Parkinson disease
&
Movement disorders

by Dr. Taim Muayqil

Done by: Malak Alkahtani

Revised by: Sarah Almubrik & Mohanad Alsuhaim

Objectives:

- **Not given**

References:
Slides - Black
Kumar - Black
Doctor's notes - Red
Step up / davidson - Blue
Extra explanation - Grey
Kaplan - purple

Optional:

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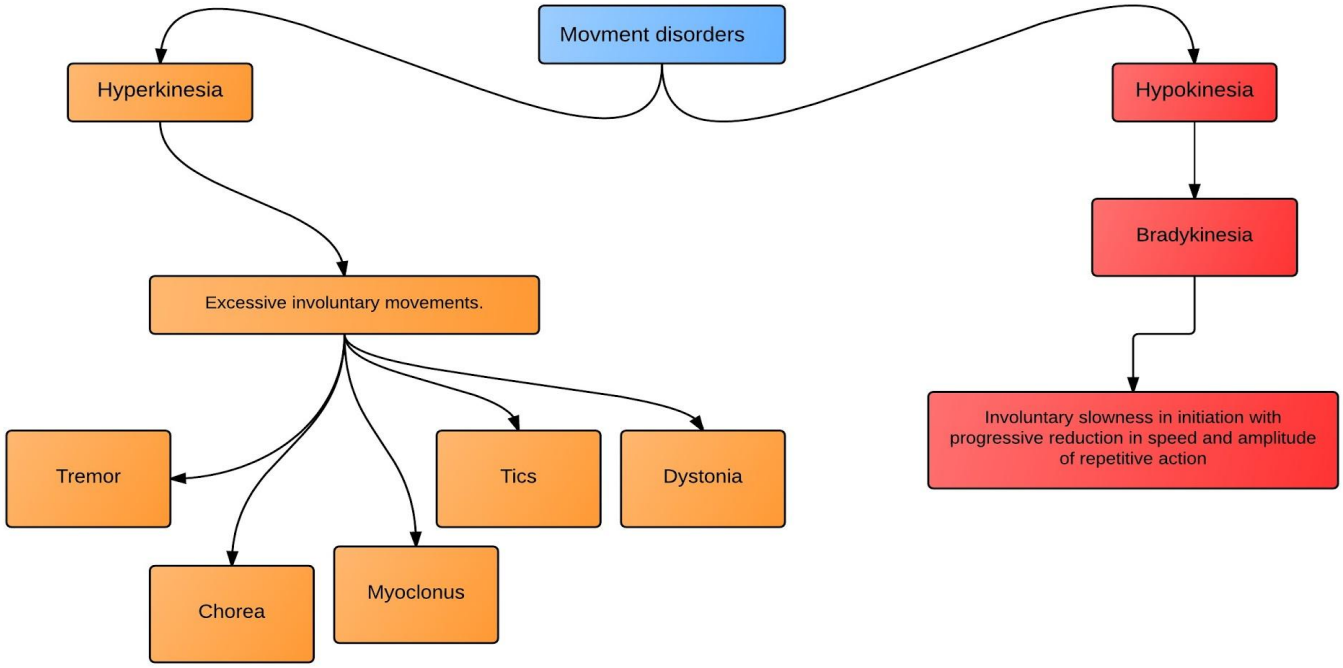
Editing file

MOVEMENT DISORDERS:

Disorders of movement divide broadly into two categories:



Both types may co-exist, for example in Parkinson's disease with both slowed movements and tremor.

Any movement disorder —> Always ask about drugs

Hyperkinetic movement disorders:

There are five hyperkinetic movement disorders (may occur in combination):

1. Tremor – Involuntary rhythmic sinusoidal oscillation ذبذبة movement around a joint axis.
2. Chorea – Involuntary excessive, irregular movements flitting from one body part to another ('dance-like') with no pattern. Resulting from a continuous flow of random muscle contractions.
3. Myoclonus – Involuntary brief single quick muscle contraction (or its inhibition) can be repeated but not rhythmic.
4. Tics – Stereotyped movements or vocalizations (may be temporarily suppressed)
5. Dystonia – Sustained or intermittent muscle contractions causing abnormal repetitive twisting movements and/or abnormal postures.(complex muscle movement)

1-Tremor:

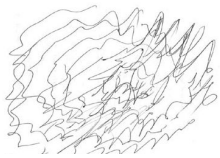
A. Physiological tremor:

1. Causes
    a. Fear, anxiety, fatigue
    b. Metabolic causes: hypoglycemia, hyperthyroidism, pheochromocytoma
    c. Toxic causes (e.g., alcohol withdrawal, methylxanthines—caffeine and theophylline)
2. Treatment: Treat the underlying cause, if known; otherwise, no treatment is necessary

DDX of ET: cervical dystonia

B-Essential tremor:

- A common often inherited autosomal dominant trait, causes a clear Action tremor, bilateral but one side is more prominent, fast >6Hz , low amplitude tremor, mainly in the upper limbs. The head and voice are occasionally involved.
- Tremor is postural (such as when holding a glass).
- Distorted handwriting is often present.



