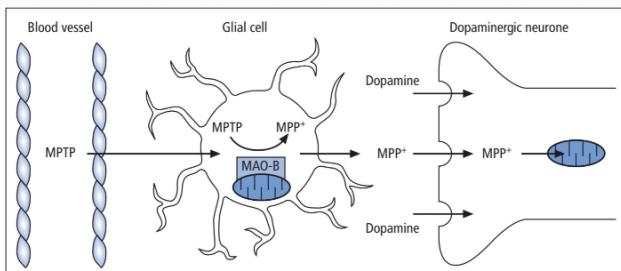


PARKINSON DISEASE



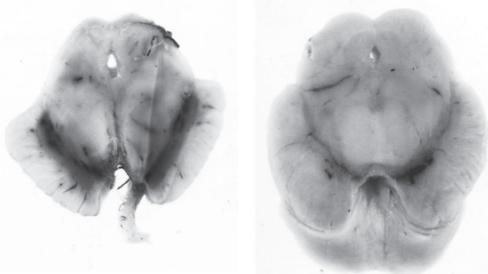
Mechanism at which MPTP heroin metabolite causes dopaminergic neuronal damage

Figure 12.1 MPTP and the aetiology of Parkinson's disease. The toxin MPTP crosses the blood-brain barrier and is converted to its active metabolite MPP⁺ by the enzyme monoamine oxidase type B (MAO-B) in glial cells. MPP⁺, a free radical, is concentrated in dopaminergic neurones, entering via the dopamine reuptake mechanism, thereby selectively damaging these cells. MPP⁺ is a mitochondrial poison, inhibiting Complex I of the respiratory chain, and hence impairing cellular energy production.



Wilson disease

- autosomal recessive defect of copper metabolism
- low ceruloplasmin
- KayserFleischer
- copper deposition in liver and basal ganglia
- akinetic-rigid syndrome, dystonia, cerebellar signs ,neuropsychiatric manifestations
- treatment copper-chelating agents (trientine and penicillamine), zink



'Punch-drunk syndrome'

- boxers
- dementia pugilistica
- Postencephalitic Parkinsonism**
- after World War I
- oculogyric crises

Multiple lacunar infarcts

- association with pyramidal and cognitive dysfunction
- Drugs** :Neuroleptics, antiemetics(metoclopramide) , amiodarone

Toxins: MPTP, manganese, chronic carbon monoxide poisoning

Lewy body : alpha-synuclein containing eosinophilic inclusion in brainstem,cerebral cortex, and sympathetic autonomic ganglia

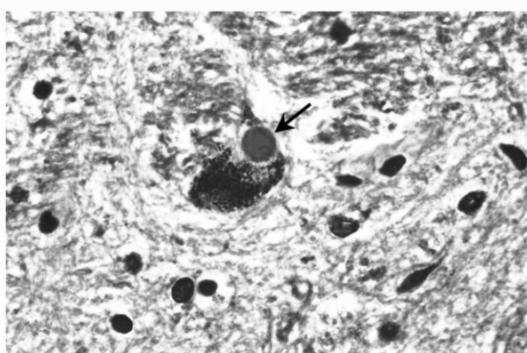
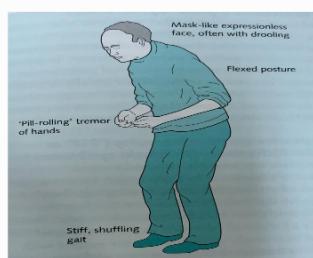
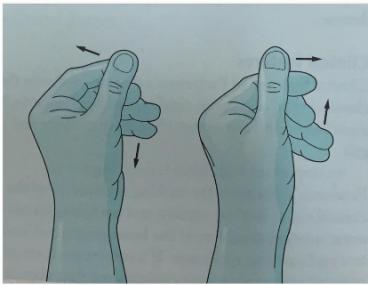
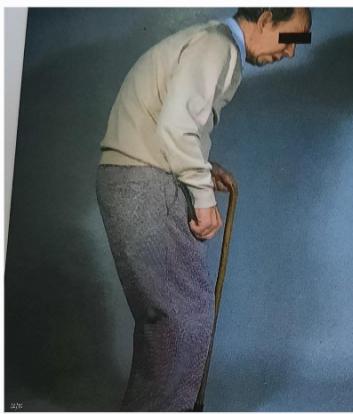


Figure 12.3 The Lewy body (arrowed).



