Pathophysiology of common diseases

Parkinson's Disease

Parkinsonism

- Parkinsonism is a clinical syndrome characterized by a group of movement abnormalities including tremor, bradykinesia, rigidity, and postural instability.
- It can result from a variety of neurodegenerative diseases, secondary causes, or medication side effects, not just Parkinson's disease.
- Parkinson's disease is the most common form of Parkinsonism, but there are several other types.

Causes

1. **Idiopathic Parkinsonism (Parkinson's Disease):**
   - Most common, due to degeneration of dopaminergic neurons in the substantia nigra.
2. **Atypical Parkinsonian Disorders:**
   - **Multiple System Atrophy (MSA)**
   - **Progressive Supranuclear Palsy (PSP)**
   - **Corticobasal Degeneration (CBD)**
   - **Dementia with Lewy Bodies (DLB)**
3. **Secondary Parkinsonism:**
   - **Drug-induced:** Antipsychotics (e.g., haloperidol), antiemetics (e.g., metoclopramide).
   - **Toxins:** Carbon monoxide, manganese, MPTP.
   - **Vascular Parkinsonism:** Multiple small strokes affecting basal ganglia.
   - **Trauma-related:** Repeated head injury (e.g., in boxers).
4. **Other Neurodegenerative Conditions:**
   - Including Alzheimer's disease and frontotemporal dementia in some cases.

Symptoms

1. **Motor Symptoms:**
   - **Tremor:** Often less prominent or absent in atypical forms.
   - **Bradykinesia:** Slowness of movement.
   - **Rigidity:** Stiffness of the limbs and trunk.
   - **Postural Instability:** Impaired balance and frequent falls.
2. **Non-Motor Symptoms:**

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- Cognitive decline, especially in dementia with Lewy bodies.
- Mood disturbances: Depression, apathy, anxiety.
- Sleep disturbances: REM sleep behavior disorder, insomnia.
- Autonomic dysfunction: Constipation, urinary incontinence, orthostatic hypotension.
- Visual hallucinations (especially in DLB).
- Speech and swallowing difficulties.

Diagnosis

1. Clinical Evaluation:

- Based on neurological examination and symptom history.
- Atypical features such as early falls, rapid progression, and poor levodopa response suggest non-PD forms.

2. Imaging Tests:

- **MRI:** To exclude structural causes (vascular damage, tumors).
- **DaTscan:** Helps assess presynaptic dopaminergic function.
- **FDG-PET or SPECT:** May be used to support diagnosis in atypical parkinsonism.

3. Levodopa Challenge Test:

- Parkinson's disease typically shows good response.
- Poor or transient response may suggest atypical parkinsonism.

Pathophysiology of Parkinsonism

1. Dopaminergic Deficiency:

- Common to most forms due to loss or dysfunction of neurons in the nigrostriatal pathway.
- Leads to reduced dopamine in the basal ganglia, causing motor symptoms.

2. Variability in Atypical Forms:

- **MSA:** Involves glial cytoplasmic inclusions and widespread autonomic failure.
- **PSP:** Affects the brainstem, leading to vertical gaze palsy and early falls.
- **CBD:** Asymmetric rigidity, apraxia, and cortical signs.
- **DLB:** Shares features with PD but has prominent early dementia and hallucinations.

3. Lewy Bodies:

- Present in PD and DLB.
- Composed of alpha-synuclein protein.

4. Neuroinflammation and Mitochondrial Dysfunction:

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- Oxidative stress and inflammation contribute to neuronal death in several types.

Treatment

1. Medications:

- **Levodopa:** Effective in Parkinson's disease; often less effective in atypical forms.
- **Dopamine Agonists:** May be used early or adjunctively.
- **MAO-B Inhibitors:** Help increase dopamine availability.
- **Amantadine:** Useful for dyskinesia or some symptomatic relief.
- **Anticholinergics:** Sometimes used for tremor (cautiously in elderly).
- **Supportive Medications:** For depression, sleep, constipation, etc.

2. Surgical Treatment:

- **Deep Brain Stimulation (DBS):** Effective in Parkinson's disease but **not recommended for atypical Parkinsonism** due to poor outcomes.

