

Parkinson Disease

Parkinson disease means dopamine-making brain cells are dying, so movement becomes slow, stiff, and shaky.

THE ONE-LINE TRUTH

Dopamine-making cells in the substantia nigra (the brain's movement-control station) are dying, so your body loses the chemical signal it needs to start and smooth out movement.

The chain — how it unfolds

1. Alpha-synuclein misfolds and clumps into Lewy bodies inside substantia nigra neurons. — why: Genetics, mitochondrial damage, oxidative stress, or environmental toxins push the protein to fold wrong; once it clumps, it poisons the cell's machinery and triggers a slow death.
2. Dopamine-making cells in the substantia nigra die, so less dopamine reaches the striatum. — why: Without dopamine, the striatum cannot green-light movement commands or set their speed, so the whole movement loop stalls.
3. You see resting tremor (shaking when the hand is still), cogwheel rigidity (muscles catch like a ratchet), bradykinesia (slow movement), and postural instability (balance problems). — why: The striatum is starved of dopamine, so it cannot start movements smoothly (bradykinesia), muscles stay tense because inhibitory signals fail (rigidity), the brain generates a 4–6 Hz oscillation in the motor loop that shows up as tremor at rest, and postural reflexes do not fire fast enough to catch a stumble.
4. Face becomes mask-like (hypomimia), handwriting shrinks (micrographia), and gait turns into a shuffling walk with short steps and a forward-leaning posture. — why: Fine motor control and automatic movements (like facial expressions, penmanship, and arm swing during walking) all depend on dopamine; when it drops, those movements shrink or freeze.
5. Non-motor symptoms appear: loss of smell (hyposmia), constipation, sleep problems (REM behavior disorder—acting out dreams), low mood (depression), anxiety, and mild cognitive slowing. — why: Lewy bodies spread beyond the substantia nigra to the olfactory bulb (smell center), the dorsal motor nucleus of the vagus (which runs gut motility), the locus coeruleus and raphe nuclei (which regulate sleep and mood with norepinephrine and serotonin), and eventually the cortex (thinking and memory areas).

6. Autonomic dysfunction develops: blood pressure drops when standing (orthostatic low blood pressure (hypotension)), sweating becomes unpredictable, bladder empties incompletely (urinary retention or urgency), and sexual function declines. — why: Dopamine and norepinephrine pathways that regulate automatic body functions (heart rate, blood vessel tone, sweat glands, bladder sphincters) are damaged by Lewy body spread.
7. Late-stage complications: severe freezing of gait (feet feel glued to the floor), falls with hip fractures, aspiration pneumonia (food or saliva goes into the lungs because swallowing is slow), dementia (Parkinson disease dementia), and autonomic crises. — why: As more brain regions accumulate Lewy bodies and lose neurons, the movement system collapses completely, swallowing and cough reflexes fail, and cortical damage impairs memory and executive function.
8. Sudden medication withdrawal or severe infection can trigger parkinsonism-hyperpyrexia syndrome (looks like neuroleptic malignant syndrome): very high fever, severe rigidity, confusion, and autonomic instability. — why: Stopping dopaminergic drugs abruptly or a systemic stressor (infection, surgery, dehydration) unmasks how fragile the remaining dopamine system is; the brain cannot regulate temperature or muscle tone, so the body overheats and muscles lock up dangerously.

Spot it — what you see, and why

- Shaking in one hand or arm while at rest (resting tremor): Dopamine (the brain messenger that smooths out movement) drops in the substantia nigra (a small control center deep in the brain), so the circuits that steady your hand when it's relaxed get noisy and fire in a rhythm, making the hand shake when you're not using it.
- Moving slowly overall (bradykinesia): Without enough dopamine, the basal ganglia (the brain's movement-planning network) can't start or scale movements quickly, so every action—walking, writing, buttoning a shirt—takes more time and effort, like a car stuck in low gear.
- Stiff, rigid muscles: Low dopamine lets the brain's brake signals overpower the go signals, so muscles stay tight even when you try to relax them; it feels like moving through thick syrup and others notice a stiff, jerky quality when they bend your arm or leg.
- Trouble with balance and walking (postural instability): As dopamine loss spreads, the brain circuits that keep you upright and adjust your posture automatically start to fail, so you shuffle, lean forward, and can't catch yourself quickly if you start to tip—this usually shows up years after the tremor and slowness begin.
- Smaller handwriting that gets tinier as you write (micrographia): The basal ganglia can't keep fine movements big and consistent, so each letter shrinks as the movement program fades, like a battery running low mid-sentence.

