Parkinsonism

Objectives: no objectives found

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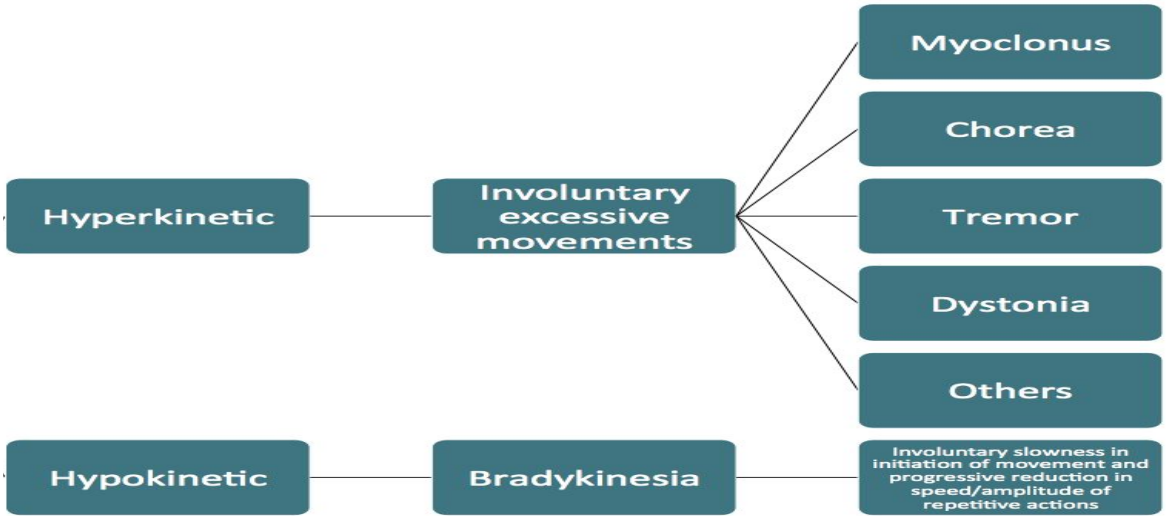
Resources: 435 team + Davidson + kumar + Recall questions step up to medicine.

- Editing file
- Feedback

Movement disorders



Terminology	
Chorea[1]	• Involuntary dancing like movements resulting from a **continuous** flow of random muscle contractions. especially when an individual wants to grab something • Chorea can occur in "Sydenham's Chorea" (Rheumatic fever-autoimmune condition) and in Huntington's disease (HD) -Ballismus: a **large** (+ faster) amplitude choreaform movement, seen after subthalamic strokes usually. same as chorea but stronger (more aggressive & faster movements) but if you said chorea for both you're right -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 - could be generalized or focal, could be lesional, drug or idiopathic
Myoclonus	Involuntary **single quick contraction or inhibition** of a muscle group. Repeatable but not rhythmic. during encephalopathies or drug related, hereditary disorders.
Tremor	Involuntary **rhythmic** (that's what differentiates between it & myoclonus) **oscillatory** movement around a joint axis, it's the most common of all involuntary movements.

[1]comes from the word dance like in "choreography"

Bradykinesia	Involuntary **slowness** of movement with progressive reduction in speed and amplitude of repetitive action.
Rigidity	abnormally increased resistance (an increased tone) to movement that is independent of the velocity of movement. while spasticity is velocity dependent.
Parkinsonism	Group of features: rigidity, bradykinesia, and resting tremor +\- postural instability. (person is at risk of falling) (like with dopamine blockers)
Parkinson's Disease	The most common neurodegenerative cause of **parkinsonism.**

Tremors:

1. **Essential tremors:** It is a benign condition (will not lead to comorbidities)
   - The most common movement disorder, they are inherited[2] 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 +exams :) but temporarily **improve** with alcohol use.
   - They may present with distorted handwriting **BUT** 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

(: Just take propanolol جايينك ضيوف وتبي تصب القهوة بدون ماتكبها على الضيوف

2. **Physiologic tremors:**
   - Physiologic tremors can occur in normal individuals but is **enhanced**[3] 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.

[2] Autosomal dominant inheritance
[3] This is called "enhanced physiologic tremor"

3. **Neurologic tremors:**
    - A manifestation of neurological disease such as parkinson disease, cerebellar disease, or wilson disease.

