bilaterally to improve symptoms.

○The most DBS targets used for PD are: the thalamus (Vim nucleus), the subthalamic nucleus (STN), and the globus pallidus internus (GPi) with estimated 50% improvement of UPDRS scores (Unified Parkinson's Disease Rating Scale) & 69% reduction of Levodopa-induced dyskinesia when compared to the off medications condition before surgery.
○The most reported complications related to DBS (especially STN DBS) and may persist in the long-term follow-up include: weight gain, eyelid opening apraxia, dysarthria/hypophonia, gait disturbances, postural instability and verbal fluency decline.
○ Deep brain stimulation (DBS) of the subthalamic nucleus (STN) may be considered as a treatment option in PD patients to improve motor function and to reduce motor fluctuations, dyskinesia, and medication usage. Patients need to be counseled regarding the risks and benefits of this procedure.
○ Bilateral globus pallidus internus (GPi) stimulation may be used in people with PD who:
- have motor complications that are refractory to best medical treatment
- are biologically fit with no clinically significant active co-morbidity
- are levodopa responsive
- have no clinically significant active mental health problems (e.g. depression or dementia).
○ Aged tremor-dominant PD patients with severe unilateral tremor can benefit more from thalamus (Vim nucleus) than STN DBS, due to the relatively less complicated thalamic procedure, simpler post-operative management, less stimulation related side effects and the usually relatively benign course of tremor-dominant PD.
○ Preoperative response to levodopa should be considered as a factor predictive of outcome after DBS of the STN but there is insufficient evidence to make any recommendations about factors predictive of improvement after DBS of the GPi or VIM nucleus of the thalamus.
○ Age and duration of PD may be considered as factors predictive of outcome after DBS of the STN. Younger patients with shorter disease durations may possibly have improvement greater than that of older patients with longer disease durations.

Treatment options for motor complications

First Line	Entacapone, Rasagiline, Pramipexole, Ropinirole
Other Options	Levodopa modified release, DBS STN, DBS GPi
Reduce Dyskinesia	Amantadine, DBS STN, DBS GPi

Other Treatment Options for PD

Previously, motor function received the primary attention of patients and physicians leading to concentration on pharmacologic therapies for PD. More recently, non-motor symptoms (*Sleep Problems, Fatigue, Sensory Issues, Autonomic Issues, Personality and Behavior issues, Cognition and Mental Issues)* have become recognized as a major source of disability and treatment focus has shifted to improve and maintain quality of life in advanced disease with using non-pharmacologic methods of treatment (rehabilitation, physical and exercise therapies)

Non-Motor Features of PD - Mental Health

Include depression, dementia and psychosis. It should be clear that standard pharmacologic treatment for these symptoms in patients without PD will not be as effective or necessarily tolerated (dopamine antagonists for psychosis) due to neurotransmitter changes present in PD

Depression

Often goes on unrecognized due to the many overlapping features common to depression and PD, both prior to and while on treatment (loss of facial expression, hypophonic speech, slowed movement, reduced appetite and sleep disorders), depression in PD.
Amitriptyline is to be considered in the treatment of depression in PD without dementia,

desipramine and citalopram were similarly efficacious in PD depression. ECT remains a potentially lifesaving treatment in major depression and has been used successfully in PD

Psychotic Symptoms

○ Once evident, typically persist as a problem through the course of their disease. There is a typical progression from illusions of presence, through pseudo hallucinations to true hallucinations. Visual hallucinations and paranoia are the most common.

○ Not all hallucinations require treatment. If they are sufficiently problematic then any precipitating medical problems should be ruled out & all non essential central nervous system active medications should be eliminated.

○ If these steps do not control the hallucinations, then reducing or stopping parkinsonian medications that have a greater potential for worsening psychosis relative to the parkinsonian benefit may be needed. Keeping in mind the risk of rapid discontinuation of dopaminergic medications worsening psychosis or causing potential neuroleptic malignant syndrome

○ If following the above suggestions is inadequate then the addition of an antipsychotic may be necessary. In choosing these, typical antipsychotic medications (phenothiazines, butyrophenones) should be avoided as may exacerbate PD motor symptoms

- Quetiapine up to 150 mg/day may have a lower potential for causing worsening of parkinsonism and is considered as a safe treatment option.

– Clozapine 25-50 mg/day is the most supported medication option in the treatment of psychosis in PD but is not easy to use as more intensive monitoring required.

Dementia

Common in those with an older age of onset and its frequency increases with disease duration. We should rule out other potential medical disorders contributing to dementia (thyroid dysfunction, B12 deficiency etc). Discontine anticholinergics, amantadine, tricyclics, tolterodine, oxybutinin and benzodiazepines.

