

45 Parkinson's Disease

Abstract: The clinical syndrome of Parkinsonism characterized by tremor, rigidity, akinesia and abnormal posture, as described by James Parkinson in 1817, is not difficult to identify and particularly if it is associated with shuffling gait, micrographia and hypophonia. However, in early stages it may resemble depressive illness or generalized asthenia (weakness). In such situation it may become necessary to carry out a therapeutic trial with anti-depressant drugs. Failure to improve upon the symptoms of "depression" in few weeks may require therapeutic challenge with levodopa therapy. In later stages, symptoms and signs of confusional state or early dementia may pose a diagnostic problem and will demand neuro-imaging studies to ascertain diagnosis and rule out conditions like "normal pressure hydrocephalus" or Alzheimer's disease. In early cases, physiotherapy and rehabilitation exercise are essential before drug therapy is started. Failure to respond to levodopa therapy often points to differential diagnosis like Parkinson plus syndromes as described in the text. By and large, medical therapy if properly administered, controls the symptoms of Parkinson's Disease (PD) and patient is able to lead normal activities. The role of surgery is limited to young patients with unilateral syndrome. Transplantation of tissues containing dopaminergic neurons has not been successful. Stem cell therapy holds promise.

James Parkinson, in 1817, wrote "Essays on Shaking Palsy" which is now commonly termed as Parkinsonism. It is a clinical syndrome characterized by tremor, rigidity, akinesia, and abnormal posture. Other clinical features include: (i) shuffling gait, (ii) micrographia, (iii) hypophonia, (iv) drooling, (v) dysphagia, and (vi) autonomic dysfunction. It affects both sexes equally. The mean age of onset of disease is around 65 years (range 31-85 years) and the mean duration of disease at the time of death is usually 12 years. Atypical clinical features such as dementia, and supranuclear vertical gaze palsy or poor response to levodopa therapy are not uncommon and may indicate alternative pathologies like "neuro-fibrillary degeneration", etc.

Etiology

- A. **Idiopathic:** This is common form of parkinsonism which occurs without obvious cause, and often called **Parkinson's disease (PD)** or **paralysis agitans**. The disease may start below 20 years of age (**Juvenile PD**) or before the age of 50 years (**Early onset**) or after the age of 50 years (**Late onset**).
- B. **Postencephalitic Parkinsonism:** Parkinsonism often developed in patients with a history of von Economo's encephalitis. Now, this type of infection is uncommon and hence cases of postencephalitic parkinsonism are becoming increasingly rare.
- C. **Drug or Toxin-induced Parkinsonism:**
 1. Neuroleptic drugs – Phenothiazines, butyrophenones, metoclopramide, reserpine, lithium, MAO inhibitors, and tetrabenzine, may cause "reversible parkinsonian" syndrome.
 2. Toxic substances – Toxins such as manganese dust or carbon disulfide may lead to parkinsonism, and such a disorder may also appear as sequelae of carbon monoxide poisoning.
 3. 1-methyl-4-phenyl-1, 2, 5, 6-tetrahydropyridine (MPTP) – A drug-induced form of parkinsonism has been described in individuals who self-administered a meperidine analogue, MPTP. This compound selectively destroys dopaminergic neurons in the substantia nigra and induces a severe form of parkinsonism in humans and in subhuman primates. The ability of this drug to reproduce neurochemical, pathologic, and clinical features of PD suggests that an environmental toxin may be responsible for the idiopathic disorder. MPTP-induced parkinsonism has provided a model which could assist in development of new drugs for treatment of this disease.
- D. **Parkinsonism Plus Disorders:** Parkinsonism that occurs in association with symptoms and signs of other neurologic disorders like *Progressive Supranuclear Palsy (PSP)*, *Frontotemporal Dementia (FTD)*, *Alzheimer's Disease (AD)* and disorders with *Tauopathies* and *Amyloidopathies*. Among the Chamorro people of Guam, PD, cognitive dysfunction and features of Amyotrophic Lateral Sclerosis (ALS) often coexist. In genetically mediated neurologic disease like Wilson's disease, *Huntington's disease* and Hallaverdon spartz disease, features of PD are often present. This list is incomplete.
- E. **Familial Parkinson's Disease:** It is a *genetically heterogeneous disease* where three molecules critical for development are (i) *Alpha synuclein*, (ii) *Parkin*, and (iii) *Ubiquitin*. Abnormal high levels of alpha synuclein in Dopamine rich nerve cells play a central role whereas Parkin and Ubiquitin are involved in natural destruction of synuclein. If alpha synuclein is not eliminated it accumulates in *Lewy Bodies* as structural component of Lewy Body fibrils. The Parkin Type II Juvenile PD is characterized by triad of (a) lower limb dystonia, (b) onset at young age with abnormal neuropsychiatric behavior and (c) Dyskinesias with levodopa therapy. Molecular testing is now available to detect various mutations in Parkin molecule and may help in genetic counseling and elucidate inheritance pattern.

