2ry parkinsonism

- Cerebral atherosclerosis.
- Viral encephalitis.
- Drugs; neuroleptics, antiemetics, reserpine and α-methyl dopa.
- Neurotoxins; pesticides, herbicides, industrial chemicals.

Multifactorial pathogenesis

- Genetic, especially in pts < 50yrs; α-synuclein gene mutations.
- Mitochondrial damage & oxidative stress.
- Inflammatory milieu.
- Apoptosis.

Clinical picture; hypokinesia

- Bradykinesia; slow movements.
- ↓ associated movements.
- Rigidity: ↑ muscle tone (flexor and extensor)
- Resting tremor
- Postural imbalance & Shuffling gait.

Later in disease process

- Autonomic deficits.
- Dementia.
- Affective disorders.
Antimuscarinic drugs

Benztropine, trihexyphenidyl

- Centrally-acting antimuscarinic → ↓ ACh action in striatum.
- Dose is **titrated up** until clinical benefit or adverse effects.
- **Gradual** withdrawal.

- **Improve** rigidity & tremor.
- **Limited** effect on bradykinesia.

- **Preferred in** drug-induced 2ry parkinsonism.
- **Poorly-tolerated** by elderly or cognitively-impaired pts.

- **AEs**: Constipation, urine retention, dry mouth, blurred vision, drowsiness, tachycardia, dementia, arrhythmia
Phase III: “Pivotal” Studies- “make-or-break” stage

Drugs to address problems associated with current formulations:

• ER carbidopa-Levodopa pills; IPX066.
• Safinamide & zonisamide, (MAOIs & anti-glutaminergics); ↑ “on-time”.
• Istradefylline (adenosine A2A antagonist); suppress dyskinesia.
• Perampanel & talampanel (AMPA antagonists).

Symptomatic drugs to address non-motor PD issues:

- Pimavanserin (5HT2A partial agonist); for psychosis & hallucinations.
- Pitolisant (H3 inverse agonist/antagonist); suppresses excessive sleepiness.

Neuroprotective therapies:

Since there is evidence relating oxidative damage of nerve cells to PD, antioxidants to deactivate "free radicals" & chemicals that damage nerve cells.

- Coenzyme Q10 (CoQ10)
- Creatine & Vitamin E (α-tocopherol); have not been found effective.
- Polyphenol (antioxidant) in green tea.

Phase IV: Post Market Studies

FDA-approved drugs for PD or for another condition, are studied to see if they might work for additional PD symptoms.

- Rasagiline; for its effects when combined with dopamine agonists.
- Naltrexone; for treating PD impulse-control disorders.
- Rivastigmine (approved for PD dementia); for treating other cognitive symptoms.
- Lubiprostone (PGE1 derivative); for alleviating PD-related constipation.