Cholinesterase inhibitors (donepezil , rivastigmine) used for the treatment of dementia in PD

Non-Motor Features of PD - Sleep Disorders

The major sleep disorders in Parkinson's disease include insomnia, excessive daytime somnolence, REM sleep behavior disorder and restless legs syndrome.

▪ Insomnia - Good sleep hygiene should be ensured. Eszopiclone & Melatonin may be used.

▪ REM Sleep Behaviour Disorder (RBD)- characterized by the loss of normal muscle tone during REM sleep & patients act out their dream content; clonazepam (0.25-1mg hs) or melatonin (3-12mg hs) can suppress RBD

▪ Restless legs syndrome (RLS)- characterized by a sensation of urge to move the legs, which is worse at night, exacerbated by rest, and relieved by activity. RLS can be treated with dopaminergic agents, opioids, or gabapentin(800-1800 mg/day split between one-third of the total dose at 12PM and two-thirds at 8PM)

▪ Excessive daytime sleepiness (EDS) - when severe, patients fall asleep even in stimulating conditions such as eating, walking, or working.

Modafinil 200- 400 mg/day may be considered but has modest effect.

Non-Motor Features of PD - Autonomic dysfunction

○Autonomic dysfunction is extremely common in PD and encompasses cardiovascular, gastrointestinal, urogenital and thermoregulatory disorders.

Orthostatic hypotension, nocturia, constipation and weight loss have significant impact on quality of life but evidence regarding specifics of management is poor.

○ Sialorrhea can be a functionally and cosmetically disabling symptom in PD. Atropine drops, ipratropium bromide spray, gum chewing and botulinum neurotoxin should be considered as options in the managements.

○ Swallowing difficulties can become an increasing concern as the disease progresses. Oro-pharyngeal dysphagia in the early stages may not require any specific investigations if it occurs infrequently (less than one time per week) and is limited to liquids. Treatment at this stage would include encouraging smaller boluses, having an increased attention to eating and reducing distractions at meals. As the dysphagia progresses monitor respiratory and nutritional status, Food consistency changes, reduce bolus volume, screen for gastroesophageal reflux disease and other upper GI tract dysfunction, reflux treatments or prokinetic (domperidone) medications for symptom management are helpful but it is important to remember to avoid the use of metoclopramide.

Urinary Dysfunction

In the form of urgency, frequency and nocturia. In men, prostatic hypertrophy must be ruled out & urological assessment is always warranted. The consumption of water or caffeinated drinks after dinner is to be restricted, specific recommendations for treatment of these symptoms include anticholinergics (oxybutynin, tolterodine) but must be closely monitored for anticholinergic related side effects such as confusion, hallucinations, dry mouth and urinary retention. Newer anticholinergics such as solifenacin (vesicare) may be used.

Constipation

Constipation can predate the onset of PD symptoms by decades.
Simple measures such as ensuring a higher content of fiber including consumption of fruits and vegetables are crucial along with a high consumption of water.
Bulk-forming laxatives (metamucil, psyllium), stool softeners (docusate) & lubricant laxatives suppositories can be used but the stimulant laxatives such as bisacodyl (Dulcolax) should not be used for more than a few days as they will cause the bowel to potentially lose tone. In some cases; domperidone might be helful.

Orthostatic Hypotension

Non-pharmacological therapy include wearing elastic stockings, head-up tilt of the bed at night, avoid aggravating factors such as large meals, alcohol, avoid or reduce drugs known to cause orthostatic hypotension if possible such as Levodopa and dopamine agonists, diuretics or antihypertensive drugs.
Drug therapy for orthostatic hypotension would include:
Domperidone 30 mg t.i.d for those with post-prandial orthostatic hypotension
Mineralocorticoids (fludrocortisones 0.1–0.2 mg/day) or alpha-receptor agonists (midodrine 2.5-10 mg t.i.d) can often raise the orthostatic blood pressure for more severe cases but both can cause supine hypertension.

Erectile dysfunction

This symptom is widespread in PD (50-75% of men with PD) due to dysautonomia, mood dysfunction, motor disability and side effects of medications. There is good evidence exists for the use of sildenafil citrate (viagra), tadalafil (cialis) and vardenafil (levitra).

