

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

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والصلاة والسلام على
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parkinsonism

ارائه توسط دکتر مهدی شفیعی ثابت
عضو هیات علمی گروه پزشکی خانواده
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Clinical Dx

- ▶ History ----> understanding the nature of the patient's problem
- ▶ Ph/E -----> Etiologic hypothesis
- ▶ Para clinic --> Confirm etiology ----> treatment -----> Increased quality of life and health

Clinical DX in neurologic problems

History -----> understanding the nature of the patient's problem and **localization**

Neurologic exam -----> **Confirm localization**

Ph/E -----> Etiologic hypothesis

Paraclinic -----> confirm etiology

Physical examination

- ▶ Looking
- ▶ Touching
- ▶ Percussion
- ▶ Auscultation

Neurological Examination

- ▶ **Mental Status and language**
- ▶ **Cranial nerves**
- ▶ **Motor system**
- ▶ **Sensory system**
- ▶ **Stance and gait**

Motor system Examination

- ▶ **Looking:** abnormal movements(location, rhythm, frequency, amplitude, association with activity and posture and emotion)
- ▶ **Touching:** muscle bulk, muscle tonus, strength, coordination
- ▶ **Percussion:** fasciculation, reflexes
- ▶ **Stance:** posture, abnormal movements, Romberg test, pull-test
- ▶ **Gait:** rhythm, speed, coordination, arm swing, abnormal movements, tandem gait

Localization of Motor system dysfunction

- ▶ Upper motor neuron lesions
- ▶ Movement disorders (Extrapyramidal disorders)
- ▶ Ataxia (disequilibrium)
- ▶ Lower motor lesions

CNS lesions

- ▶ **Cortex**
- ▶ **White matter**
- ▶ **Diencephalon**
- ▶ **Basal ganglia**
- ▶ **Cerebellum**
- ▶ **Spinal cord**

Lower motor lesions

- ▶ Anterior horn cell
- ▶ Radicles
- ▶ Plexus
- ▶ Neurons
- ▶ Neuromuscular junctions
- ▶ muscles

Etiologic Dx

- ▶ Cerebrovascular diseases (ischemic or hemorrhagic, cerebrovascular thrombosis)
- ▶ Disturbances of CSF and its circulation (hydrocephalus, NPH, low-pressure syndrom)
- ▶ Neoplastic disorders (primary tumors or metastatic, paraneoplastic disorders)
- ▶ Infectious diseases (bacterial, viral, fungal, parasitic, prion)
- ▶ Inflammatory-immune diseases (demyelinating diseases, vasculitis)

- ▶ Toxic disorders (due to toxins, drugs and other chemical agents)
- ▶ Acquired metabolic disorders and nutritional deficiency
- ▶ Traumatic insults
- ▶ Congenital-Genetic diseases of nervous system (Developmental , Inherited metabolic diseases)
- ▶ Degenerative disorders (dementia, movement disorders)
- ▶ Functional disorders

Parkinsonism

- ▶ 1) Tremor at rest
- ▶ 2) Brady kinesia _ Hypo kinesia
- ▶ 3) Rigidity
- ▶ 4) Flexed posture
- ▶ 5) Loss of postural reflexes
- ▶ 6) Freezing

Definite Dx is clinical: At least two of six which should include at least one of “1 & 2”

Rest Tremor

- ▶ Frequency of 4 to 5 Hz
- ▶ Is present in: the limbs, lips, chin and tongue
- ▶ In the limbs: almost always distally; classic “pill-rolling”, disappears with action but reemerges as the limbs maintain a posture, in hands increases with walking (may be an early sign) , worsens with stress.