Pathology

In idiopathic parkinsonism, pathologic examination shows loss of pigmentation and cells in the substantia nigra and other brain stem centres, cell loss in the globus pallidus and putamen, and the presence of *eosinophilic intraneural inclusion granules (Lewy bodies)* in the basal ganglia. A *severe loss of neuromelanin containing neurons in the pars compacta of substantia nigra and locus coeruleus with Lewy bodies* are considered minimum confirmatory postmortem criteria. These inclusion bodies are not seen in postencephalitic parkinsonism, but instead there may be nonspecific *neurofibrillary degeneration in a number of diencephalic structures* as well as changes in the substantia nigra.

Pathogenesis

Both dopamine and acetylcholine are present in the corpus striatum, where they function as neurotransmitters. In idiopathic parkinsonism, it is generally believed that the normal balance between these two antagonistic neurotransmitters is disturbed because of *dopamine depletion in the dopaminergic nigrostriatal system*. Other neurotransmitters, such as norepinephrine, are also depleted in the brains of patients with parkinsonism, but the clinical relevance of this deficiency is less clear (Figs 1A to C). In Parkinson plus syndrome (e.g. PSP) mutation in *Tau gene* is often considered responsible; however, it is not simply the genetic trigger which can explain as to how members of the same family with the same mutations develop different clinicopathologic syndromes. Identification of biological markers for specific entities needs to be developed. Such information may elucidate pathogenesis and pathophysiology of syndromes like PSP (progressive supranuclear palsy).

Clinical Findings

- A. **Tremors:** The tremors in parkinsonism, *4- to-6 Hz in frequency are characteristically conspicuous at rest*, and increased at times of emotional stress, but *often improve during voluntary activity*. It commonly begins in the hand or foot, where it takes the form of rhythmic flexion-extension of the fingers (pill-rolling type) or of the hand or foot-or rhythmic pronation-supination of the forearm. It frequently involves the face around the mouth but spares the head. Although it may ultimately be present in all of the limbs, it is not uncommon for the tremor to be confined to one limb- or to the 2 limbs on one side- for months or years before it becomes more generalized.
- B. **Rigidity:** Rigidity or increased tone, i.e. increased resistance to passive movement - is a characteristic clinical feature of parkinsonism. The resistance is typically uniform throughout the range of movement at a particular joint and affects both agonist and antagonist muscles alike - in contrast to the findings in spasticity, where the increase in tone is often greatest at the beginning of the passive movement (clasp-knife phenomenon) and more marked in some muscles than in others. In some instances, perhaps due in part to the presence of tremor, *the rigidity in parkinsonism is described as cogwheel rigidity because of ratchet-like interruptions of passive movement*. The disturbance in tone is responsible for the flexed posture of many patients with parkinsonism. Muscle rigidity is often complained as painful stiffness.
- C. **Hypokinesia:** The *most disabling feature of this disorder is insidious onset of slowness of movements (hypokinesia sometimes called bradykinesia)* associated with reduction in amplitude in individual movements, e.g. such as loss of swinging of the arms while walking. Fine or rapidly alternating movements are impaired, but power is preserved. Often patients are unable to carry out two tasks at a time. The patient has relatively immobile, masklike facies with widened palpebral fissures, infrequent blinking, monotonous speech, certain fixity of facial expression, and a smile that develops and fades slowly (hang-dog appearance). *The voice is of low volume (hypophonia) and tends to be poorly modulated. The handwritings are small, tremulous, and hard to read (micrographia)*. Above symptoms are often attributed to

“getting old” or “being tired”. Lack of energy, drive and initiative, are often misdiagnosed as apathy or amotivation or even depression. *Depression is not uncommon* and it is a reaction to disabling illness and an integral feature of PD. It is often attributed to disturbances in noradrenergic, cholinergic, serotonergic and peptidergic systems. *Mood disturbances may result from impairment of mesocortical and mesolimbic pathways.* Even low levels of serotonin may be found. Thus depression requires analysis and treatment.