ESSENTIAL TREMOR ET

The diagnosis of ET requires one of the following:
• Bilateral postural or kinetic tremor of the hands.
• Isolated head tremor without evidence of dystonia.
The exclusion criteria are
(1) other abnormal neurologic signs,
(2) recent neurologic trauma preceding the onset of tremor,
(3) presence of known causes of enhanced physiologic tremor (eg, drugs, anxiety, depression, hyperthyroidism),
(4) history or presence of psychogenic tremor,
(5) sudden onset or stepwise progression,

(6) primary orthostatic tremor (predominantly in the legs upon standing),
(7) isolated position- specific or task-specific tremors (occupational tremors, primary writing tremor),
(8) isolated tremor in the voice, tongue, chin, or legs

ET commonly affects the hands or forearms, head, and larynx. The arms are involved bilaterally, though often asymmetrically. Amelioration with alcohol and a positive family history is supportive historical information. Occasionally, cognitive and personality disturbances may occur, involving verbal fluency, mental set-shifting, disinhibition, emotional blunting, and depression.
The anticonvulsant primidone 50–100 mg bid may be the most effective agent for treating ET, but it is often poorly tolerated.
ß-blockers are the preferred alternative: propranolol 120–160 mg bid,
atenolol 50–100 mg/day
Benzodiazepines, including alprazolam 0.25 - 0.5 mg tds & the anticonvulsant topiramate 50-100 mg bid can also benefit patients with ET.
Deep brain stimulation of the ventral intermediate nucleus of the thalamus can provide good long-term benefits in cases of severe, medically intractable ET, including good efficacy for head tremor with bilateral surgery.

DYSTONIA
It is a sustained muscle contraction, frequently causing repetitive twisting movements or abnormal postures. The diagnosis of dystonia is clinical, the core being abnormal postures (with or without tremor) and the recognition of specific features, e.g. gestes antagonistes, overflows, mirror movements.
Dystonia is a dynamic condition that often changes in severity depending on the posture assumed and on voluntary activity of the involved body area.
Dystonia is divided into focal (affecting a single body region), segmental (two or more adjacent areas) or generalized (involving the legs, or one leg and the trunk, plus at least one other area of the body). Focal dystonias include cervical dystonia (spasmodic torticollis), blepharospasm, oculogyric crisis, oromandibular dystonia, spasmodic dysphonia or laryngeal dystonia, and focal hand dystonia

The classification is based on three axes:
(a) aetiology (b) age at onset of symptoms, (c) distribution of body regions affected.
The aetiological axis defines primary (idiopathic) dystonia with no identifiable exogenous cause nor evidence of neurodegeneration (i.e. no progressive loss of neural cells) or dystonia can be secondary to a known structural lesion of the brain.
Primary dystonias are classified as pure dystonias, dystonia-plus syndromes or paroxysmal dystonias
Adult onset primary dystonia can present mainly with tremor, which could be misdiagnosed as Parkinson's disease.
○Assessment should be performed using a validated rating scale for dystonia.
○ A diagnostic levodopa trial is warranted in every patient with early onset dystonia without an alternative diagnosis.
○ Appropriate investigations are required if the initial presentation or the course suggest heredo-degenerative or secondary (symptomatic) dystonia.
Genetic testing should be performed after establishing the clinical diagnosis.
- DYT1 testing is recommended for patients with limb-onset, primary dystonia with onset before age 30, as well as in those with onset after age 30 if they have an affected relative with

early onset dystonia. In dystonia families, DYT1 testing is not recommended in asymptomatic individuals.
- DYT6 testing is recommended in early-onset dystonia or familial dystonia with cranio-cervical predominance or after exclusion of DYT1.
- DYT11 testing is recommended in individuals with early-onset myoclonus of the arms or neck, particularly if positive for autosomal dominant inheritance and if triggered by action.
○ Neuro-physiological tests are not routinely recommended for the diagnosis or classification of dystonia; however, the observation of tests abnormalities typical of dystonia is an additional diagnostic tool in cases where the clinical features are insufficient to the diagnosis.
○ Structural brain imaging is not routinely required when there is a confident diagnosis of primary dystonia in adult patients, because a normal study is expected in primary dystonia. Structural brain imaging (MRI) is necessary for screening of secondary forms of dystonia.
○Botulinum neurotoxins (BoNT), in properly adjusted doses, are effective and safe treatments of cranial (excluding oromandibular), cervical dystonia, writer's cramp and is possibly effective in other types of upper limb dystonia.
BoNT must not be used in patients affected by disorder of neuromuscular transmission or presence of infection at injection site & the recommended dosage should not be exceeded.
○ Pallidal deep brain stimulation DBS is considered a good option for primary generalized or segmental dystonia, cervical dystonia after medication or BoNT have failed to provide adequate improvement but it is less effective in secondary dystonia with the exception of tardive dystonia and should not be used in patients with dementia or in patients with disability due to secondary fixed deformities.
○ Physical therapy and rehabilitation procedures have an important role in the care of patients with dystonia especially in cases of upper limb dystonia.