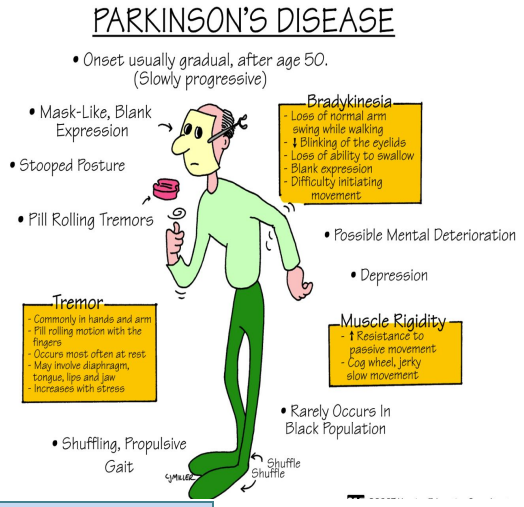
Huntington disease:

- HD is an autosomal dominant disorder with progressive chorea, cognitive impairment and psychiatric features develop. Some pt start with depression & high risk of suicide because of their condition 'cognitive impairment, chorea …..'
- may develop parkinsonism features with chorea (think of huntington) usually younger patients
- **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.

Parkinsonian disorder

★ 1. idiopathic Parkinson's disease (PD):

- **Parkinsonism** "Parkinsonian features"[4] .
- 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.

Motor Symptoms

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

Pill rolling tremor

- May progress to an action tremor. There is a trick to differentiate between: (1) parkinson rest tremor (because parkinson rest tremor sometimes will occur during action) to differentiate that from the (2) typical action tremor like in central tremor or somebody who is hypoglycemic, somebody who took a drug which cause a tremor. These action tremors (2) are pure action tremors (will not be there at rest) but as soon as they raise their hands immediately you will see the tremor, where the parkinson pt. have something called **re-emergence** (delayed response) so it go up, then the tremor will start after somewhile (aprox. 3 mins).
- Frequency: 4-6 Hz.

- Predominantly rest. You have to be careful about the rest tremor, the best way to see the rest tremor is to have the pt. to walk, because when they're walking

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

they're not using their hands, so I tell the pt. to walk to examine him while I'm really looking into their hands.

- 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 (increase) with emotional stress and mental concentration. If you asked the pt. to do something mental, mathematic or count, the tremor will become more prominent.

2. Bradykinesia: slowness of initiation (So if you asked a pt. to get up & walk they will pause before they actually start walking) with progressive reduction in speed and amplitude of repetitive action. (So if you asked them to do finger tap or open & close your hand, they will begin to gradually slow down)

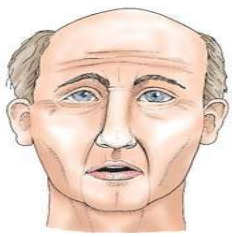
- The **cardinal clinical feature** of parkinsonism and the **main cause of disability**.
- The upper limb is usually affected first.
- Almost **always unilateral** for the first years.
- Akinesia is tested clinically by asking the patient to perform rapid alternating movements such as opening and closing 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. Rigidity: Characteristic abnormally increased resistance to movement (**independent** of the velocity of the movement). (Spasticity: Velocity **dependance**, the faster you move the arm the more the more the tendon will catch the spasticity)

- 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.

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[5] stare.



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

[5] A serpentine is basically a snake, they have the gaze of a snake...
[6] difficulty in articulating words
[7] small handwriting.

Non-motor Symptoms

Important - before the motor symptoms manifest

1. REM[8] sleep behavior disorder (RBD)[9]. => LBD (Lewy body dementia)

2. Anosmia[10]: 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 والله من زمان

- Both 1 & 2 might start earlier before the disease, pt will say "I haven't been able to smell in the past 10 years"

3. Hallucinations (typically visual hallucinations: Seeing things that are not there, NOT auditory hallucinations, if the patient doesn't have parkinsonism and has auditory hallucinations refer him to a psychiatrist)

4. Impairment of cognitive function (+dementia) **in advanced disease.** (Later on, if it happened early at the start with parkinsonism (within 1 year) that means it is LBD. But, if he have parkinson disease for 1 or 2 years & then cognitive problems start then it's probably parkinson disease dementia)

5. Autonomic dysfunction: can lead to orthostatic hypotension, constipation, increased sweating and oily skin. (a lot of time pt say they feel dizzy, they stand up & they feel light headache because they don't have a good autonomic regulation of their blood pressure. Other examples is erectile dysfunction, bladder control difficulties, severe constipation that start before the disease by years)

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

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[8] Rapid Eye Movement

[9] 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.

[10] the loss of the sense of smell, either total or partial.

progressive course, significant disability usually present within 5 to 10 years, indirectly leads to increased mortality.

Investigations: When you have the criteria (rest tremor, rigidity, bradykinesia slowly progressive over a year) you don't even need imaging sometimes

- Investigations and imaging are usually **normal** in typical PD.