Bradykinesia

- ▶ The most common feature of parkinsonism
- ▶ Slowness of movement, difficulty initiating movement, and loss of automatic movement
- ▶ Can affect;

Face: masked facies or hypomimia, decreased frequency of blinking

Speech: hypophonia, monotonous tone of voice, aprosody(lack of inflection), dysarthria, tachyphemia(running the words together)

Swallow: drooling saliva

**Hands: difficulty in shaving, brushing,
combing hair, buttoning,
micrographia(small and slow handwriting)**

Trunk: difficulty rising from a chair

**Gait: slow with a shortened stride length
and a tendency to shuffle, decreased arm
swing.**

Rigidity

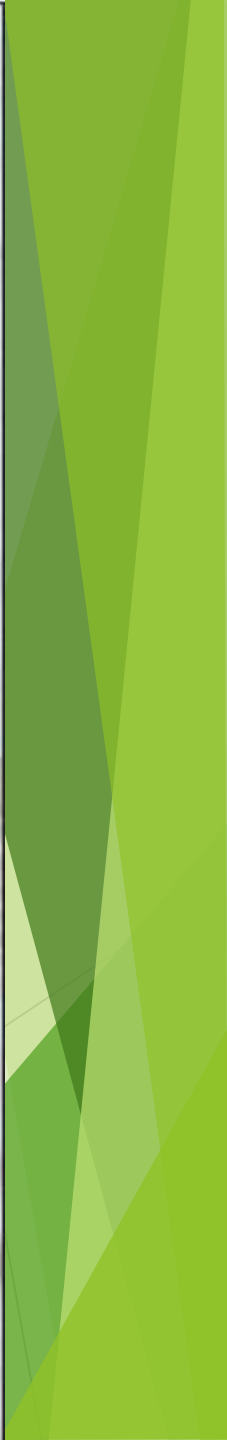
- ▶ An increased muscle tone in passive movement of patient's limbs, neck or trunk.
- ▶ In all direction
- ▶ Cogwheel
- ▶ Rigidity in limb increases when another limb is engaged in voluntary active movement.

Flexed posture

- ▶ Commonly begins in the arms, spreads to involve the entire body.
- ▶ Head is bowed, the trunk is bent forward, the back is kyphotic, the arms are held in front, the elbows, hips, and knees are flexed
- ▶ Deformities of the hands include ulnar deviation of the hands, flexion of the metacarpophalangeal joints and extension of the interphalangeal joints.
- ▶ Deformities of feet include inversion and dorsiflexed big toes (hallux toe).







Loss of postural reflexes

- ▶ **Stance: sitting en bock, inability to stand unassisted**
- ▶ **Gait: festination, leads to falling**

Freezing (motor block)

Suddenly transient inability to perform active movements, lasting usually no more than several seconds and includes:

Walking: occurs when patient begins to walk(start hesitation), attempts to turn while walking, approaches a destination(destination hesitation) and inability to deal with perceived barriers or time-restricted activities.

Eyelid: apraxia of lid opening or levator inhibition

Speaking: palilalia

writing

Biochemical pathology

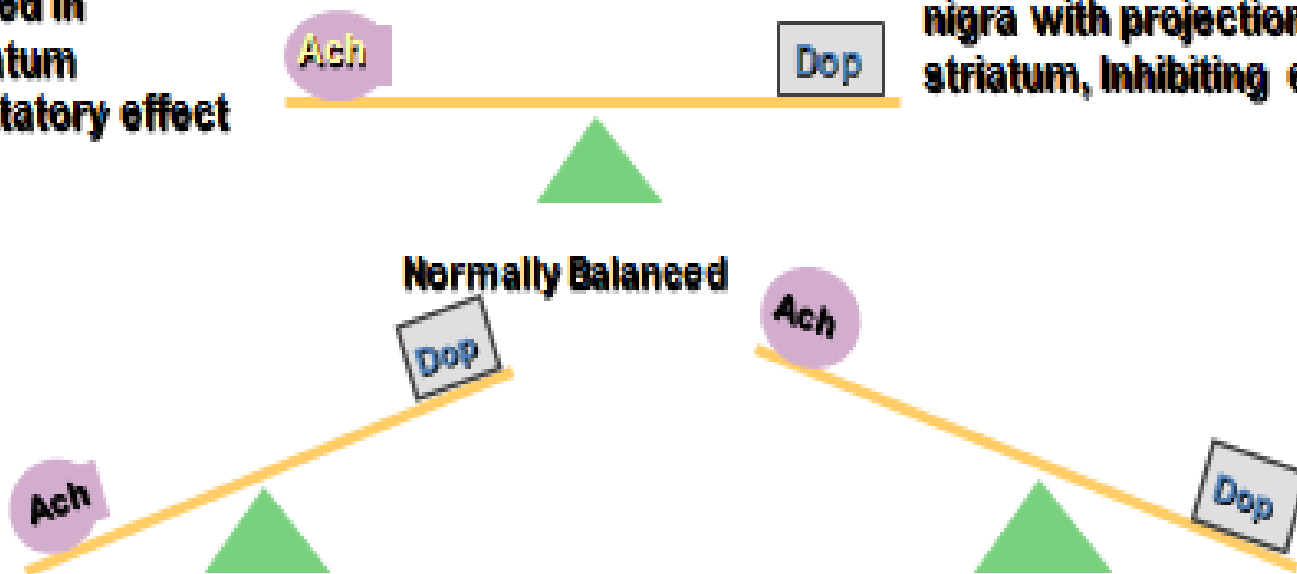
Core biochemical pathology is decreased dopaminergic neurotransmission in the basal nuclei -----> disinhibition of subthalamic nucleus and medial Globus pallidus-----> decreased VA/VL drive to cortex -----> less motor activity;

