# Parkinson’s disease

# Definition

**Progressive neurodegenerative disease, results from loss of dopamine-containing neurons in substantia nigra of midbrain.**

**Onset is usually after age of 50.**

**Parkinson disease is essentially a clinical diagnosis, laboratory tests play no role is diagnosis.**

**It is a movement disorder disease .**

- While the idea of initiating a movement starts in the motor cortex, The basal ganglia receives signals from the overlying motor cortex, processes that information before sending the signal on down the spinal cord to the muscles that are going to perform the movement. (make movement +don't make unwanted movement)
- The processing of movement in the basal ganglia involves a direct pathway and an indirect pathway. In simple terms, the direct pathway encourages movement, while the indirect pathway does the opposite (inhibits it). The two pathways work together like a carefully choreographed symphony.
- Under normal circumstances the dopamine neurons release dopamine in the basal ganglia that excites the direct pathway and inhibits the indirect pathway (to make sure we don't inhibit muscles too much). This acts as a kind of lubricant for movement.

With the loss of dopamine neurons in Parkinson's disease, however, there is an increased amount of activity in the indirect pathway. As a result, the thalamus is kept inhibited. With the thalamus subdued, the overlying motor cortex has trouble getting excited, and thus the motor system is unable to work properly. And this is the reason why people with Parkinson's disease have trouble initiating movement.

((cant initiate movement in direct pathway Cant prevent excessive reduction in indirect pathway))

Results in >> Slowing down movement or loss of movement))

# Pathophysiology

- In Parkinson’s disease the dopaminergic neurons projecting from substantia nigra into striatum of the basal ganglia are affected.
- Dopamine is an inhibitory neurotransmitter, with the loss of dopamine inhibitory influences are lost and excitatory mechanisms are unopposed , leading to overstimulation of the neurons in the basal ganglia causing the symptoms of the disease.

# Movement signs and symptoms

## 1-Tremor:

- **Involuntary repetitive rhythmic movement.**
- **Primarily affects the hands (described as pill rolling), but it may involve upper and lower limbs.**
- **Present at rest(resting tremor) and exacerbated by anxiety or stress.**
- **Improves and may disappear on action.**

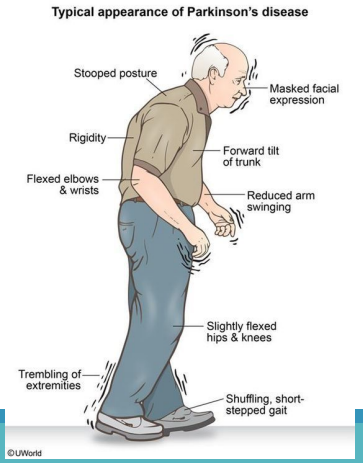
# Movement signs and symptoms

## 2-Rigidity:

Lead pipe rigidity: muscular rigidity that produces steady resistance to passive movement of the limbs.

Cogwheel rigidity: Resistance starts and stops (jerky movements) as the limb is moved through its range of motion.

- Rigidity effects posture and person starts to bend over time until stooped posture.
- It effects all muscles including facial muscles so patients will experience loss of facial expressions **(masked faces).**



# Movement signs and symptoms

## 3-Bradykinesia:

It is the most disabling manifestation of Parkinson’s disease.

Patients with Parkinson’s disease may complain that they have “ slowed down”

Physically.

Difficulties along the whole course of the movement process, from planning to initiation to execution, leading to difficulty with everyday tasks, e.g. dressing, eating, bathing.

# Movement signs and symptoms of Parkinson's disease

- **Patients gait :**

**1-Pt is adopted flexed (apelike)**
**2-Unable to maintain normal stance in response to pressure from behind they may fall forward propulsion or from in front falling backward retropulsion**
**3-Freezing : pt unable to start the walking or unable to turning ,they will stop in their place unable to move themselves**
**4-Steps are small and shuffling (festinant gait)**
**5-Normal arm swing on walking is lost**

# Movement signs and symptoms of Parkinson's disease

## 4-Postural instability

**Unstable and imbalance when standing because of (postural reflexes) stop working**
**Increase risk of falling**

- **Other symptoms:**

**Dysarthria**
**dysphagia(even his own saliva result in sialorrhoea) Quite monotonous speech(same tone when he is happy, sad, angry ..)**
**Micrographia (small hand writing)**