3. Physical Therapy:

- Focuses on improving mobility, gait, balance, and posture.

4. Occupational Therapy:

- Aims to help with activities of daily living and adaptations.

5. Speech and Swallowing Therapy:

- Address hypophonia (low voice), speech clarity, and dysphagia (swallowing difficulties).

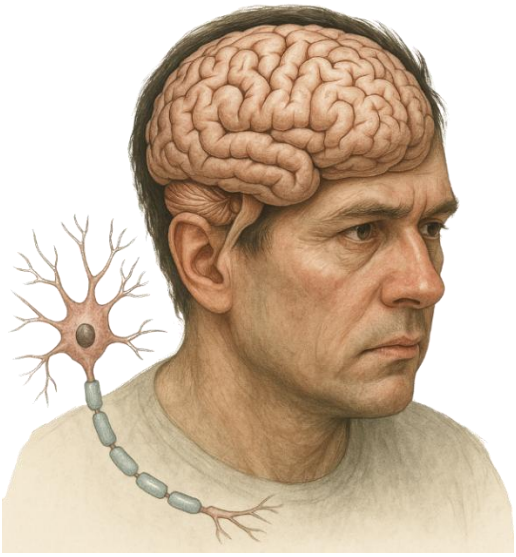
6. Multidisciplinary Care:

- Essential in managing complex and progressive symptoms, especially in atypical cases.

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Schizophrenia

- Schizophrenia is a chronic and severe mental health disorder that affects how a person thinks, feels, and behaves.
- It is characterized by episodes of psychosis, including hallucinations, delusions, and disorganized thinking.



Causes

1. **Genetic Factors**: Strong genetic component; having a close relative with schizophrenia increases the risk.
2. **Neurobiological Factors**: Abnormalities in brain structure and neurotransmitter systems, particularly dopamine and glutamate.
3. **Environmental Factors**: Prenatal exposure to infections, malnutrition, or stress, and psychosocial factors.
4. **Substance Use**: Use of psychoactive or psychotropic substances can trigger or worsen symptoms.

Symptoms

1. **Positive Symptoms**: Hallucinations (hearing voices), delusions (false beliefs), thought disorders, and movement disorders.
2. **Negative Symptoms**: Reduced emotional expression, lack of motivation, social withdrawal, and neglect of personal hygiene.
3. **Cognitive Symptoms**: Impaired executive function, attention, memory, and difficulty understanding or using information.

Diagnosis

1. **Clinical Evaluation**: Based on a detailed history and symptom assessment, often using criteria from the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition).
2. **Mental Status Examination**: To assess the individual's thought processes, mood, and behavior.

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3. **Imaging and Laboratory Tests**: To rule out other medical conditions or substance abuse that might cause similar symptoms.

Pathophysiology of Schizophrenia

1. Dopaminergic Imbalance:

- **Mesolimbic pathway** hyperactivity → **positive symptoms** (hallucinations, delusions).
- **Mesocortical pathway** hypoactivity → **negative symptoms** (apathy, social withdrawal).

2. Glutamate Hypofunction:

- Dysfunctional **NMDA receptors** disrupt synaptic connectivity and cognitive function.

3. Structural Brain Abnormalities:

- Enlarged lateral ventricles.
- Cortical thinning and reduced gray matter in prefrontal and temporal regions.

4. Neurodevelopmental Factors:

- Prenatal stress, viral infections, obstetric complications may affect brain maturation.

Treatment

1. **Medications**: Antipsychotics are the mainstay of treatment. Typical antipsychotics (e.g., haloperidol) and atypical antipsychotics (e.g., risperidone, olanzapine) help manage symptoms.
2. **Psychotherapy**: Cognitive-behavioral therapy (CBT) for psychosis, supportive therapy, and family therapy.
3. **Social and Vocational Rehabilitation**: Programs to improve social skills, vocational training, and employment support.
4. **Hospitalization**: In severe cases, to ensure the safety of the patient and others.
5. **Community Support**: Peer support groups and case management services.

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