Parkinsonism

435 medicine teamwork

[Important | Notes | Extra | Editing file]

Lecture objectives:

Not given.

Done By: Wael Al Oud, Raghda AlQassim, Reem Alaqeel

Edited By:Omar AlSulaiman

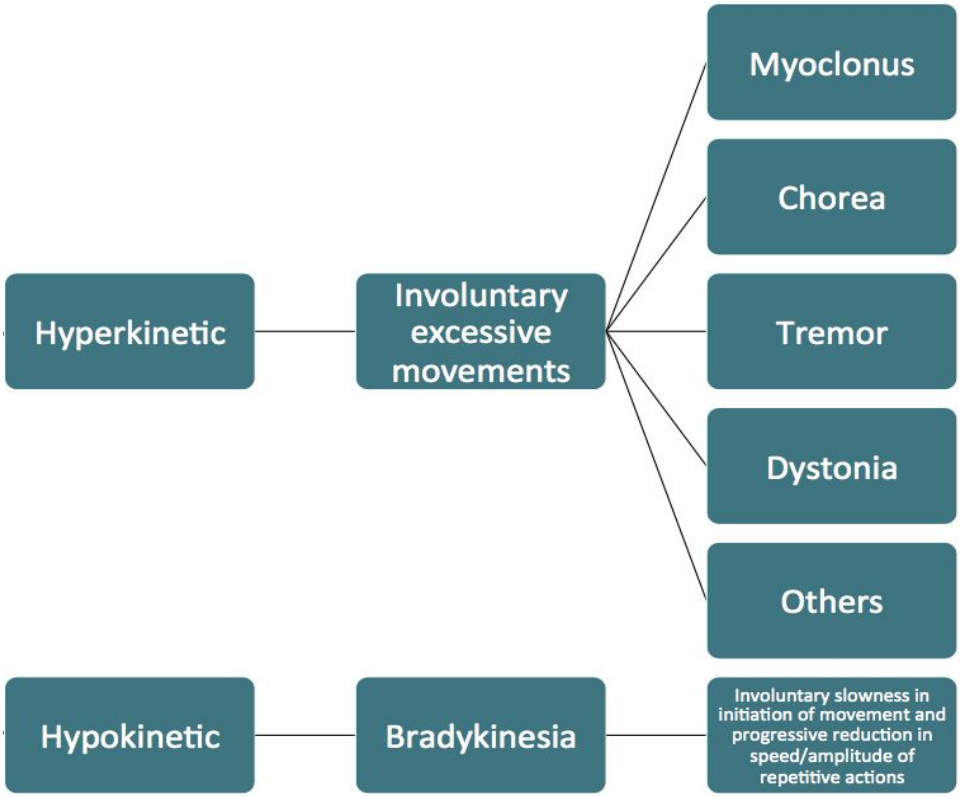
Revised By: Ahmed Alyahya

References: Doctors' Slides/notes + Davidson +Master the board + Step up

Movement disorders

Prelude:

Classification of movement disorders:



Terminology (we're sure you know them but just in case)	
Chorea	Involuntary movements resulting from a **continuous** flow of random muscle contractions. - **Ballismus:** stronger form of chorea (more aggressive movement) - **Athetosis:** chorea of the fingers
Dystonia	A movement disorder characterized by **sustained or intermittent** muscle contractions causing abnormal and repetitive movements, postures, or even both. (patient may present with his head 'stuck' to the left or right and faces difficulty when attempting to move)
Myoclonus	Involuntary **single quick contraction or inhibition** of a muscle group. Repeatable but not rhythmic.
Tremor	Involuntary **rhythmic oscillatory** movement around a joint axis, it's the most common of all involuntary movements.
Bradykinesia	Involuntary slowness of movement.
Parkinsonism	Group of features: rigidity, bradykinesia, and resting tremor. (like with dopamine blockers)
Parkinson's Disease	The most common neurodegenerative cause of **parkinsonism.**

Tremors:

1. Essential tremors:

- Essential tremors are the most common movement disorder, they are inherited[1] in up to ⅓ of individuals who have them.
- They are slowly progressing **ACTION** tremors meaning that they **disappear at rest.**
- They **worsen** with physical activity, caffeine and stress but temporarily **improve** with alcohol use. (depending on the community you are in, this can be useful to you in diagnosing a patient).
- They may present with distorted handwriting **BUT** there bradykinesia, rigidity, shuffling gait, and postural instability are **ALL ABSENT.** Some patients may have one side with more severe symptoms than the other one "nothing in the world is 100% symmetrical"
- So how will I differentiate between a parkinson's tremor and an essential tremor during a physical exam? When you ask the patient to lift their hand, you'll have to wait for the parkinson's tremor but the essential tremor will be instantaneous.
- **Management?** Propranolol

2. Physiologic tremors:

- Physiologic tremors can occur in normal individuals but is **enhanced**[2] in individuals with an underlying cause for the tremor.
- Causes of physiologic tremors include:
  - **Fear, anxiety, fatigue**
  - **Metabolic:** hypoglycemia, hypothyroidism, pheochromocytoma
  - **Toxic:** alcohol withdrawal, valproic acid, lithium, methylxanthines, caffeine, and theophylline.

Treatment? Treat the underlying cause.

3. Neurologic tremors:

- A manifestation of neurological disease such as parkinson disease, cerebellar disease, or wilson disease.

Huntington disease:

- **Huntington disease/Huntington chorea** is a progressive brain disorder that causes uncontrolled movements, emotional problems, and loss of thinking ability (cognition).
- Adult-onset Huntington disease, the most common form of this disorder, usually in the age of 30s/40s.
- It's autosomal dominant → lack of Fhx: unlikely to be Huntington
- Caused by mutation on **chromosome 4** → CAG leads to loss of GABA-producing neurons in striatum.
- **Clinical features:**
  - **Chorea:** chorea involving face, head, neck, tongue, trunk, and extremities.
  - **Altered behaviour:** irritability, changes in personality, antisocial behaviour, depression, obsessive compulsive features, and or psychosis.
  - **Impaired mentation:** progressive dementia is a key feature of Huntington disease, 90% are demented before the age of 50.
  - **Gait abnormalities:** unsteady/irregular
  - **Bradykinesia/rigidity**
  - **Incontinence**
- **Diagnosis:**
  - **MRI:** you'll see atrophy of the head of caudate nuclei
  - **DNA:** confirms the diagnosis.
- **Treatment?** sadly no curative treatment, we treat symptomatically. Dopamine blockers may help with the psychosis and chorea.

---

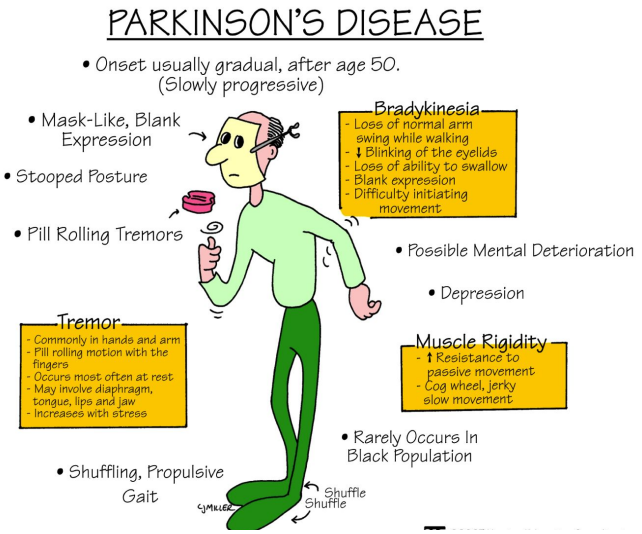
[1] Autosomal dominant inheritance

[2] This is called "enhanced physiologic tremor"

Parkinsonian disorder

1- idiopathic Parkinson's disease (PD):

General characteristics:



- **Parkinsonism** "Parkinsonian features"[3] .
- Parkinson's disease occurs due loss of dopamine containing neurons-nerve cells that are located in the pigmented **substantia nigra** and the **locus coeruleus** in the midbrain.
- Onset is usually after age of 50.
- PD is the imbalance of dopaminergic (too little) and cholinergic (too much - unopposed) tone on the basal ganglia.
- PD is clinically and pathologically distinct from other parkinsonian syndromes.