- D. **Abnormal Gait and Posture:** The patient generally finds it difficult to get up from bed or an easy chair, and on standing tends to adopt a flexed posture. It is often difficult to start walking, so that the patient may lean farther and farther forward while walking in place before he is able to advance (**cadence**). *The gait itself is characterized by small, shuffling steps and loss of arm swing* that normally accompanies locomotion, there is generally some unsteadiness on turning, and there may be *difficulty in stopping suddenly (propulsion or retropropulsion)*. In advanced cases the patient tends to walk with increasing speed to prevent a fall (**festinating gait**) because of the altered center of gravity that results from the abnormal posture.
- E. **Other Clinical Feature:** There is often mild **blepharoclonus** (fluttering of the closed eyelids) and occasionally **blepharospasm** (involuntary closure of the eyelids). The patient may drool, perhaps because of impairment of swallowing. There is typically no alteration in the tendon reflexes, and the plantar responses are flexor. Repetitive tapping (about twice per second) over the bridge of the nose produces a *sustained blink response (Myerson’s sign)*, whereas in normal subjects the response is not sustained. **Cognitive dysfunction:** In Parkinson’s disease disruption of motor functions, facial expression, body language and communication can all interfere with perception of patient’s emotional life. Patient may appear disinterested including abulia, and psychomotor retardation. *Cognitive disturbances in PD* may manifest in cognitive defects to overt dementia. Difficulty in logical analysis and abstract reasoning is frequent. *Despite impaired verbal fluency, apraxia, agnosia and aphasia are not present.*

DIAGNOSIS OF PD

1. **Clinical Diagnosis:** *Slowness and difficulty of movement are early symptoms* and evident when patient is asked to get out of a chair. *Pill rolling type tremor* may be present when the limb is relaxed but may be unilateral. These symptoms respond to levodopa therapy. Factors which do not favor PD are (i) symmetry of motor signs, (ii) lack of tremors, (iii) poor response to levodopa, (iv) early falls, (v) dysautonomia, and (vi) rapid progression within one year.
2. **Levodopa challenge testing:** When diagnosis of PD is in doubt, levodopa and apomorphine challenge are considered justifiable tests. *Therapeutic challenge with levodopa drugs and a reliable response* and relief of clinical symptoms (improvement of motor score) is present in 70% of patients. In 30% there may be false positive or false negative response.
3. **Radiological Evaluation:** Imaging studies like CT or MRI are useful to exclude (i) multi-infarct state, (ii) normal pressure hydrocephalous, (iii) lesions of Wilson’s disease or basal ganglia pathologies. *Positron Emission Tomography (PET) and Single Photon Emission CT (SPECT) or 18F Dopamine uptake studies often show depletion in uptake in striatal dopamine neurons.*
4. **Neuropathologic Diagnosis:** The major findings are *loss of pigmented dopaminergic neurons in substantia nigra and the presence of Lewy bodies.* However, there are no standard criteria for neuropathologic diagnosis. Lewy Body stain for alpha synuclein or Ubiquitin are not very specific.

Differential Diagnosis

The diagnosis may be difficult to make in mild cases.

Depression may be accompanied by a somewhat expressionless face, poorly modulated voice, and reduction in voluntary activity and can thus simulate parkinsonism. Moreover, the two diseases may coexist in the same patient. A trial of antidepressant drug treatment may be helpful if the diagnostic uncertainty cannot be resolved by the presence of more widespread neurologic signs indicative of parkinsonism.

Essential (benign familial) tremor: An early age at onset, *family history of tremor*, beneficial effect of alcohol on the tremor, and *lack of other neurologic signs* distinguish this disorder from parkinsonism. Furthermore, *essential tremor commonly affects the head (causing a nod or head shake)*, whereas parkinsonism often affects the face and lips rather than the head.

Wilson's disease can also simulate parkinsonian syndrome, but other varieties of abnormal movements are usually present as well. Moreover, the early age at onset and the *presence of Kayser-Fleischer rings* should distinguish Wilson's disease from Parkinson's disease, as should the abnormalities in serum and urinary copper and serum ceruloplasmin that occur in Wilson's disease.

Normal-pressure hydrocephalus leads to a gait disturbance (often mistakenly attributed to parkinsonism), urinary incontinence, and dementia, and *CT scanning reveals dilatation of the ventricular system of the brain without cortical atrophy*. The disorder may follow head injury, intracranial hemorrhage, or meningoencephalitis, but the cause is often obscure. Surgical shunting procedures to bypass any obstruction to the flow of cerebrospinal fluid (CSF) are often beneficial.