- ▶ 1] Degeneration of nigrostriatal dopamin system
- ▶ 2] Degeneration of the striatum with loss of dopamine receptor
- ▶ 3] Drug induced: a)blockade of dopamine receptor or ,
b)depletion of dopamine storage.

Balancing Acts.....

Acetylcholine:
Synthesized and stored in striatum
Excitatory effect

Dopamine:
Synthesized by substantia nigra with projections in striatum, Inhibiting effect



Ach > Dop = Parkinson's

(Block Ach with anticholinergic drugs or
Increase Dopamine)

Ach < Dop = Chorea

(Reduce dopamine or block
dopamine receptors)

Classification of major parkinsonian syndromes

- ▶ Primary parkinsonism:

parkinson disease-sporadic and familial

- ▶ Secondary Parkinsonism:

Vascular; multi-infarct state, Hypoxia, Hemiatrophy-hemiparkinsonism, Hydrocephalus; NPH, Tumor, Infectious; postencephalitic, Toxin: Mn, CO, MPTP, cyanide, Metabolic; parathyroid dysfunction, Trauma

► **Parkinson-plus syndromes:**

Cortical-basal ganglionic degeneration, Dementia syndromes (AD, DLB dis, FTD), MSA syndromes (Striatonigral degeneration, Shy-drager syndrome, Sporadic olivopontocerebellar degeneration, motor neuron disease-parkinsonism), Progressive pallidal atrophy, PSP, Lytico-Bodig (Guamanian parkinsonism-dementia-ALS)

► **Heredodegenerative disease:**

Hallervorden-Spatz disease, Huntington disease, Lubag (X-linked dystonia-parkinsonism), Mitochondrial cytopathies with striatal necrosis, Neuroacanthocytosis, Wilson diseases

History of Parkinson's Disease

- ★ **First described in 1817 by an English physician, James Parkinson, in “An Essay on the Shaking Palsy.”**
- ★ **The famous French neurologist, Charcot, further described the syndrome in the late 1800s.**

James Parkinson, 1817

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Famous Faces of Parkinson



Michael J. Fox



Muhammad Ali



Katharine Hepburn



Pope John Paul II



Mao Tse Tung

Stages of PD

- Initially, symptoms are typically mild and on one side of the body
- (Hemi parkinsonism).
- Tremors are usually the first symptom to appear, but not all patients develop a tremor.
- Over time, the tremor usually becomes worse and patients develop bradykinesia (slowness of movement) and akinesia (lack of movement), rigidity, and difficulty with balance.

Stages of PD

- Symptoms eventually spread to the other side of the body, affecting both the UE and LE.
- Other symptoms can develop such as shuffling gait, freezing episodes, “poker face” (lack of facial expression), drooling, and muffled speech.
- Later stages may include a severe loss of mobility and independence.
- This can lead to the most serious risk of PD, bronchopneumonia, which is the leading cause of death.