Risk factors:

- Incidence rate increases sharply with **age** (>70 years)
- Higher in **men** (1.5:1 M:F)
- Environmental factors: Pesticide exposure, Smoking.
- Genetic factors: Idiopathic Parkinson's disease is not usually familial

Clinical features:

Motor Symptoms

1. Pill rolling tremor at rest: tremor fades away when performing routine tasks.

Pill rolling tremor

- May progress to an action tremor.
- Frequency: 4-6 Hz.
- Re-emergence with maintained posture. (Re-emergence means it comes later, not like essential tremor > means if they lift their hand up, you should wait to see the tremor.)
- Worsens with emotional 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.

2. Bradykinesia: slowness of initiation with progressive reduction in speed and amplitude of repetitive action.

- The **cardinal clinical feature** of parkinsonism and the main cause of disability.
- The upper limb is usually affected first.
- Almost **always unilateral** for the first years.
- 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.
- Sialorrhea (excessive drooling): as a result of **both** bradykinesia AND rigidity of the oral and pharyngeal muscles

[3] Refers to symptoms and signs of parkinson's disease (features of rigidity, bradykinesia, rest tremor) +/- postural instability and can be a result from many conditions (medications) in drug induced.

3. Rigidity: Characteristic abnormally increased resistance to movement (independent of the velocity of the movement).

- Cogwheel rigidity: refers to a ratchet-like jerking, which can be elicited by testing the tone on one limb while the patient clenches the opposite fist. it's stiffness with tremor.
- Lead pipe rigidity (video): stiffness on passive limb movement, it presents throughout the range of movement.

4. Spasticity: increased resistance to the passive movement of a joint due to abnormally high muscle tone (hypertonus) which **varies with the amplitude and speed** of displacement.
While **rigidity** is an increased resistance to the passive movement of a joint which is constant throughout the range of joint displacement and **not related to the speed** of joint movement.

5. Poor postural reflexes: difficulty in initiating the **first step** and walking with ***small shuffling*** steps (shuffling gait), **stooped posture**.

6. Mask facies (expressionless face OR hypomimia): frequency of spontaneous blinking diminished, producing a serpentine[4] stare.

7. Dysarthria[5], dysphagia, and micrographia[6].

Non-motor Symptoms

Important - before the motor symptoms manifest

1. REM[7] sleep behavior disorder (RBD)[8].

2. Anosmia[9]: the olfactory bulb is one of the **first** structures to be affected and it usually comes before the development of parkinson's تسأله تأثرت عندك حاسة الشم؟ يقول و الله من زمان

3. Hallucinations: (they "see" or "hear" stuff that aren't real)

4. Impairment of cognitive function (dementia) in advanced disease.

5. Autonomic dysfunction: can lead to orthostatic hypotension, constipation, increased sweating and oily skin. (+urinary incontinence)

6. Personality changes present in early stages of the disease; patients become withdrawn, apathetic and dependent on others.

7. Depression is common and can be significant cause worsening of parkinsonian symptoms.
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. Follows progressive course, significant disability usually present within 5 to 10 years, indirectly leads to increased mortality.

---

[4] A serpentine is basically a snake, they have the gaze of a snake...
[5] difficulty in articulating words.
[6] small handwriting.
[7] Rapid Eye Movement
[8] In a person with REM sleep behaviour disorder, the paralysis that normally occurs during REM sleep is incomplete or absent → this allows the person to 'act out' his or her dreams physically. This usually occurs in dreams that are vivid, intense, and violent.
[9] the loss of the sense of smell, either total or partial.