Progressive supranuclear palsy is a disorder in which there may be bradykinesia and rigidity, but its *characteristic features are loss of voluntary control of eye movements (especially vertical gaze), dementia, pseudobulbar palsy, dysarthria*, and axial dystonia. The disorder responds poorly, if at all, to antiparkinsonism drugs.

Huntington's disease may occasionally be mistaken for parkinsonism when it presents with rigidity and akinesia, but the *family history and accompanying dementia* should suggest the correct diagnosis.

Shy-Drager syndrome is a degenerative disorder, characterized by parkinsonian *features, autonomic insufficiency (leading to postural hypotension, anhidrosis, disturbance of sphincter control, impotence, etc.)*, and signs of more widespread neurologic involvement (pyramidal or lower motor neuron signs and often a cerebellar deficit). There is no treatment for the motor deficit, but the postural hypotension may respond to a liberal salt diet, fludrocortisone, 0.1-1 mg/d; indomethacin, 25-50 mg 3 times daily; wearing waist high elastic stockings; and sleeping in the head-up position at night.

Creutzfeldt-Jakob disease may be accompanied by parkinsonian-features, but *dementia is usually present, myoclonic jerking is common*, and ataxia is sometimes prominent; there may be pyramidal signs and visual disturbances, and the electroencephalographic findings of periodic discharges are usually characteristic.

Treatment

The *aims of therapy* are (i) *to relieve symptoms of PD*, (ii) *to achieve functional independence* with minimum side effects. Early parkinsonism requires no drug treatment, but it is important to discuss with the patient the nature of the disorder and the availability of medical treatment if symptoms become more severe. This can be achieved by: (a) dopamine precursors, (b) increasing pre-synaptic release of dopamine, (c) increasing dopaminergic receptor activity, (d) inhibiting dopamine metabolism and (e) correcting striatal neurotransmitter imbalance. *At present, five*

groups of drugs are available: (i) anticholinergics, (ii) amantadine, (iii) levodopa, (iv) dopamine agonists, (v) neuroprotectors (selegiline).

- A. **Anticholinergic drugs:** Muscarinic anticholinergic drugs are *more helpful in alleviating tremor and rigidity rather than hypokinesia* but are generally less effective than dopaminergic drugs. A number of different preparations are available, and different patients tend to favor different drugs. Among the most commonly prescribed drugs are trihexyphenidyl (Artane: 6-20 mg), benztropine (Cogentin: 1-6 mg), procyclidine (Kemadrin: 7.5-30 mg), and orphenadrine (Disipal: 150-400 mg), ethopropazine (Parsidol: 150-300 mg), biperiden (Akineton: 2-12 mg). Common side effects include dryness of the mouth, constipation, urinary retention, and defective papillary accommodation, which result from muscarinic receptor blockade in parasympathetic end organs; and confusion (especially in the elderly) due to antimuscarinic effects in the brain. Treatment is started with a small dose of one of the anticholinergics; the dosage is then gradually increased until benefit occurs or side effects limit further increments. If treatment is not helpful, the drug is withdrawn and another anticholinergic preparation is tried.
- B. **Amantadine:** Amantadine can be given for mild parkinsonism either alone or in combination with an anticholinergic agent. Its precise mode of action is unclear, but it may potentiate the release of dopamine from pre-synaptic neurons and possibly inhibits dopamine reuptake. *Its advantages are that it improves nearly all (akinesia, tremor and rigidity) clinical features of Parkinsonism in about two-thirds of patients.* Its side effects (restlessness, confusion, skin rashes, edema, and disturbances of cardiac rhythm) are not uncommon. It has rapid action and given in a standard dose of 100 mg orally twice daily, but many patients fail to respond to this drug, or *its benefit is short-lived*. Motor fluctuations and dyskinesias are often seen in later stages.
- C. **Levodopa:** Levodopa, which is converted in the body to dopamine, ameliorates clinical features of parkinsonism (akinesia, rigidity and to a lesser extent tremors). *There is controversy about the best time to introduce dopaminergic therapy.* Some feel that in many patients levodopa loses its efficacy with time and accordingly the drug should be reserved for patients with definite disability. However, *the weight of present evidence suggests that any decline in therapeutic response relates to disease duration and progression rather than to duration of treatment*, and argues for early treatment with dopaminergic drugs which may be most effective before the disease is far advanced.