- Soft, mumbled speech and a flat facial expression (hypomimia): The same slowness and stiffness that affect arms and legs also hit the muscles of the face, throat, and voice box, so your voice loses volume and your face looks less animated, even when you feel the emotion inside.

Red flags — act now

- Falls or severe balance problems within the first year of symptoms
- Eye-movement trouble, especially looking up or down (vertical gaze palsy)
- Blood pressure that drops sharply when standing, severe constipation, or loss of bladder control early in the illness
- Symptoms that are exactly the same on both sides of the body from the start (true Parkinson usually begins on one side)
- No improvement at all after a fair trial of levodopa (the main Parkinson medicine)

Treat it — in this order

1. Carbidopa-levodopa (25/100 mg three times daily, titrated up) → Levodopa crosses into the brain and gets converted to dopamine by the remaining substantia nigra cells and other neurons, replacing what the dying cells can no longer make. Carbidopa blocks levodopa breakdown outside the brain so more reaches the brain. This fixes tremor, stiffness, and slow movement at their source — the dopamine shortage in the striatum.
2. Physical therapy and structured aerobic exercise (30–60 minutes, 3–5 times per week) → Movement practice wakes up the brain's backup pathways for balance and coordination (the cerebellum and premotor cortex), bypassing the damaged dopamine system. Aerobic exercise boosts brain-derived neurotrophic factor (BDNF, a growth signal that protects neurons) and slows brain cell death. Resistance and balance training reduce fall risk and keep muscles strong.
3. MAO-B inhibitors (rasagiline 1 mg daily or selegiline 5 mg twice daily) → These drugs block monoamine oxidase B (MAO-B, the enzyme that breaks down dopamine in the brain), making each remaining dopamine-making cell work harder and last longer. This smooths motor symptoms in early disease and delays the need for levodopa by 6–12 months.
4. Dopamine agonists (pramipexole 0.5–4.5 mg daily or ropinirole 3–24 mg daily) for younger patients (age < 60–65) → These drugs mimic dopamine's signal directly on dopamine receptors in the striatum, bypassing the need for the dead substantia nigra cells to make dopamine. They delay motor fluctuations and dyskinesias seen with long-term levodopa use.

5. Catechol-O-methyltransferase (COMT) inhibitors (entacapone 200 mg with each levodopa dose) → COMT inhibitors block the enzyme that breaks down levodopa in the bloodstream, so more levodopa reaches the brain and lasts longer. This extends each levodopa dose by 30–60 minutes and smooths motor fluctuations (the 'wearing off' between doses).

Your top priorities at the bedside

1. Assess fall risk at every visit using the Timed Up and Go test, and check orthostatic vital signs (blood pressure and heart rate lying, sitting, and standing after 1 and 3 minutes). — why: Parkinson disease damages the basal ganglia (the brain's balance and posture control center) and the autonomic nervous system (which keeps blood pressure stable), so patients can fall from poor balance or from blood pressure dropping 20 or more points when they stand, causing dizziness and fainting.
2. Give carbidopa-levodopa exactly on schedule, ideally 30 to 60 minutes before meals, and never hold or delay a dose without calling the provider. — why: Levodopa is the brain's replacement dopamine supply. Patients develop a narrow therapeutic window where even one missed dose causes wearing-off (return of tremor, stiffness, and freezing). Taking it with food reduces absorption because protein competes for the same transporter in the gut.
3. Monitor for sudden confusion, high fever, muscle rigidity, or inability to swallow, and escalate immediately if any appear. — why: These are signs of parkinsonism-hyperpyrexia syndrome (PHS), a life-threatening condition caused by suddenly stopping dopamine drugs or by severe infection or dehydration. The body loses all dopamine signaling at once, causing muscle breakdown (rhabdomyolysis), kidney failure, and death if untreated.