Investigations:

- Investigations and imaging are usually **normal** in typical PD.
- Parkinson's disease is essentially a clinical diagnosis. Laboratory studies play no role in diagnosis.
- Lewys bodies (hyaline inclusion bodies) are a pathological hallmark neuronal finding in brains of patients with parkinson's disease.
    - Lewy bodies will contain tangles of α-synuclein and ubiquitin.

Management:

There is no cure, the goals are to delay disease progression and to relieve symptoms.
The basal ganglia/striatal region normally operates as a balanced system consisting of the dopaminergic system and the central cholinergic system. In PD, dopaminergic pathway is compromised and the cholinergic system is unopposed. As such goal of treatment is either to enhance dopamine influence or to inhibit acetylcholine influence.

- **Levodopa (L-dopa) AND Carbidopa**. DRUG OF CHOICE for treating parkinsonian symptoms.
    - REMEMBER: Levodopa changes into dopamine in the brain, carbidopa prevents the breakdown of levodopa in the blood stream.
    - Side effects include:
        - Dyskinesias[10] that can occur after 5-7 years of therapy. This is a major concern, and may warrant delay in initiating the drug for as long as possible.
        - N/V, anorexia, HTN, hallucinations.
        - '**on-off phenomenon**'[11] during treatment, which results in episodes of insufficient dopamine "off" characterized by bradykinesia. and "on" effect (too much dopamine) resulting in dyskinesia. This is due to dose-response relationships.
- **Dopamine agonists** (Pramipexole, Rotigotine, Bromocriptine)
    - may control the symptoms and delay need for Levodopa for several years.
    - initiate one of these agents when you have established the diagnosis.
    - Pramipexole is the most commonly used.
- **MAO B inhibitors** Used as an adjuvant to L-dopa and carbidopa (Selegiline, Rasagiline)
- **COMT inhibitors** metabolizes L-dopa peripherally (Entacapone), prolongs activity of Levodopa in blood Used as an adjuvant to L-dopa and carbidopa, use when there is "on/off" phenomena to even out the dopamine level(it prolongs the On time) , or when the response to therapy is inadequate.
- Amantadine. (antiviral)
- Anticholinergics (Trihexyphenidyl and Benztropine)
    - Particularly helpful in patients with tremor as a major finding.
    - do not use in older patients or demented patients.
- **Amitriptyline** is useful in the treatment of parkinson's disease both as an anticholinergic agent and as an antidepressant.
- BOTOX: is injected specifically into the overactive muscles causing either the foot cramps, eye twitching or drooling (salivary glands). The effect comes on gradually over several days, with the peak effect reached in approximately 2 weeks. The results last for about 3 months, so injections are repeated at 3 month intervals to maintain ongoing benefits.
- **Surgery:** Deep brain stimulation (DBS) used in patients unresponsive to Levodopa/Carbidopa

2- Drug-induced parkinsonism:

Mainly bilateral manifestations, and it could be reversible, partially reversible, or irreversible.

Medications that cause parkinsonian side effects:

- Neuroleptic drugs: Chlorpromazine, haloperidol, perphenazine.
- Dopamine antagonists: Metoclopramide.
- Antihypertensive: Reserpine.

[10] Involuntary, often choreic movements.
[11] The on-off phenomenon can be avoided using *duopa* which is carbidopa/levodopa administered continuously through an intraintestinal pump but have other side effects of their own.

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:

1. Progressive supranuclear palsy (PSP) (Steele-Richardson-Olszewski syndrome) (they can't look up or down)
    a. Like parkinson's disease: it **causes** bradykinesia, limb rigidity, cognitive decline and follows a progressive course.
    b. Unlike parkinson's disease: **DOES NOT cause tremor** -- **BUT CAUSES ophthalmoplegia.**
2. **Multiple system atrophy (MSA)/Shy-drager syndrome:** = parkinsonian symptoms + autonomic insufficiency. Symptom wise, both MSA and PD Symptom-wise cause slowness of movement with rigid posture, tremor and unstable shuffling gait. **MSA** can be distinguished from Parkinson's disease in certain notable ways:
    a. MSA patients parkinsonism symptoms occur unilaterally, while true PD is bilateral.
    b. Postural instability usually manifests earlier and progresses more rapidly in MSA than in PD.
    c. PD = pill rolling tremor, **MSA = NO pill rolling tremor!**
3. Corticobasal degeneration.
4. Lewy body dementia = parkinsonism with dementia.much faster onset.