- bradykinesia, rigidity, shuffling gait, or postural instability **are all absent.**
- Patient with essential tremor have a long standing history of tremor, occurs at any age but usually starts in early life, slowly progressive and varies in severity.
- Anxiety, exercise, caffeine, and Beta agonist exacerbates the tremor, While Alcohol reliefs the tremor.
- Treatment is often unnecessary. Small amounts of alcohol, beta-blockers (propranolol).

C. Neurologic diseases (e.g., Parkinson disease, cerebellar disease, Wilson disease)

What are the types of tremors:

Type	Description
Resting tremor	occurs when the patient is not moving (resting) and typically decreases with voluntary activity.
Intention tremor	which typically has cerebellar origins, appears as the patient moves a limb toward a target, and is often irregular in amplitude and trajectory.
Postural tremor	the most common cause of which is essential tremor, appears as the patient actively holds the limbs in a position against gravity.

Sympathomimetics (e.g. salbutamol) make all tremors worse.

SUMMARY	Parkinsonian	Cerebellar	Essential
Characteristic	Rest	With action—"intention tremor"	With certain postures
Description	Pill-rolling	Coarse	Fine
Associated Features	Rigidity, bradykinesia, shuffling gait	Ataxia, nystagmus, dysarthria	Head tremor, vocal tremulousness
Improved By	Action	Rest (no tremor at rest)	Alcohol

2- Chorea

Causes include:

1. Systemic disease – thyrotoxicosis, SLE, antiphospholipid syndrome, primary polycythaemia
2. Genetic disorders – Huntington's disease, neuroacanthocytosis, benign hereditary chorea
3. Structural and vascular disorders affecting the basal ganglia (unilateral + sudden —> think stroke)
4. Drugs (e.g. levodopa and OC pill)
5. Post-infectious (Sydenham's chorea), months after strep infection or acute rheumatic fever

Treatment is of the underlying cause, but dopamine blocking drugs such as phenothiazines (e.g. sulpiride) and dopamine depleting drugs (tetrabenazine) reduce chorea.

Child with chorea —> Always ask about Drugs + Rheumatic fever

Huntington's disease (HD):

A autosomal dominant disease It's caused by a mutation on chromosome 4 (expanded triplet repeat sequence) — CAG leads to a loss of GABA-producing neurons in the striatum. Presenting in middle life (between 30 - 50), initially with subtle 'fidgetiness' (state of nervousness marked by sudden jerky movements) followed by development of progressive psychiatric (depression) and cognitive symptoms.

What neurotransmitter is reduced in the basal ganglia in Huntington's disease and how does this relate to the hyperkinetic motor abnormalities seen in Huntington's disease?

GABA, the major inhibitory neurotransmitter of the CNS, is reduced. In Huntington's disease, loss of inhibitory signals within the basal ganglia results in disinhibition of the motor thalamus, explaining the hyperkinetic motor abnormalities.

Note that the deficiency of GABA within the basal ganglia has the opposite effect (i.e., hyperkinesia) from that seen with the deficiency of dopamine associated with Parkinson's disease (i.e., hypokinesia).

- Clinical features:
1. Chorea
2. Altered behavior— irritability, personality changes, antisocial, depression, obsessive-compulsive features, and/or psychosis.
3. Impaired mentation — progressive dementia is a key feature; 90% of patients are demented before age of 50.
4. Gait — unsteady and irregular, ultimately bradykinesia and rigidity dominate.
5. Incontinence.

- Diagnosis: 1. MRI shows atrophy of the head of caudate nuclei.
2. DNA testing confirms the diagnosis.

- Treatment: No curative treatment. Although chorea can improve with treatment, but progressive neurodegeneration leads to dementia and ultimately death after 10–20 years

Hemiballismus:

A violent swinging movements of one side caused by infarction/haemorrhage in the contralateral subthalamic nucleus. Acute chorea-hemiballismus also occurs after diabetic non-ketotic hyperglycaemia, with signal change seen in the basal ganglia on CT or MRI, thought to be due to osmotic shifts causing myelinolysis.

severe chorea = ballism

3- Myoclonus

Cortical myoclonus is usually distal (hands and fingers especially) and stimulus sensitive (spontaneous but also triggered by touch or loud noises) and caused by a wide variety of pathologies affecting the cerebral cortex; spinal and brainstem myoclonus are caused by localized lesions affecting these structures.

Primary myoclonus

- Physiological myoclonus: Nocturnal myoclonus consisting of sudden jerks (often with a feeling of falling) on dropping off to sleep or waking – most common and not pathological. The startle response is also a form of brainstem myoclonus.
- Myoclonic dystonia (DYT11): Myoclonic 'lightning jerks' often with dystonia.