It might be a little bit asymmetrical one side is more than the other but it usually a bilateral disease

- 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. Levodopa replace the missing dopamine, carbidopa & MAO B inhibitors keep Levodopa longer in the blood so both don't have any action by themselves but you add it to Levodopa (prevents the breakdown of levodopa in the bloodstream).
    - Side effects include:
        - Dyskinesias[11] 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'**[12] during treatment, which results in episodes of insufficient dopamine "off" characterized by bradykinesia. and "on" effect (too

[11] involuntary, often choreic movements.

[12] 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.

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** "COMT 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 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.

It is a surgical procedure (while pt is awake) they implant a device & it changes the tremor response. Done in advanced cases of parkinsonism.

★ 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.

★ 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), impaired vertical gaze** (they can't look up or down, you tell them to look up & then just their eyebrows goes up because they can't move their eyes) (Cranial nerves are intact)
    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. parkinsonism + orthostatic hypotension = shy drager syndrome
    c. PD = pill rolling tremor, **MSA = NO pill rolling tremor!**

3. **Corticobasal degeneration:** Cortical impairments (Sensory: Astereognosis (gnosis= knowledge, knowing the dimension of an object, ex) you give the pt a key while his eyes are closed & ask him to recognize what is it) , agraphesthesia (agraphia= loss of graphic sensation, esthasis= sensation, draw a number or a letter on the pt hand the he should be able to tell that number\letter. Brain should be able to process this changes in stimulants) , apraxia (praxia= practice, to do something "skills", you ask the pt to show you how to brush his teeth but he won't be able to tell, he forgot how to handle the brush & clean his teeth).
4. Lewy body dementia = parkinsonism with dementia.much faster onset.
5. Ataxia+parkinsonism = olivopontocerebellar atrophy

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. multisystem atrophy
- limited eye movements. (Progressive supranuclear palsy)
- Pyramidal, cerebellar or sensory symptoms. multisystem atrophy or stroke
- 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. comes with UMN signs

★ 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**

Summary

Parkinsonian disorder

General characteristics	• occurs due to loss of dopamine containing neurons-nerve cells in the pigmented **substantia nigra** and the **locus coeruleus** in midbrain. • Onset after age of 50.(incidence rate increase>70) • It is the imbalance of (dopaminergic↓) and (cholinergic↑) tone on the basal ganglia. • Higher in Men (1.5:1 M:F)

Clinical Features

Motor symptoms	**Non-Motor symptoms** (Important) Before motor symptoms manifests
1. Pill rolling tremor at rest 2. Bradykinesia (main cause of disability) 3. Rigidity 4. Spasticity 5. Poor postural reflexes (small shuffling steps) 6. Mask facies (hypomimia) 7. Dysarthria, dysphagia, and micrographia	1. REM sleep behavior disorder 2. Anosmia (first to be affected) 3. Hallucinations 4. Impairment of cognitive function 5. Autonomic dysfunction 6. Personality changes 7. Depression

Investigations

- Essentially a clinical diagnosis. (Investigations and imaging normal in typical PD).
- Lewys bodies are pathological hallmark finding in brains of patients.

Management

The goal is: 1. Delay progression 2. Relieve symptoms (No Cure)

- Levodopa, Carbidopa. (drug of choice) for treating symptoms.
- Dopamine agonists (Pramipexole)
- MAO B inhibitors (Selegiline)
- COMT inhibitors (Entacapone)
- Anticholinergics (Benztropine, Amitriptyline)

Questions

1. A 40-year-old female presented with bradykinesia and shuffling gait, you suspect parkinson's how will you diagnose the patient?

A. Take full history and perform a complete physical exam
B. Brain MRI
C. CSF analysis
D. Genetic testing

2. What is the drug of choice in a newly diagnosed parkinson's patient?

A. MAO Inhibitor
B. TCA
C. Levodopa
D. Pramipexole

3. You recently diagnosed a 53 year old male with Parkinson's. Which of the following structures is first to be affected?

A. Spinal tract
B. Olfactory bulb
C. Optic chiasm
D. Cerebral cortex

4. A 27-year-old female comes to your clinic complaining of shaking during exams, and class presentation. Her symptoms do not appear at rest. She denies having postural instability, rigidity or bradykinesia. How will you manage this patient?

A. Start her on levodopa
B. Refer her to neurosurgery for deep brain stimulation
C. Prescribe propranolol to manage her symptoms
D. Admit patient and start high dose prednisolone

5. Which of the following will make you reconsider the diagnosis of parkinson's?

A. Shuffling gait

B. Early autonomic dysfunction

C. Blank face

D. Old age

6. Parkinson's occurs due to loss of which of the following structures?

A. Substantia nigra

B. Cerebellum

C. Medial longitudinal fasciculus

D. Spinothalamic tract

7. Which clinical feature will help you distinguish parkinson's disease from multiple system atrophy?

A. Memory

B. Rigidity

C. Shuffling gait

D. Pill rolling tremor

Answers:

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