Clinical manifestations

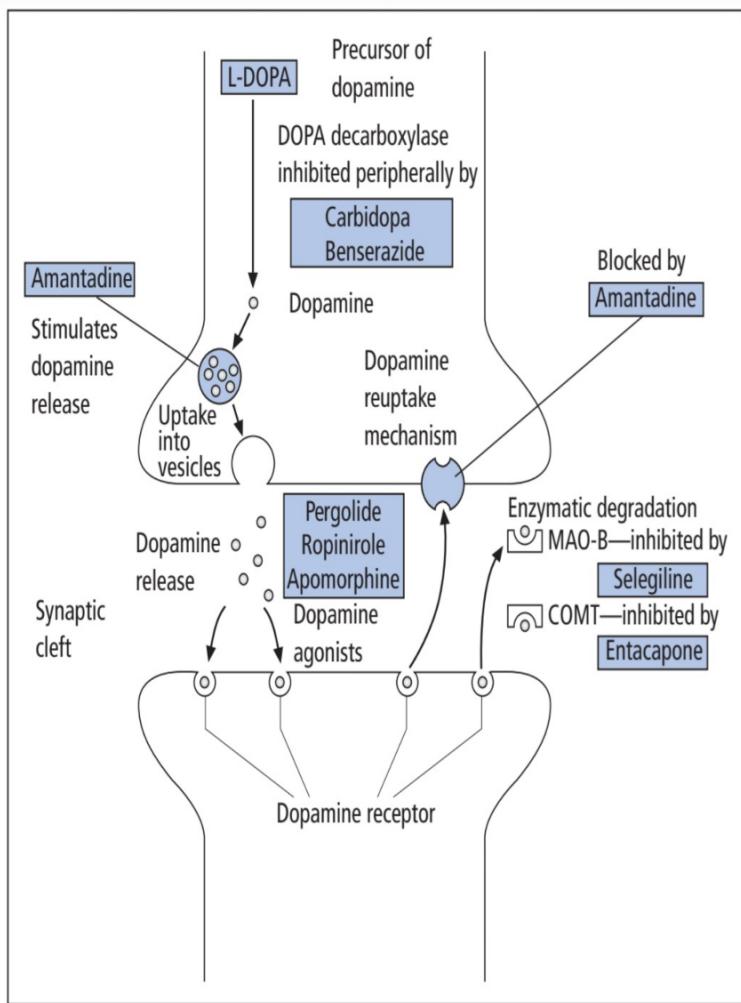
- TRAP (tremor, rigidity, akinesia, and postural instability)
- Tremor: resting , pill rolling , worse with distraction , asymmetric



non-motor symptoms :

- (REM) sleep behaviour disorder, failure to induce Antonia during sleep
- depression
- hallucinations
- Psychosis
- Dementia
- Sleep disorder

Autonomic symptoms: greasy seborrheic skin ,Constipation, bladder disturbance,Anosmia



Treatment

Levodopa combined with carbidopa(inhibitor of peripheral dopa decarboxylase)
-Later >dyskinesias

MAO-B inhibitors

- rasagiline and selegiline
- dopamine agonists**
- pramipexole and ropinirole are
- mild or early PD
- Rotigotine patch form

Anticholinergics

- benztrapine and trihexyphenidyl are used to treat tremor

Amantadine

- dyskinesias and dystonia

COMT inhibitors

- entacapone
- Patients with wearing off

Deep brain stimulation of the subthalamic nucleus (STN)