Myoclonus in epilepsy

Progressive myoclonic epilepsy-ataxia syndromes

Rare genetic & metabolic disorders where myoclonus accompanies progressive epilepsy, cognitive decline and/or ataxia.
Lafora body disease, neuronal ceroid lipofuscinosis and Unverricht–Lundborg disease

Secondary myoclonus

Myoclonus may be seen in a wide variety of metabolic disorders including

- Asterixis (flapping tremor) due to hepatic and renal failure, (flapping tremor is a negative myoclonus — the movement occurs due to the loss of movement not muscle spasm)
- Dementias and neurodegenerative disorders (e.g. Alzheimer's disease)
- encephalitis.
- Post-anoxic myoclonus

4- Tics (Was not mentioned by the doctor)

Tics are common (15% lifetime prevalence), brief stereotyped movements usually affecting the face or neck but which may affect any body part including vocal tics. Unlike other movement disorders they may be transiently suppressed, leading to a build-up of anxiety and overflow after release.
Simple transient tics (e.g. blinking, sniffing or facial grimacing) are common in childhood, but may persist. Adult onset tics are rare and usually secondary.

• Motor tics (e.g., facial grimace, blinking, head jerking, shoulder shrugging)
• Phonic tics (e.g., grunting, sniffing, clearing throat, coprolalia, repetition of words)
• Conditions that must be ruled out include seizures, tardive dyskinesias, and Huntington disease.

Tourette's syndrome

Commonest cause of tics, starting in childhood. Boys are more affected (3:1). Behavioural problems including ADHD and OCD are common. There is sometimes explosive involuntary swearing (coprolalia) and gestures (copropraxia) or echolalia (copying what other people say). Cause is not known but it may be due to problem with histaminergic neurotransmission.

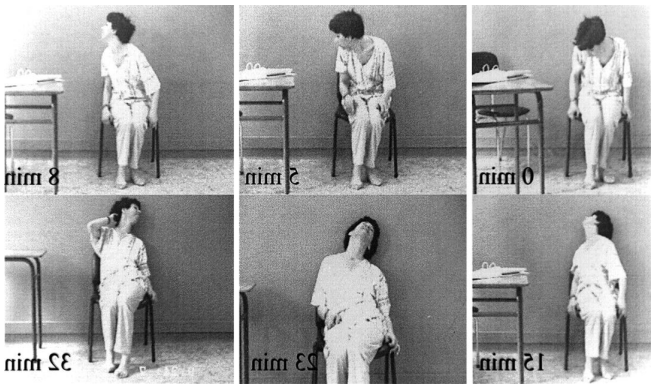
- Clinical features (occur frequently and regularly). Must have both motor and phonic tics. starts in childhood and persisting longer than a year (before age 21)
    1. Motor tics (multiple)
    2. Phonic tics (at least one kind)

- Treatment (Clonidine - Pimozide - Haloperidol)

5- Dystonias:

Dystonia is most usefully classified by etiology, into:

- Primary dystonias – where dystonia is the only/main clinical manifestation (usually genetic)
- Secondary dystonia – due to brain injury, cerebral palsy or drugs.
- Heredo-degenerative dystonia – as part of a wider neurodegenerative disorder
- Paroxysmal dystonias – rare genetic, attacks of sudden involuntary movements with elements of dystonia and chorea.



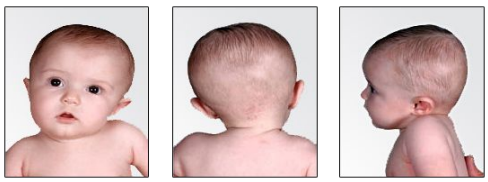
Primary dystonias

-Young onset: Mutations in DYT1 gene, seen in the Ashkenazi Jewish population, cause limb-onset dystonia (usually foot) before age of 28.

-Adult onset: The commonest type of primary dystonia. Onset is usually around 55 and dystonia is usually focal (particularly affecting the head & neck unlike DYT1 dystonia). **Various patterns are recognized:**

Torticollis

Dystonic spasms gradually develops in neck muscles causing the head to turn (torticollis) or to be drawn backwards (retrocollis).



Writer's cramp and task-specific dystonias

A specific inability to perform a previously highly developed repetitive skilled movement, e.g. writing. The movement provokes dystonic posturing. Other functions of the hand remain normal. Overuse may lead to task-specific dystonias in certain occupations, e.g. musicians, typists and golfers.

Blepharospasm and oromandibular dystonia

-Spasms of forced blinking

-involuntary movement of the mouth and tongue (e.g. lip-smacking and protrusion of the tongue and jaw).

Dopa-responsive dystonia (DRD)

Neuroleptics and movement disorders

Neuroleptics (antipsychotic drugs used to treat schizophrenia) and antiemetics (e.g. metoclopramide) can cause a variety of movement disorders.

-Akathisia: This is a restless, repetitive and irresistible need to move

-Parkinsonism: Due to D1 and D2 dopamine receptor blockade

-Acute dystonic reactions: Spasmodic torticollis, trismus and oculogyric crises (episodes of sustained upward gaze) develops dramatically and unpredictably after single doses.

-Tardive dyskinesia: mouthing and lip-smacking grimaces occur after several years of neuroleptic use.

Treatment

-Injection of botulinum toxin into affected muscles is the treatment for all focal dystonias

-Antimuscarinics (e.g. trihexyphenidyl).