Common side effects of levodopa therapy are: nausea, vomiting, orthostatic hypotension, abnormal movements (off-period dystonia or choreathetosis from peak-dose dyskinesia), restlessness, confusion or hallucinations and occasionally cardiac arrhythmias. Late side effect of levodopa therapy are: (a) wearing off or shorter duration of response resulting in *morning akinesia or end of dose akinesia*, (b) unpredictable fluctuations in the severity of parkinsonism occurs at frequent intervals during the day ("*on-off*" phenomenon), apparently without any relationship to the last dose of levodopa, (c) *freezing phenomenon*", and (d) "delayed on" response or short duration response. This problem is sometimes very disabling, and it is unaffected by concomitant administration of carbidopa; it can be controlled partly by varying the dosage-intervals, administering levodopa one hour before meals, restricting dietary protein intake, or treatment with dopamine agonist (bromocriptine). Other treatment options for *peak-dose dyskinesia* are: (i) lower dose of levodopa, (ii) altering the dose of dopamine agonist, and (iii) add or omit amantadine therapy.

Carbidopa is a drug that inhibits dopa decarboxylase (the enzyme *responsible for the breakdown of levodopa to its active metabolite: dopamine*) but *does not cross the blood brain barrier*. If levodopa is given in combination with carbidopa, the breakdown of levodopa is largely prevented outside the central nervous system, and thereby the incidence of side effects like nausea, vomiting, hypotension and cardiac irregularities are reduced. Levodopa (**Sinemet**) is generally given combined with carbidopa in a fixed proportion (1:10 or 1:4).

Treatment is started with small dose such as Sinemet-10/100 mg or Sinemet-25/100 mg orally 3 times daily, and gradually increased depending on the response. Most patients ultimately require Sinemet-25/250 mg 3 or 4 times daily.

- D. **Dopamine agonists (DA):** Bromocriptine, an ergot derivative, is DA that directly stimulates dopamine receptors. It is perhaps slightly less effective than levodopa in relieving the symptoms of parkinsonism but is *less likely to cause dyskinesias or the on-off phenomenon*. In consequence, it has been recommended that when dopaminergic therapy is to be introduced, the patient be started on Sinemet-25/100 3 times daily and bromocriptine is then added. The starting dose is 1.25 mg/d for 1 week and 2.5 mg/d for the next week, after which the daily dose is gradually, increased by 2.5 mg increments every 2 weeks depending on the response and the development of side-effects. Maintenance doses are usually between 2.5 and 10 mg orally 3 times daily. Side-effects are similar to those associated with levodopa therapy, but *psychiatric effects such as delusions or hallucinations are especially common, and bromocriptine is therefore contraindicated in patients with a history of psychotic disorders*. Relative contraindications to its use are recent myocardial infarction, severe peripheral vascular disease and active peptic ulceration. The other issues include (i) dyskinesias, (ii) motor fluctuations, (iii) postural hypotension, and (iv) sleep attacks. Other DA's (Pergolide, Cabergoline, Lisuride, Ropenirole, Apomorphine, Piribedil) are not much in vogue. However, Pramipexole has rapid action with tremorolytic effect (0.125 mg thrice daily) and is frequently prescribed with levodopa.
- E. **Deprenyl:** Deprenyl or Selegine inhibits monoamine oxidase type B and thereby reduces the metabolic breakdown of dopamine. It thus *enhances the antiparkinsonism effect of levodopa and may reduce mild "on-off" fluctuations or freezing of gait*. Recent studies of MPTP-induced parkinsonism in animals suggest that deprenyl may also reduce disease progression, and clinical studies are currently being conducted to determine whether the natural progression of PD in humans is altered by deprenyl. Side-effects like insomnia, confusion, sympathetic over-activity are not uncommon. It is advisable to avoid evening dose.
- F. **Neupro Patch:** It is a silicone based patch that slowly releases dopamine agonist like Rotigotine transdermally. It is replaced once in 24 hours. Side effects like skin rash, nausea, dizziness, insomnia or drowsiness may interfere with occupation or activities of daily life.
- G. **COMT inhibitors:** Catechol-o-methyl transferase inhibitors are currently in preclinical trials. Its use is limited to experimental studies. It may be useful in patients with frequent on-off phenomenon.
- H. **Stem Cell Therapy** for Parkinson's disease (PD). The *aim of embryonic stem cell therapy as a novel strategy is to reconstruct nigrostriatal neuronal pathways, using endogenous neural stem cells or precursor cells or grafting dopaminergic neurons*. Alternatively, stem cell derived dopaminergic neurons have been transplanted into the striatum hoping to establish local synapses or release of dopamine from grafted cells. It is believed that embryonic stem cells are pluripotent, proliferate and differentiate as potential donor source of dopamine or dopaminergic neurons. It should be noted that graft survival is highly variable and may not be equally effective in releasing dopamine. Furthermore, inflammatory immune responses may compromise graft survival and function. However, limited tissue availability and for ethical reasons this form of therapy is in experimental stage. The future rests upon the hope that effective neuro-restorative or neuro-regenerative therapies based on gene and stem cell therapy may help subjects with Parkinson's disease, and other progressive neuro-degenerative disorders like Alzheimer's disease. The development of recombinant *adenoviral (AAV) vector* is making **gene therapy** for PD as a feasible therapeutic option, in experimental models.^{1,2}
- I. **Surgery:** Surgical treatment of parkinsonism by thalamotomy is rarely required, since pharmacologic treatment is usually effective. *Nevertheless, surgery is sometimes helpful in*