Clinical features of PD

- Resting tremor: Most common first symptom, usually asymmetric and most evident in one hand with the arm at rest.
- Bradykinesia: Difficulty with daily activities such as writing, shaving, using a knife and fork, and opening buttons; decreased blinking, masked facies, slowed chewing and swallowing.
- Rigidity: Muscle tone increased in both flexor and extensor muscles providing a constant resistance to passive movements of the joints; stooped posture, anteroflexed head, and flexed knees and elbows.

Additional clinical features of PD

- Postural instability: Due to loss of postural reflexes.
- Dysfunction of the autonomic nervous system:
 - . Impaired gastrointestinal motility
 - . Bladder dysfunction
 - . Sialorrhea
 - . Excessive head and neck sweating
 - . Orthostatic hypotension.
- Cognitive impairment
- Psychiatric Symptoms

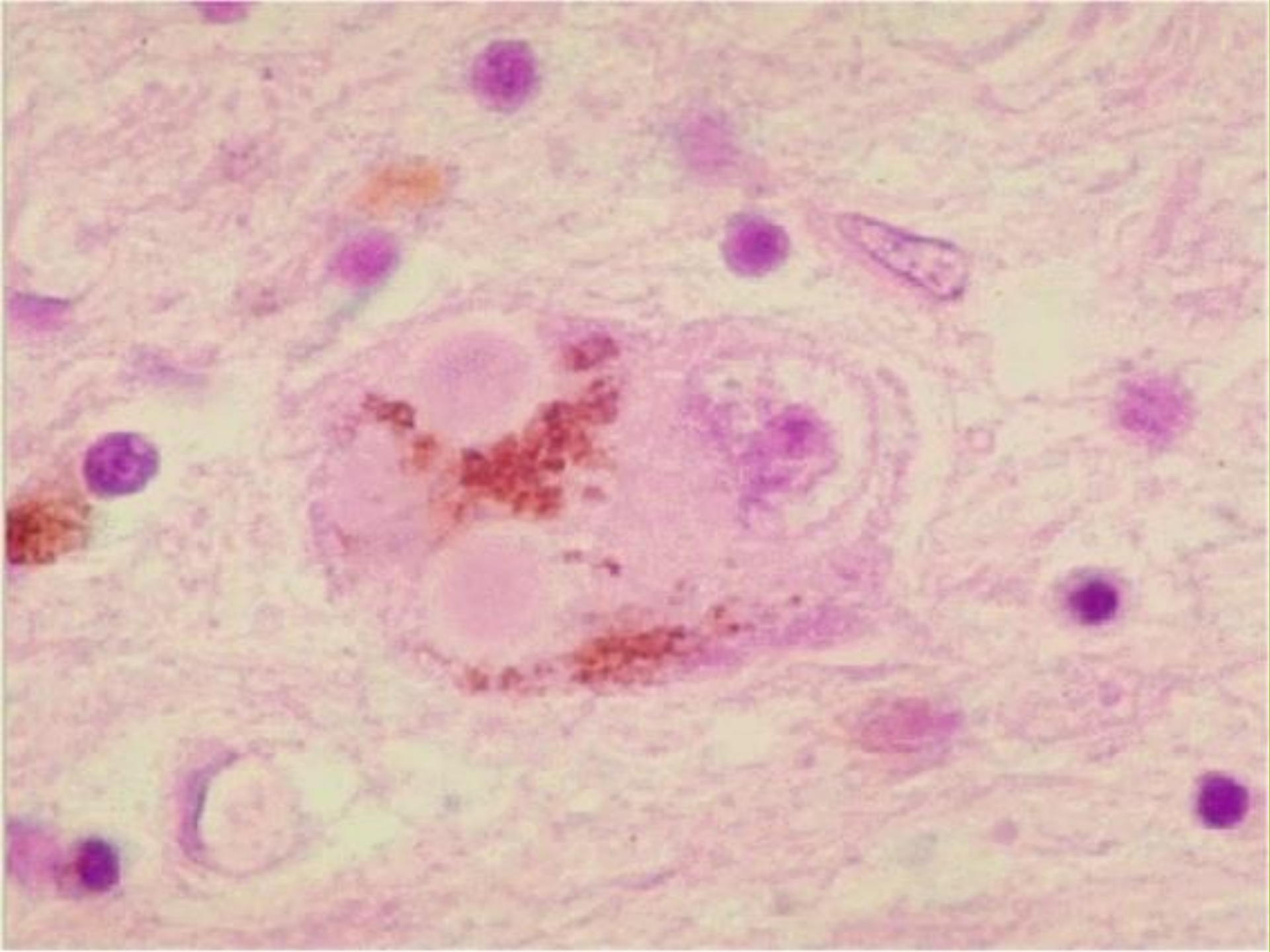
Neuropathology

- ▶ Degeneration of the neuromelanin containing neurons in the brain stem specially in the substantia nigra pars compacta and locus ceruleus
- ▶ Many of surviving neurons contains eosinophilic cytoplasmic proteinaceous inclusions known as Lewy bodies the pathologic hallmark of the disease.
- ▶ Lewy body First described in 1912 by a German neuropathologist, Friedrich Lewy.

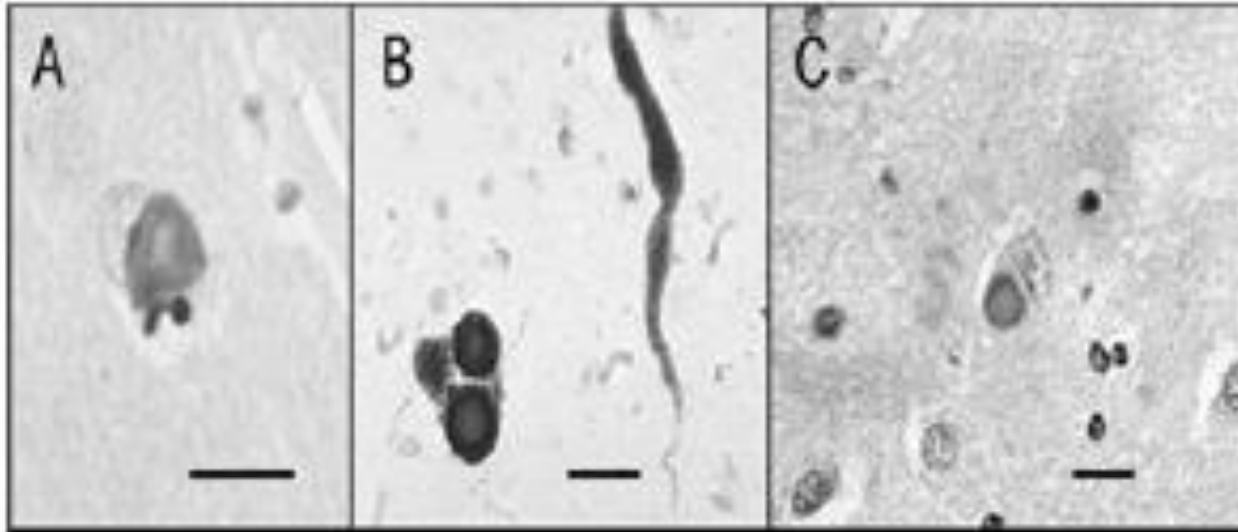
Neuropathology of PD:

Where are Lewy Bodies?

- Not limited to Substantia Nigra also in found in:
- Locus coeruleus
- Motor nucleus of the Vagus nerve
- Hypothalamus
- Nucleus basalis of Meynert
- Cerebral cortex,
- Olfactory bulb
- Autonomic nervous system.