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 suggest one of these disorders.

Red flags:

If any of the following are present, suspect conditions **other than** parkinson's disease:

- Neuroleptic/antiemetic drug use. (neuroleptics for example work as dopamine receptor blockers and as such may manifest similar symptoms)
- Early/prominent autonomic dysfunction.
- limited eye movements.
- Pyramidal, cerebellar or sensory symptoms.
- Cognitive impairment: Lewy bodies dementia.
- Symmetrical presentation and absence of tremor.
- Levodopa unresponsiveness (or poor response)
- early falls, within one year.
- Additional neurological features.

4- Vascular Parkinsonism:

Caused by a 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 ceruloplasmin). Intellectual impairment develops. Diagnosis and treatment is with the chelating agent penicillamine. **Wilson's disease** (WD) patients often present with **Parkinson's disease** (PD). Furthermore, most patients with PD have reduced ceruloplasmin, a characteristic of **Wilson's disease**.

MCQs

1) A left-handed 79 year-old man presented with resting tremor in his left hand. Tremor is evident in his writing, and in regards to his writing he also complained that it's smaller than usual. His wife complains that he sometimes kicks her while they are in bed asleep. When he wakes up in the morning he feels a little woozy but that resolves after a while. On examination he blinks 3 times per minute, his face does not show much emotion, he has a slow shuffling gait. He holds his feet slightly apart to steady himself. Which of the signs and symptoms is not commonly associated with parkinsonism?

a. Postural instability
b. Hypomimia
c. Broad-based gait
d. Autonomic instability

2) What is the frequency of the pill-rolling tremor?

a. 2-4 Hz
b. 4-6 Hz
c. 6-8 Hz
d. 8-10 Hz

3) Which of the following is *NOT* associated with progressive supranuclear palsy?

a. Bradykinesia
b. Limb rigidity
c. Cognitive decline
d. Tremors

4) A 75 year-old woman was diagnosed with Parkinson's disease. Her initial symptoms were depression, stooped posture, loss of energy, dragging leg, difficulty walking, tremors, and a loss in her arm swing. What would be the best initial treatment?

a. Levodopa/carbidopa
b. Amantadine
c. Trihexyphenidyl
d. Benztropine

5) A patient who is diagnosed with Parkinson's disease states, "I can't tie my shoelaces anymore." The student recognizes that this patient's problem is due to a deficiency in which of these neurotransmitters?

a. Glutamate
b. Dopamine
c. Norepinephrine
d. Serotonin

6) An OSCE station doctor asks you why do we give carbidopa *and* levodopa. How should you respond?

a. Levodopa turns carbidopa into dopamine when it reaches the brain
b. Carbidopa prevents the breakdown of levodopa
c. Better compliance
d. Levodopa prevents the breakdown of Carbidopa

7) When taking history of a patient diagnosed with Parkinson's disease, which of the following symptoms should you anticipate the patient to tell you?

a. My eyes have become very sensitive to light.
b. Sometimes I feel like my feet are glued to the floor
c. I used to be able to walk up the stairs without getting losing my breath
d. I've been getting really severe headaches lately

8) Which of the following speech patterns is consistent with Parkinson's disease?

a. Bubbly and spirited
b. Clear and rhythmic
c. Pressured and hurried
d. Slow, slurred, and monotone.

Answer key:

1 (C) | 2 (B) | 3 (D) | 4 (A) | 5 (B) | 6 (B)| 7(B)| 8 (D)