TARDIVE DYSKINESIA TD

Dyskinesia refers specifically to rapid, repetitive, stereotypic movements that mostly involve the oral, buccal, and lingual areas though this term is now often used more globally to describe various tardive syndromes.
Tardive syndromes are characterized by abnormal involuntary movements (most often choreiform or dystonic) or akathisia (a sensation of restlessness that causes often uncontrollable movements) caused by exposure to a dopamine receptor–blocking agent within 6 months of the onset of symptoms and persisting for at least 1 month after cessation of the offending drug. Elderly patients, especially those with dementia, are the most susceptible population.
The American Psychiatric Association has required 3 months of exposure to an offending drug for a diagnosis of TD, although TD has been reported occasionally in elderly persons after as little as 1 month of exposure.
Among neuroleptics: clozapine and quetiapine have the lowest reported incidence of TD and have been convincingly shown to induce TD only in patients who were exposed to additional neuroleptics.
The most important intervention for TD is preventive i.e. to avoid any agents that block the dopamine receptor, including metoclopramide that must be prescribed only after establishing medical necessity.
When possible, the offending agent should be discontinued immediately with the hope of facilitating a remission though this condition may persists and can be disabling.
Switching to an atypical neuroleptic may be considered in patients with active psychosis or in whom TD is brought on or worsened as a result of lowering the inciting agent.
Reserpine 0.375–2 mg/day, Tetrabenazine 100–200 mg/day, Clonazepam 1–4 mg/day are

considered among potential treatments for TD. Deep brain stimulation appears to be effective for treating medically intractable TD, including its oro-facial symptoms.

RESTLESS LEGS SYNDROME RLS

Is an autosomal dominant pattern of inheritance & defined by four obligatory criteria:

- Urge to move the legs
- Worsening of symptoms with rest
- Relief with activity
- Intensification during the evening

Offending medications (selective serotonin re-uptake inhibitors, monoamine oxidase inhibitors, lithium, antihistamines, and neuroleptics) should be discontinued.

Morning fasting serum ferritin, vitamin B_{12}, folate levels should be measured and iron therapy should be instituted to achieve a ferritin level of ≤ 50 μg/L (low-normal range).

Milder cases can occasionally be tempered with a sedative to promote sleep.

For resistant cases Pramipexole 0.25–0.5 mg at bedtime, Ropinirole 1–2 mg at bedtime, , Carbidopa/ levodopa 25/100 mg bedtime and Methadone 5–25 mg/day can be used.

HUNTINGTON`S DISEASE HD

Chorea, the clinical hallmark of HD, is a progressive disease and consists of involuntary, continual, abrupt, rapid, brief, un-sustained, irregular movements that flow randomly from one body part to another with inability to maintain voluntary contraction that results in the dropping of objects and clumsiness. Some of the movements can be partially and temporarily suppressed by incorporating them into semi-purposeful activities (parakinesia).

In addition to chorea, other presenting symptoms of HD include cognitive decline and psychiatric impairment, gait and balance difficulties, irritability, depression, clumsiness, speech difficulty, memory loss, lack of motivation, paranoia, intellectual decline, sleep disturbance, hallucination, weight loss, and sexual problems.

Besides chorea, other motor symptoms that typically affect patients with HD include dystonia, postural instability, ataxia, slow saccades, bruxism, myoclonus, tics and tourettism, dysarthria, dysphagia, and aerophagia.

The Unified Huntington's Disease Rating Scale (UHDRS) is used to assess and quantify various clinical features of HD, specifically motor function, cognitive function, behavioral abnormalities, and functional capacity. Hung-up and pendular reflexes are also typically present in patients with HD.

Caudate atrophy(measured by the ratio of inter-caudate to outer-table distances) has traditionally been used as an index of striatal atrophy in HD. Subsequent studies, however, have shown that a reduction in the volume of putamen, as measured by magnetic resonance imaging (MRI), is a more sensitive index of neurologic dysfunction than caudate atrophy.

The Indications to treat chorea include (Interference with work activities, physical injury, loss of balance, social stigma, sleep disturbance)

Single drug treatments are often unsuccessful and require addition of other drugs or drug combinations related to the complexity of HD

Tetrabenazene is considered first line of treatment of chorea started at 12.5 mg/day and should be increased slowly up to 100 mg/day in divided doses as required.

If there is associated (depression, psychosis, aggression) then antipsychotic are used first.

Amantadine 300–400 mg/ day recommended right after tetrabenazine and before riluzole.

Riluzole 200 mg/day though has limited functional benefits and need to monitor hepatic alanine aminotransferase levels so not recommended routinely as anti-choreic therapy.

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