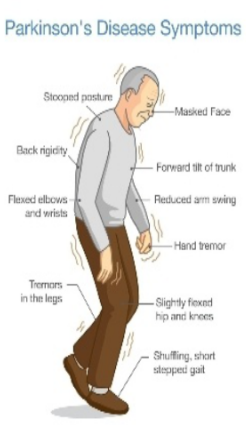
Disease	Feature	Cause	Sign & Symptoms	Histology & Microscopically	Other
Parkinson Disease (PD) 	• Neurodegenerative disease • prominent **hypokinetic movement disorder** that is caused by **loss of dopaminergic neurons** from the **substantia nigra** • Complex **progressive** neurodegenerative disease characterized by tremor, rigidity, and bradykinesia, with postural instability	• **Protein (α-synuclein) aggregation**, mitochondrial abnormalities, & neuronal loss in the **substantia nigra & elsewhere in the brain** • Due to **defects in autophagy & lysosomal degradation** • **Dopaminergic neurons degeneration**→ reduction in **dopamine** in the **striatum**	• Gradual slowness of spontaneous movement. • loss of postural reflexes • poor balance and motor coordination 1. **Triad** of(tremor ,rigidity & , bradykinesia), in the absence of toxic injury or other etiology. 2. progresses over 10 to 15 years ,eventually producing severe motor slowing→ near immobility. 3. Death usually is the result of **aspiration pneumonia** or **trauma** from falls caused by postural instability.	1. Dgeneration and loss of nigrostriatal dopaminergic innervation. 2. Neuronal inclusions containing α-synuclein (Lewy bodies)(insoluble cytoplasmic protein aggregates)(single or multiple, cytoplasmic, eosinophilic, round inclusions (dense core with pale halo))	• Second most common neurodegenerative disease after Alzheimer's disease • Alpha-synuclein is a protein which is abundant in dopamine producing nerve cells, normally cleared by autophagy
Huntington Disease (HD) 	• **Autosomal dominant** disease of **progressive movement disorders** & **dementia** caused by **degeneration of the striatal neurons** • **involuntary jerky movements** (dystonic sometimes) of all parts of the body→ **Chorea**.	• **Accumulation of Huntington protein CAG** trinucleotide repeat in a gene on **ch. 4**, encodes the **protein Huntingtin mHTT** (potential injuries) • Normal alleles contain 6 to 35 copies → larger numbers of repeats resulting in earlier-onset disease .	• Involuntary jerky movements (dystonic sometimes) of all parts of the body→ **Chorea**. • **Presymptomatic phase :** Neuropsychiatric : irritability ,disinhibition . • **Diagnostic phase:** 1. Hyperkinetic phenotype: prominent chorea (uncontrollable jerking movements) and dystonia (involuntary muscle contractions, often painful) 2. Hypokinetic phenotypes : bradykinesia(slowness of movement) ,gait disturbance ,imbalance 3. Cognitive dysfunction : poor executive function and speech impairment 4. Neuropsychiatric : depression and suicidal ideation	• The **brain** is **small** and shows striking **atrophy** of the **caudate nucleus** and the **putamen**. • The **lateral** and **third ventricles** are **dilated**. • **Profound shrinkage** of **cortex** and **caudate**	• Usually progressive • Death after an average 15 years. 
Amyotrophic Lateral Sclerosis (ALS)	• The **most common** neurodegenerative disease • affecting the motor system • A chronic, progressive disorder of **loss of upper motor neurons** in the cerebral cortex (Betz cells) and **lower motor neurons** in the spinal cord and brainstem	• Mutations in the superoxide dismutase gene ,**SOD1**, on **chr. 21** • Abnormal misfolded forms of the SOD1 protein are generated→ trigger 'unfolded protein response' in cells→ **apoptosis**. 1. Death of **upper motor neurons**, causes degeneration of the descending corticospinal tracts. 2. Death of **anterior horn cells (lower motor neurons)** with loss of innervation causes atrophy of skeletal muscles.	• Motor neuron loss results in **progressive** and **irreversible** loss of motor function ,muscle weakness and wasting and ultimately death, usually due to respiratory failure • **Upper motor neuron** 1. Brisk tendon reflexes 2. Spasticity • **Lower motor neuron** 1. Skeletal muscle weakness and wasting 2. Fasciculations