Parkinsonian disorders:

1-Idiopathic Parkinson's disease

Defined as a neurologic syndrome resulting from the deficiency of the neurotransmitter dopamine located in the pigmented substantia nigra and locus ceruleus in the midbrain. As a consequence of degenerative, vascular, or inflammatory changes in the basal ganglia. Onset is usually after age 50 years.

PD is the imbalance of dopaminergic (too little) and cholinergic (too much - unopposed) tone on the basal ganglia.

Parkinson's disease is clinically and pathologically distinct from other parkinsonian syndromes.

There are multiple risk factors that might be linked to parkinson disease:

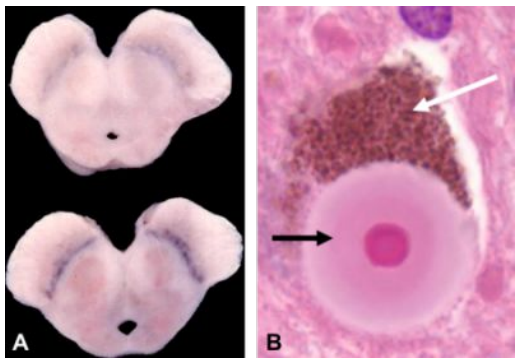
1- Age & gender: Prevalence increases sharply with age (particularly > 70 years), higher in men (1.5:1 M:F)
2- Environmental factors:
- Pesticide exposure: The compound MPTP, a potent mitochondrial toxin, causes severe Parkinsonism.
- Smoking: Studies consistently show that *non-smokers* have a higher risk of PD

3- Genetic factors: -Idiopathic PD is not usually familial
-Several genetic loci for Mendelian inherited monogenic forms of PD have been identified designated PARK gene.

Pathology

The pathological hallmarks of PD are the presence of neuronal inclusions called Lewy bodies and loss of the dopaminergic neurones from the pars compacta of the substantia nigra in the midbrain that project to the striatum of the basal ganglia.

Lewy bodies contain tangles of α-synuclein and ubiquitin and become gradually more widespread as the condition progresses, spreading from the lower brainstem, to the midbrain and then into the cortex. Degeneration also occurs in other basal ganglia nuclei. The extent of nigrostriatal dopaminergic cell loss correlates with the degree of akinesia.



(A) Cross section of the midbrain showing the normal pigmented substantia nigra (bottom) and depigmented nigra in a brain with PD (upper).
(B) Microscopic section of a substantia nigra containing neuromelanin (white arrow) and a Lewy body (black arrow) within the cytoplasm of the neuron.

Diagnosis

- Diagnosis of parkinson is **clinical** by recognizing the classical physical signs and distinguishing idiopathic PD from other Parkinsonian syndromes. There is no laboratory test
- MRI imaging: is **normal.**
- Dopamine transporter (DaT) imaging: uses a radiolabelled ligand binding to dopaminergic terminals to assess the extent of nigrostriatal cell loss. It may be needed to distinguish PD from other causes of tremor, or drug-induced Parkinsonism, but it cannot discriminate between PD and other akinetic-rigid syndromes.

In the classical clinical picture of PD there is no need for a scan. Only in the unclassical picture (Eg: patient with rigidity + dystonia —> not a classical picture —> do a scan)

Symptoms and signs:

PD almost always presents with the typical motor symptoms

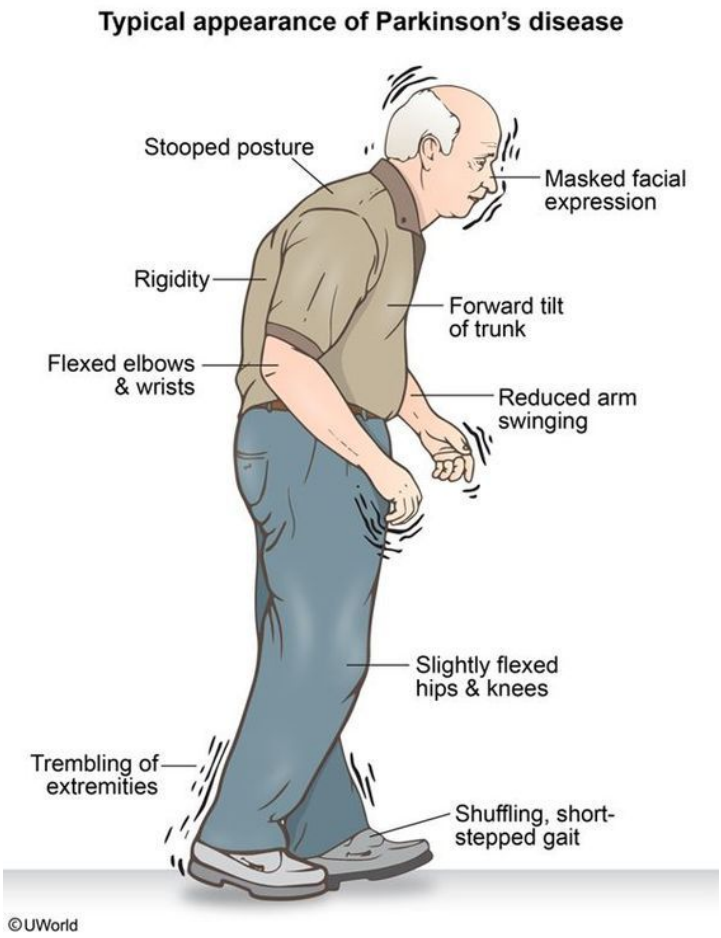
- **B**radykinesia (manifested by slow movements, mask facies, reduction of automatic movements)
- **R**igidity (cogwheel)
- **I**nstability (postural)
- **T**remor (resting)

