

Secondary Parkinsonism

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DRUG-INDUCED PARKINSONISM

- dopamine receptor-blocking drugs:** neuroleptics (phenothiazines, butyrophenones), antiemetics (metoclopramide).
most offensive neuroleptics are **potent D₂ receptor antagonists** + have **little anticholinergic effect**: piperazine phenothiazines, haloperidol, thiothixene.
 - dopamine-depleting agents:** reserpine, tetrabenazine.
 - α -methyl dopa, lithium, flunarizine, cinnarizine, amiodarone.
- drugs** cause 8% of all parkinsonism cases!
 - women and elderly have increased risk.
 - signs usually develop within 3 months of starting causal agent.
 - all cardinal signs of parkinsonism syndrome.
 - typically symmetric!!!
 - tremor is less common.
 - upon withdrawal of offending drug, symptoms slowly disappear (in weeks or months; if persist > 6 months – it is PD).
 - treatment of neuroleptic-induced parkinsonism:
 - discontinue drug / substitute with greater anticholinergic potency or “atypical” neuroleptic
 - add **anticholinergic** (e.g. **TRIHEXYPHENIDYL**, **BENZTROPINE**)
Remember, anticholinergics + phenothiazines potentiate **tardive dyskinesia!**
 - add **AMANTADINE**.

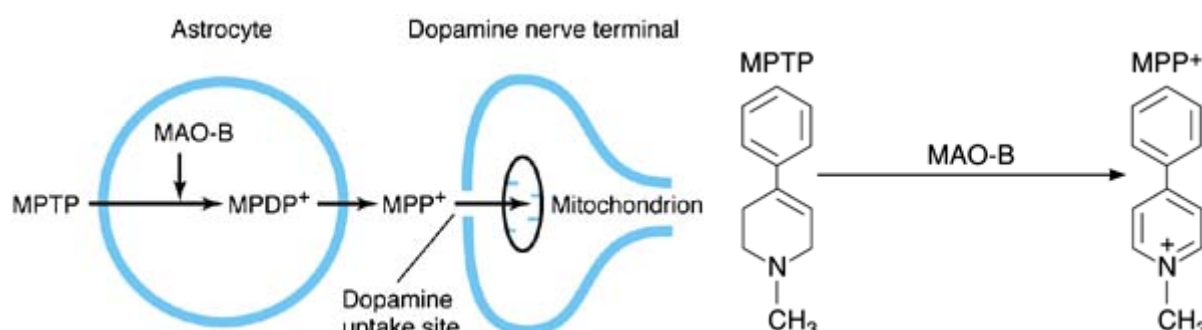
N.B. LEVODOPA is not effective (dopamine receptors are occupied by offending drug) and may worsen underlying psychotic disorder!

MPTP-INDUCED PARKINSONISM

Best studied experimental model of parkinsonism!

1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP):

- derivative of meperidine.
- by-product of synthesis of opioid (first developed during production of illicit heroin).
- opioid preparations heavily contaminated with MPTP led to several cases of parkinsonism in early 1980s (drug dealer in northern California supplied homemade "synthetic heroin").



- MPTP enters brain and is converted (by MAO-B in astrocytes) to *N*-methyl-4-phenyl-dihydropyridine (MPDP⁺).
- MPDP⁺ diffuses across glial membranes and extracellularly undergoes nonenzymatic oxidation and reduction to active metabolite *N*-methyl-4-phenylpyridinium (MPP⁺).
- MPP⁺ is taken up by plasma membrane transporters (that normally reuptake dopamine from synapses).
- internalized MPP⁺ is concentrated in mitochondria → inhibits oxidative phosphorylation (by interacting with complex I of mitochondrial electron transport chain) → reduced metabolism of molecular oxygen → **increased formation of active radicals** → cell injury.

Intravenous injection → highly focused damage of substantia nigra pars compacta → **acute severe irreversible parkinsonism** (in humans and primates).

N.B. other neurons (including other dopaminergic neurons) are left intact!

Clinical syndrome is indistinguishable from PD and responds to LEVODOPA.

POSTENCEPHALITIC PARKINSONISM

- was most prominent **sequela of pandemics of ENCEPHALITIS LETHARGICA (von Economo disease)** that occurred between 1919 and 1926. see p. Inf9 >>
- today vanishingly rare.
- causative agent (was never established) affected mainly midbrain.
other viruses (Coxsackie, Japanese B, western equine encephalitis) can cause parkinsonism!
- pathology - **NEUROFIBRILLARY TANGLES** in remaining nigral neurons.
- clinical features:
 - parkinsonism similar to PD (but onset at young age with slower progression).
 - oculogyric crises** - forced, sustained deviation of head and eyes to fixed position for minutes to hours.
 - grimaces, torticollis, torsion spasms, myoclonus, facial and respiratory tics, bizarre postures and gaits, behavioral disorders, ocular palsies may appear.
- treatment - **limited tolerance to LEVODOPA** (dyskinesias at low dosages); **anticholinergics** are tolerated well.

HEMIPARKINSONISM-HEMIATROPHY SYNDROME

Etiology - brain injury early in life (possibly even perinatally).

Relatively benign uncommon syndrome:

- HEMIPARKINSONISM** - begins in young adults and remains as hemiparkinsonism*; sometimes with unilateral dystonic movements; nonprogressive (or slowly progressive compared to PD).
*sometimes becomes bilateral.
- Ipsilateral BODY HEMIATROPHY** (or **contralateral CORTEX HEMIATROPHY**) - completely unnoticed by patient (comparative examination of size of hands and feet may be necessary to diagnose condition)

Responds poorly to medications.

“LOWER-BODY PARKINSONISM”

1. **NORMAL PRESSURE HYDROCEPHALUS** - gait with shuffling short steps and loss of postural reflexes and sometimes freezing.
2. **VASCULAR PARKINSONISM** - resulting from lacunar disease: gait is profoundly affected, with short steps, freezing and loss of postural reflexes.
3. **IDIOPATHIC GAIT DISORDER OF ELDERLY.**

BIBLIOGRAPHY for ch. “Movement disorders, Ataxias” → follow this [LINK >>](#)

Viktor's NotesSM for the Neurosurgery Resident
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