Lewy Body



✦ **Confined largely to neurons;
glial cells only rarely affected.**



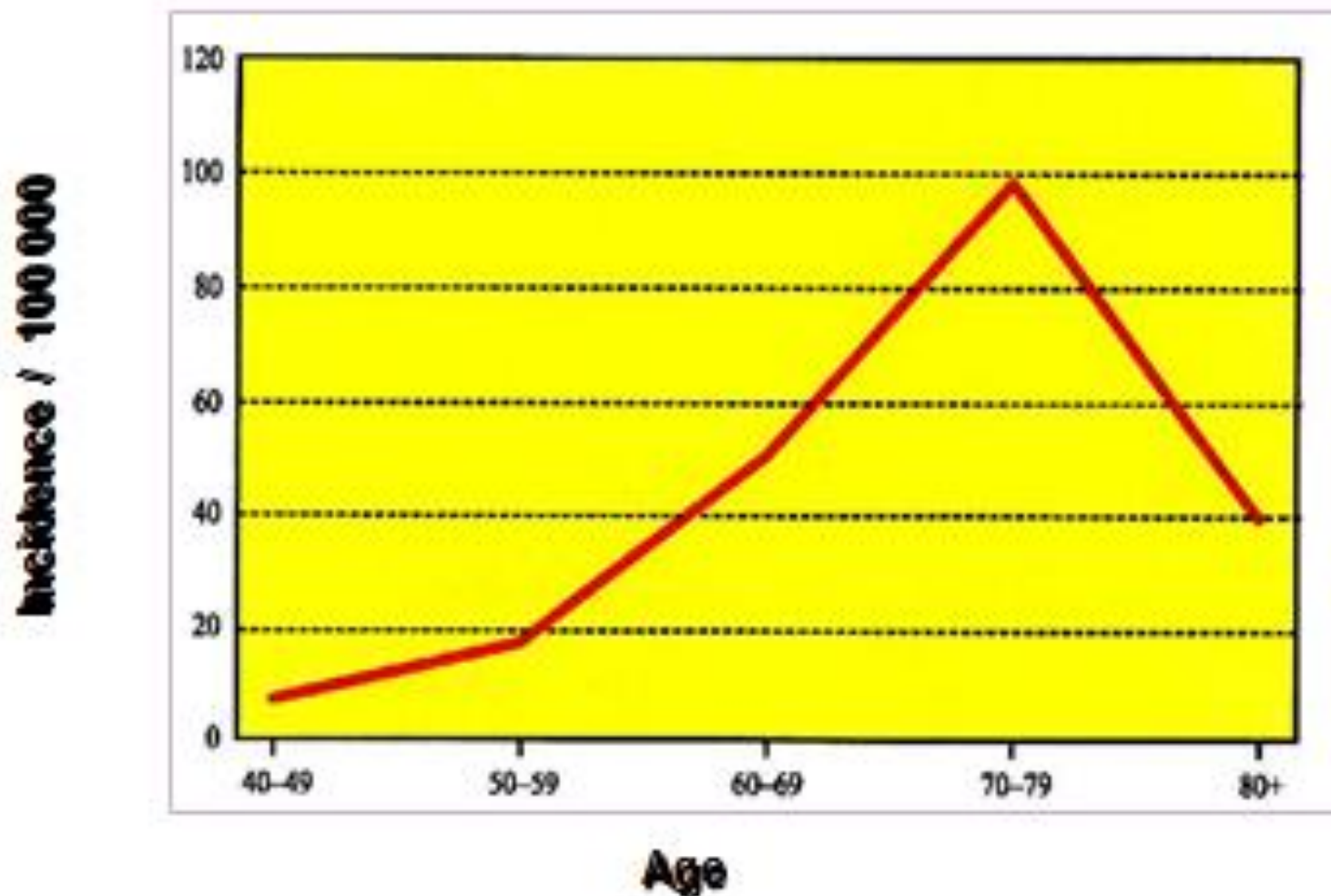
F.H. Lewy (1885-1950)

Description des corps de Lewy : F.H. Lewy 1912

Epidemiology

- ▶ Prevalence rates in men are slightly higher than in women; reason unknown, though a role for estrogen has been debated.
- ▶ May be less prevalent in China and other Asian countries, and in African-Americans.
- ▶ Average age of onset is 60 y/o.

Incidence of PD



- ▶ **Juvenile parkinsonism: onset at younger than 20 years; primary(usually familial) or heredodegenerative diseases(such as Huntington disease and wilson disease)**
- ▶ **Young onset PD: onset of primary parkinsonism between 20 and 40 years**