It's likely that the pathological process starts many years before these symptoms develop. By the time of first presentation, on average 70% of dopaminergic nigrostriatal cells have already been lost.

- Prodromal premotor symptoms:
Patients also develop a variety of nonspecific non-motor symptoms during the approximately seven years, sometimes longer, before the motor symptoms become manifest. These include:

1. Anosmia (present in 90%) – the olfactory bulb is one of the first structures to be affected (usually start early before the disease develops)
2. Depression/anxiety (50%) – due to involvement of serotonergic and adrenergic systems.
3. Aches and pains
4. REM sleep behaviour disorder (REMBD) – act out their sleep
5. Autonomic features – urinary urgency, Constipation, orthostatic hypotension, erectile dysfunction,
6. Restless legs syndrome.
7. cognitive impairment – is common in late stage PD (80%) and may develop into dementia
8. Hallucinations – visual and more common at night

- Speech and swallowing: Dysarthria, Speech becomes quiet and flat. Drooling and Dysphagia is a late feature that may eventually lead to aspiration pneumonia as a terminal event.



- Motor symptoms:
These develop slowly and insidiously. The core motor features of PD are:

Idiopathic PD is almost always initially more prominent on one side.

1. Akinesia (bradykinesia):

- The cardinal clinical feature of Parkinsonism and the main cause of disability.
- There is difficulty initiating movement.
- The upper limb is usually affected first
- Almost always unilateral for the first years.
- Rapid skilled movements are impaired causing difficulty writing (**micrographia**), and doing up buttons/zips.
- Facial immobility gives a **mask-like semblance of depression**.
- Frequency of spontaneous blinking diminishes, producing a serpentine stare.
- Akinesia is tested clinically by asking the patient to perform rapid alternating movements such as opening and closing the hand repetitively, looking for progressive slowing and decrement in amplitude of repetitive movement.(distinguishes Parkinsonian disorders from other causes of slowness of movement)

2. Tremor:
Present In 70% of patients. Almost always starts in the fingers and hand, unilateral initially, spreading later to the leg on the same side and then the opposite arm.
The tremor is present at **rest** (reduces/stops completely when the hand is in motion but re-emergence with maintained posture). But might progress to action tremor.
The frequency is 3–6 Hz and it is often described as **pill-rolling** because the patient appears to be rolling something between thumb and forefinger. As with most tremors it is made worse by emotion, stress and mental concentration.
To assess resting tremors —> ask the patient to walk (you'll see the tremor because normally while walking you don't use your hands)

3. Rigidity:
Definition: Abnormally increase resistance to movement that is independent of the velocity of the movement.
Stiffness on **passive** limb movement is described as **'lead pipe'** as it is present throughout the range of movement.
When stiffness occurs with tremor (not always visible), a ratchet-like jerkiness is felt, described as **cogwheel rigidity.**

Difference between Rigidity and spasm —> R: independent velocity
S: velocity dependent

4. Postural and gait changes: stooped posture is characteristic.
Gait gradually becomes small shuffling and slow multi step turns.
Postural stability eventually deteriorates, leading to increased risk of falls.

Treatment:

Since Parkinson disease is the imbalance of dopaminergic (too little) and cholinergic (too much) tone on the basal ganglia.
The first step when considering medication is evaluating the patient's functional status.
patients with compromised functional status (more significant bradykinesia) —> the best initial therapy is carbidopa/levodopa.

Patients with intact functional status (less bradykinesia) —> Age <60 use anticholinergic medication
Age >60 use amantadine.