relatively young patients with predominantly unilateral tremor and rigidity that have failed to respond to medication. Diffuse vascular disease is a contraindication to this approach.

- J. **Physical Therapy and Aids for Daily Living:** Physical therapy and speech therapy are beneficial to many patients with parkinsonism, and the quality of life can often be improved by providing simple aids to daily living. Such aids may include extra rails or banisters placed strategically about the home for additional support, table cutlery with large handles, nonslip rubber table mats, devices to amplify the voice, and chairs that will gently eject the occupant at the push of a button.

SUMMARY

The clinical syndrome of parkinsonism characterized by tremor, rigidity, akinesia and abnormal posture, as described by James Parkinson in 1817, is not difficult to identify, and particularly if it is associated with shuffling gait, micrographia and hypophonia. However, in early stages it may resemble depressive illness or generalized asthenia (weakness). In such situation it may become necessary to carry out a therapeutic trial with anti-depressant drugs. Failure to improve upon the symptoms of "depression" in few weeks may require therapeutic challenge with levodopa therapy. In later stages, symptoms and signs of confusional state or early dementia may pose a diagnostic problem and will demand neuro-imaging studies to ascertain diagnosis and rule out conditions

like "normal pressure hydrocephalus" or Alzheimer's disease. In early cases physiotherapy and rehabilitation exercise are essential before drug therapy is started. Failure to respond to levodopa therapy often points to differential diagnosis like Parkinson plus syndromes as described in the text. By and large, medical therapy if properly administered controls the symptoms of Parkinson's Disease (PD) and patient is able to lead normal activities.³ The role of surgery is limited to young patients with unilateral syndrome. Transplantation of tissues containing dopaminergic neurons has not been successful. Stem cell therapy holds promise.^{1,2}

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MULTIPLE CHOICE QUESTIONS

1. The "Parkinsonism" is characterized by, except two of the following:
 - A. Tremors
 - B. Seizures
 - C. Rigidity
 - D. Headache
 - E. Abnormal posture
2. Parkinson plus syndrome occurs in association with, except one of the following:
 - A. Progressive supranuclear palsy
 - B. Alzheimer's disease
 - C. Epilepsies
 - D. Frontotemporal dementia
3. Principal neurochemical abnormality in Parkinsonism is:
 - A. Acetylcholine deficiency
 - B. Dopamine depletion
 - C. GABA deficiency
 - D. MPTP deficiency
4. The frequency of parkinson tremor at rest is:
 - A. 8-12 Hz per sec
 - B. 4-6 Hz per sec
 - C. 4-12 Hz per sec
 - D. 6-8 Hz per sec
5. Rigidity in parkinsonism is often described as:
 - A. Clasp-knife rigidity
 - B. Cog-wheel rigidity
 - C. Nonspecific spasticity
6. Low volume/low pitch voice in parkinsonism is called:
 - A. Micrographia
 - B. Hypophonia
 - C. Cadence
 - D. Blepharospasm
7. Specific treatment of idiopathic parkinsonism is one of the following:
 - A. Muscle relaxants
 - B. Mood elevators
 - C. Levodopa
 - D. Multivitamin drugs

1. B, D 2. C 3. B 4. B 5. B 6. B 7. C