***Early in Parkinson these physical signs are typically markedly asymmetrical even unilateral ***

# Non-movement symptoms of Parkinson's disease

Personality changes in (early stages)
Depression
Apathetic
Anxiety
Panic
Hallucinations

Sleeping problems
Insomnia

Impairment of cognitive function
Dementia (advanced stages)

# Cont..

Autonomic Dysfunction

Constipation
Increased sweating
Orthostatic hypotension
Oily skin
Bladder disturbance

**Symptoms of Parkinson's disease appear when about 60-80% of nigrostriate dopaminergic neurons have been lost**

# Aetiology

- About 80% - 85% of patients with Parkinson disease Have what is called primary parkinsonism or Idiopathic Parkinson's disease
- Risk factors

-**Genetic**: 10 – 15% cases are familial

Some genes affect the risk of developing Parkinson's disease, but they do not cause symptoms.

The gene known as ***GBA*** is the most common of these. This gene makes the enzyme glucocerebrosidase.

NOTE: In most cases, the condition does not seem to run in families.

-**Age** (>60 years Old)

-**Sex**: males > females

- **Environmental Factor** is weak associated with Disease

eg: exposure to wood pulp and pesticides

# Secondary parkinsonism

Atypical parkinsonism, They are also called akinetic-rigid syndromes

They have the same clinical features as Parkinson Disease

(Bradykinesia, Rigidity, tremor) but the cause of the disease tend to be Known .

The Key difference that Primary Disease Patient tends to respond well to drugs that work by increasing or substituting dopamine molecules in the brain But Patient with secondary type doesn’t respond well to dopaminergic medications such as levodopa.

# Causes of an akinetic-rigid syndrome

- Inherited
  - Wilson disease
- Traumatic
  - "punch-drunk syndrome" chronic head injury in boxers
    patients have parkinsonian features often in combination with cerebellar damage a cognitive defect
- Inflammatory: postencephalitic parkinsonism
- Neoplastic : Tumours of the basal ganglia presenting with contralateral hemi parkinsonism (rare)

# Cont..

- Vascular : multiple lacunar infracts may occasionaly result in pseduparkinsonism features but usually associated with pyramidal and cognitive dysfunction

- Drugs: Antipsychotics

  Antiemetics

  Amiodarone

- Toxins : MPTP (a synthetic heroin by-product) , manganese ,Chronic Carbonic monoxid poisoning