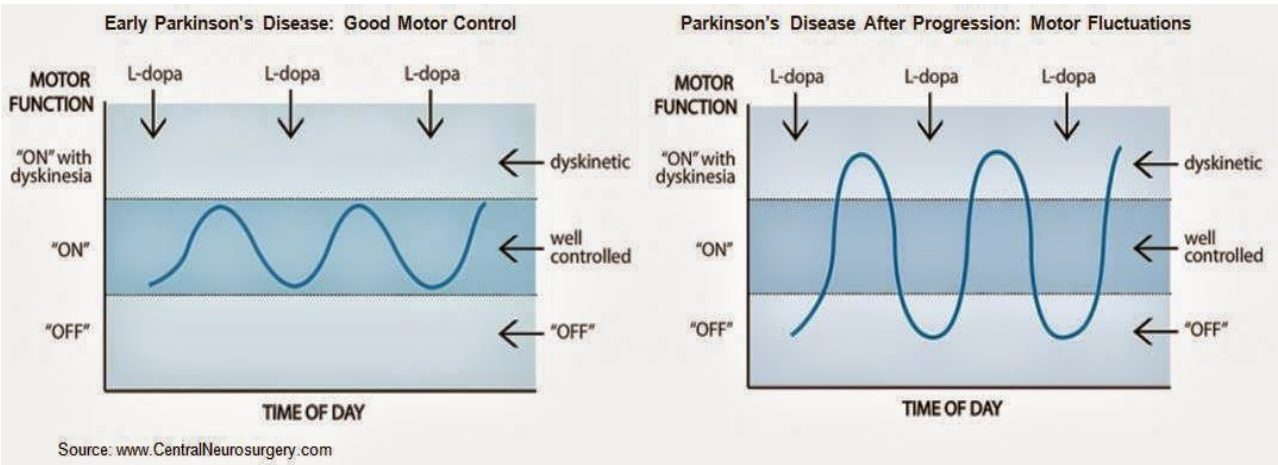
Treatment of non-motor symptoms such as depression, constipation, pain and sleep disorders is also necessary and significantly improves quality of life.

Levodopa/carbidopa
levodopa is a precursor to dopamine, can cross the blood-brain barrier and increases CNS dopamine levels once converted by dopa decarboxylase. Levodopa remains the most effective form of treatment. It is combined with a dopa decarboxylase inhibitor – benserazide (co-beneldopa) or carbidopa (co-careldopa). The response is often dramatic.

Why is levodopa typically administered along with carbidopa?
Carbidopa cannot cross the blood-brain barrier, so it inhibits the peripheral metabolism of L-dopa to dopamine. This both increases the delivery of L-dopa to the brain and minimizes the side effects of peripheral L-dopa/dopamine. These side effects include autonomic symptoms such as orthostatic hypotension, nausea/vomiting, confusion, hallucinations.

late complications to carbidopa/levodopa therapy:
• Dyskinesias (involuntary, often choreic movements) can occur after 5 to 7 years of therapy, which might lead to delay in initiating carbidopa-levodopa for as long as possible.

As the disease progresses, medical therapy for PD becomes more difficult as higher doses of dopamine replacement therapy are required and response becomes more unpredictable with the development of motor fluctuations and dyskinesias, takes longer to start working, but response to dopaminergic drugs is never lost.



Approximately 10% of patients per year develop motor complications in the form of 'wearing off' (the duration of effect of individual doses of LD becomes progressively shorter), dyskinesias and eventually, on/off phenomenon (sudden, unpredictable transitions from mobile to immobile). Eventually, patients may alternate between the on state with dopamine-induced dyskinesias and periods of complete immobility rigidity (off).

As patients gets older —> increase neuronal loss —> less response and effective therapy.

Dopamine agonists (DA)
May be used in combination with levodopa or as initial monotherapy in younger patients (below age 65–70) with mild to moderate impairment. Non-ergot DAs (Pramipexole and ropinirole or rotigotine) are used in preference to ergot-derived drugs, which may be associated with fibrotic reactions including cardiac valvular fibrosis. Domperidone is used as an antiemetic when initiating DA therapy (other antiemetics should not be used as they may worsen symptoms by blocking central dopamine receptors).

COMT inhibitors
Inhibits the action of catechol-O-methyl transferase (responsible of dopamine break down) hence to prolong duration of levodopa action

Other drugs used in PD
- Selegiline - rasagaline (monoamine oxidase B inhibitor) reduces catabolism of dopamine have a Mild symptomatic effect. Can be used in those with a declining or fluctuating response to levodopa.
- Amantadine (antiviral agent)
- Anticholinergics (e.g. trihexyphenidyl) may help tremor + in young (age <60) —> relatively contraindicated in elderly patients is because the side effects (dry mouth, urinary retention, constipation, confusion/hallucinations) occur more frequently and severely. Avoid with BPH and glaucoma.
-Apomorphine (subcutaneous DA)

Long-term response to treatment

Deep brain stimulation (DBS)
Stereotactic insertion of electrodes into the brain has proved to be a major therapeutic advance in selected patients (usually under age 70) with disabling dyskinesias and motor fluctuations not adequately controlled with medical therapy.
Targets include:
- Subthalamic nucleus – response similar to levodopa with reduction in dyskinesia
- Globus pallidus – improves dyskinesia but levodopa still required for motor symptoms
- Thalamus – for tremor only.

Surgery (last resort)
Should only be considered for patients who cannot tolerate or respond to medical therapy. The procedures usually performed are pallidotomy or thalamotomy.

The clinical evaluation of PD
PD worsens slowly over the years. Most patients respond well to treatment and there is generally a period of several years in which symptoms are well controlled with relatively little disability.
The rate of progression is very variable, with a benign form running over several decades. Usually the course is over 10–20 years, with death resulting from bronchopneumonia and immobility.

Other akinetic-rigid syndromes

2- Drug-induced Parkinsonism

Dopamine blocking/depleting drugs, particularly neuroleptics(Antipsychotic), opiates and antiemetic (Metoclopramide) induce Parkinsonism or worsen symptoms in affected patients.