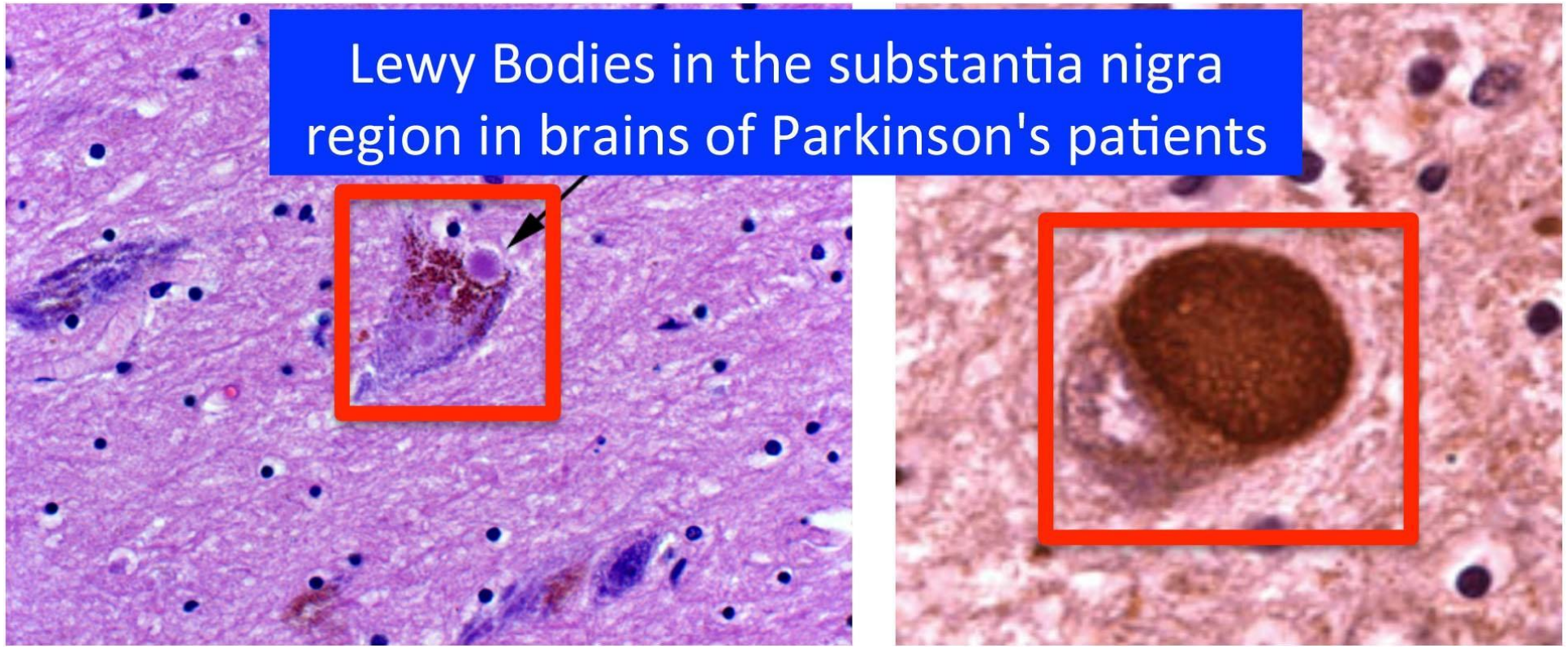
# Diagnosis

Diagnosis based on **clinical features** (asymmetry of signs at onset is important)

Patient shows **response to l-dopa treatment** (important discrimination from idiopathic akinetic-rigid symptoms)

Brain CT and MRI are **unhelpful**

In autopsy you will find **pallor** of substantia nigra and **lewy bodies** (intracytoplasmic esinophilic inclusions)


Lewy Bodies in the substantia nigra region in brains of Parkinson's patients

# Course and prognosis

Parkinson's disease is a progressive it may be divided into three stages:

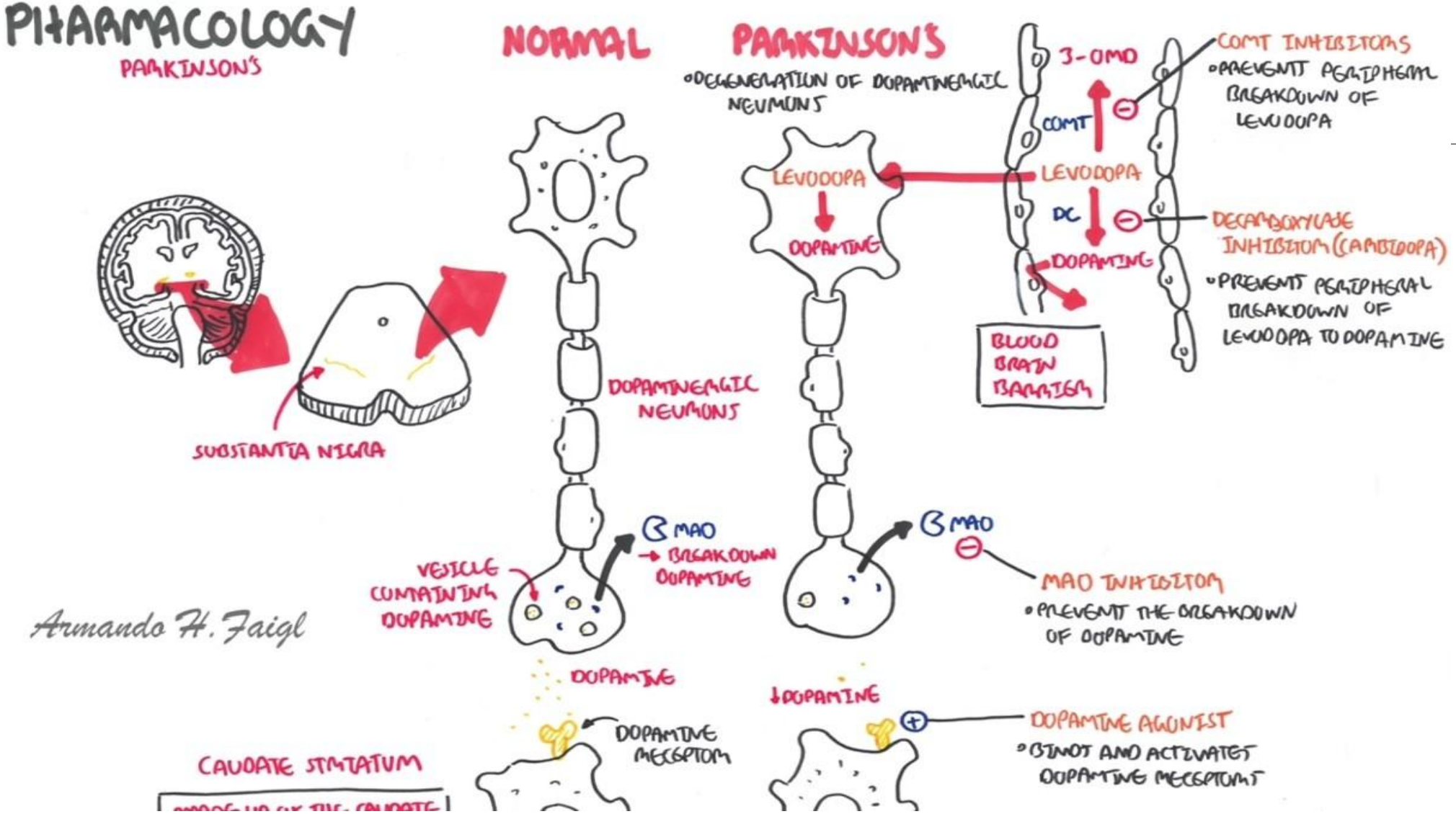
**Early-stage** : When symptom is good

**Mid-stage** : When motor fluctuations and dyskinesias develop

**Late-stage** : when treatment-resistant features such as dementia and falls occur.

**Untreated patients** with threat to life from the risk of bronchopneumonia, septicemia or pulmonary embolus after 7-10 years of disease on average

# Treatment of Parkinson



# Treatment

No cure , goal is to delay disease progression and relieve symptoms

Antiparkinsonian Drugs aim to restore DA/Achbalance

1. Decrease Cholinergic Activity

Anticholinergics.

Benzhexol - BenztropineII.

## 2. Increase Dopaminergic Activity

## Dopaminergic Drugs

1. Levodopa. (DA precursor)
2. Bromocriptine- pramipexoleropinirole. (D2 agonists)
3. Amantadine. (increase DA release)
4. Entacapone. (decrease DA degredation)
5. Selegiline (decreasecDA degredation)
6. (DA is not used as it cannot crossBBB)

levodopa (L-dopa)

(Mainstay of Therapy)

a. L- dopa is a DA precursor that crosses BBB & is decarboxylated to DA inthe CNS.

b. It is given with the peripheral decarboxylase inhibitor; carbidopa as L-dopa/carbidopa (sinemet).

c. Carbidopa prevents peripheral decarboxylation of L-dopa to DA dose of L-dopa by 75%.

d. (without carbidopa, 99% of L-dopa is converted to DA peripherally which cannot cross BBB) and also cabidopa decreas peripheral side effects of L-dopa

e. L-dopa is the most effective antiparkinsonian drug; improves all features especially bradykinesia, but benefits decreasin a few years due to gradual neuronal degeneration

f. better reserved till symptoms becometroublesome.

## Adverse Effects & Contraindications (CI) of L-dopa

A. Peripheral (due to DA peripherally; - with carbidopa)

1. GIT: Nausea - vomiting CI: active peptic ulcer.

2. CVS: postural hypotension & arrhythmias (CA).

B. Central (due to DA centrally; with carbidopa)

1. Dyskinesia (choreoathetosis; head, lip or tongue movements).

2. Confusion, psychosis; hallucinations; Cl: psychosis.

C. Fluctuations in Response (due to short t 2 & fluctuation in L-dopa level??)

1. On-off effect (sudden swings from mobility to bradykinesia).

2. End-of-dose akinesia: gradual loss of effect (wearing off) before next dose

## To decrease fluctuation in response

1. Entacapone or selegiline are added to L-dopa/carbidopa (delay break down of dopamin)

2.Shortening interval between doses

3. Using slow release preparations of L dopa/carbidopa.

## Parkinson Plus(Like Parkinson's) BUT:

1-More severe and higher mortality

2-Symmetrical Presentation (Bradykinesia and Rigidity)

3-No tremor

4-Increase d orthostatic failure or Postural Instability

5-Dementia

(If 4 & 5 were early symptoms it's Parkinson Plus, if they were late symptoms it's Parkinson's)

6-Poor response to L-Dop

# THANK YOU