3- Atypical Parkinsonism

Some neurodegenerative disorders affect the basal ganglia causing prominent Parkinsonism as part of the clinical picture and may be mistaken for idiopathic PD in the early stages. These include:

- Progressive supranuclear palsy (Steele–Richardson–Olszewski syndrome): Causes Parkinsonism, postural instability with early falls, vertical supranuclear gaze palsy (cannot move their eyes upward and downward - tend to fall down stairs) , pseudobulbar palsy and dementia. Tau deposition seen pathologically.

- Multiple system atrophy: severe Autonomic symptoms and ataxia cerebellar signs occur in addition to Parkinsonism. Pathologically α-synuclein positive glial cytoplasmic inclusions occur.

- Corticobasal degeneration:
  -Cortical impairments (sensory):
    Apraxia (inability to preform a skillfull task with a normal sensory and motor function).
    Finger agnosia (loss the ability to distinguish, name, or recognize the fingers).
    loss of Stereognosis (tactile gnosis)(loss of the ability to recognize the form of an object in the absence of visual and auditory information, eg: two point discrimination, coin test).
    loss of Graphesthesia (loss the ability to recognize writing on the skin purely by touch).
    Alien limb phenomena.
  -Myoclonus.
  -Dementia.

These disorders are relentlessly progressive, which are characterized by their relative lack of response to therapy with levodopa/carbidopa, and usually die within a decade. **'Red flag'** symptoms suggesting one of these disorders include:

- Symmetrical presentation and absence of tremor
- Levodopa unresponsiveness (or poor response)
- Early falls (within first year)
- Additional neurological features.
- Cognitive impairment: Dementia with Lewy bodies
- Neuroleptic/ antiemetic drug use
- Early /prominent autonomic dysfunction
- limited eye movement
- pyramidal, cerebellar or sensory symptoms

4- vascular parkinsonism: stroke in the basal ganglia.

5- Wilson's disease:

An autosomal recessive inherited disorder of copper metabolism, its rare and treatable as Copper deposition occurs in the basal ganglia, cornea and liver (cirrhosis). All young patients (below 50) with a akinetic-rigid syndrome or hyperkinetic movement disorder, or liver cirrhosis should be screened for Wilson's disease (check serum copper and caeruloplasmin). Intellectual impairment develops. Diagnosis and treatment with the chelating agent penicillamine.

Case scenario (Not important)

CASE 1: A 70-year-old man presents with a tremor in one hand that causes him to appear to be rolling something between his fingers. During the interview, you note that the tremor appears at rest and disappears when the patient either extends his arms parallel to the floor or reaches for a pen. However, he has difficulty initiating movement to reach for a pen, finally doing so successfully, albeit slowly. You also note an expressionless face, decreased spontaneous blink rate, and forward stooped posture. On physical examination, the patient maintains this posture and walks with a slow, narrow-based, festinating gait. Motor examination shows that his muscles demonstrate a cogwheel rigidity, in which muscle rigidity gives way to passive stretching in series of successive jerks.

1. With what actions is this tremor most likely to appear?
More likely a resting tremor, most prominent when the arms are relaxed.

2. In light of these signs, what is the most likely diagnosis for the tremor?
This is a classic presentation for Parkinson's disease, which is the most common cause of resting tremor. Parkinson's disease frequently presents with a triad of resting tremor, bradykinesia, and cogwheel rigidity, as well as characteristic masked facies, stooped posture, and festinating gait.

3. How does a festinating gait differ from an ataxic gait?
-A festinating gain is due to lesions of the substantia nigra pars compacta, a member of the basal ganglia, and manifests as an unsteady, shuffling gait consisting of narrow-based steps. When directed to turn around, patients often do so "en bloc," by taking many small steps without twisting the torso.
- An ataxic gait is due to lesions of midline cerebellar structures and manifests as unsteady wide-based steps, with staggering side to side. A subtly ataxic gait can be detected with heel-to-toe gait testing.

4. Why should we ask if the patient is taking medications such as haloperidol or metoclopramide?
Certain antipsychotic and antiemetic agents may cause or exacerbate parkinsonian symptoms such as rigidity, bradykinesia, and resting tremor. When making the diagnosis, it is critical for physicians to distinguish Parkinson's disease from parkinsonism.

When you see the patient 6 months later, you note marked improvement of his bradykinesia and resting tremor. You attribute this success to the patient's current treatment course.

5. What medication did you start the patient on, and why is it, rather than dopamine, used to treat Parkinson's disease?
Dopamine cannot cross the blood-brain barrier. However, levodopa (L-dopa) is a precursor to dopamine, can cross the blood-brain barrier and increases CNS dopamine levels once converted by dopa decarboxylase. In fact, parkinsonian syndromes are often initially misdiagnosed as Parkinson's disease, and the diagnosis later corrected when the patient does not respond to L-dopa.

6. What would a pathologist look for to establish the diagnosis of Parkinson's disease in evaluation of the brain at autopsy?
Bilateral depigmentation of the midbrain substantia nigra, due to loss of dopaminergic, neuromelanin-containing neurons, The presence of neuronal Lewy bodies in degenerated substantia nigra neurons (eosinophilic, cytoplasmic inclusions containing a-synuclein and ubiquitin)

Case scenario (Not important)

CASE 2: A 40-year-old man has become notably demented and has developed involuntary movements, such as facial grimaces and a dance-like gait in which his legs move in sudden, rapid, jerky movements. During the interview, you note that the patient makes continuous jerky movements with his arm, which he seems to complete as purposeful movements to smooth his hair. The patient also complains that his mind does not feel as sharp as it used to be.

1. What term describes the patient's movements, and what conditions may cause these movements?
Chorea describes involuntary, sudden, rapid movements of a body part.

2. What is the differential diagnosis of chorea?
- Huntington's disease,
- Sydenham's chorea (poststreptococcal autoimmune, and often accompanied by rheumatic fever)
- Wilson's disease (abnormal copper accumulation)
- cerebrovascular causes,
- senile-related chorea.

3. Why might medications such as haloperidol and L-dopa cause chorea?
they cause a side effect called tardive dyskinesia, which as the name implies, develops slowly after medication is started and may persist after the medication is discontinued. The most common presentation is choreoathetosis of the face and distal extremities.

While talking with the patient and his wife, the wife tells you that the patient saw a psychiatrist a few years ago due to some gradual changes in his mood.

4. What sort of psychiatric changes might the patient's wife be referring to?
She might describe a gradual development of emotional lability, increased aggression and irritability, hypersexuality, or depression.

5. If a mini-mental status examination shows the patient to be mildly demented, with deficits in organization, concentration, and short-term memory, what is the most likely diagnosis?
The classic clinical triad of dementia, behavioural (aggression and depression) and chorea points toward Huntington's disease. This diagnosis is often supported by the family history.

6. What pathologic lesion would be visible on imaging?
MRI of the head is notable for significant atrophy of the basal ganglia, especially the caudate nucleus.

After discussions of your initial diagnosis, the patient reveals that he has known for a while that this was going to happen to him because he had tested positive for the gene that caused his father to have similar problems. However, the patient is upset because the disease has developed several years earlier in his life than in his father's.

7. What is the mode of inheritance?
Autosomal dominant manner.

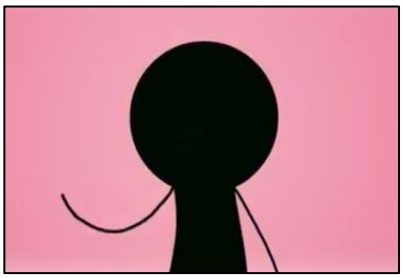
8. What type of gene mutation gives rise to Huntington's disease?
A trinucleotide repeat (CAG) expansion, located in the huntingtin gene on chromosome 4, translates into insertion of a polyglutamine tract in the huntingtin protein.

9. Why might it make sense to measure levels of serum ceruloplasmin in patients who present with similar motor abnormalities and a similar family history?
Serum ceruloplasmin is a screening test for Wilson's disease (hepatolenticular degeneration), which is also hereditary and causes movement abnormalities. In this disease, serum levels of copper are abnormally high and serum levels of ceruloplasmin, a serum protein that transports copper, are abnormally low.

Huntington's Chorea
54 sec

Essential tremor
59 sec

Bradykinesia
2:09 min



Myoclonic jerks
5:25 min

Dystonia
2:32 min

Parkinsonian gait
2:31 min

MCQ’s

1- Dominantly inherited disease: associated with progressive chorea and dementia; related to neurotransmitter imbalance:
A) Wilson's disease
B) tardive dyskinesia
C) Tourette's syndrome
D) Huntington's disease

2-Irregular, unpredictable, involuntary muscle contractions:
A) dystonia
B) tics
C) chorea
D) akinesia

3-Effective in managing essential tremor:
A) propranolol
B) metoprolol
C) primidone
D) diazepam

4- Alien limb phenomenon is typically seen in which of the following disorders?
A) Corticobasal degeneration
B) Huntington’s disease
C) Multiple system atrophy
D) Parkinson’s disease

5- A 72-year-old man presents to the emergency department after a fall. He states that he has fallen frequently over the past 8 months. On examination, he has no tremor, but he has generalized rigidity (mostly axial), bradykinesia, increased gag reflex, and difficulty with vertical gaze. What is this patient’s most likely diagnosis?
A) Multiple system atrophy
B) Parkinson’s disease
C) Parkinsonism-dementia-amyotrophic lateral sclerosis
D) Progressive supranuclear palsy

6- All of the following statements regarding essential tremor are correct EXCEPT:
A) Essential tremor is secondary to decreased dopaminergic neurotransmission in the basal ganglia
B) Symptoms may improve with alcohol intake
C) Symptoms respond to propranolol and primidone
D) Tremor is typically postural and kinetic

1-D 2-C 3-A 4-A 5-D 6-A

Thank you

If you have any question please contact with us at:
Internalmedicineteam434@gmail.com