Psychiatry disorders

Schizophrenia

Introduction / Epidemiology

- Schizophrenia is a chronic, severe psychiatric disorder characterized by disturbances in thought processes, perceptions, emotional responsiveness, and behavior.
- It is classified as a psychotic disorder and affects how a person thinks, feels, and behaves.

Epidemiology:

- **Global prevalence**: ~1% lifetime prevalence across most populations.
- **Incidence**: 15-20 per 100,000 people per year.
- **Gender**: Slightly more common in males; earlier onset in males (typically 15-25 years) than females (25-35 years).
- **Onset**: Typically late adolescence or early adulthood.
- **Course**: Chronic and relapsing in most cases, with variable functional outcomes.

Risk Factors:

- Genetic predisposition (family history).
- Perinatal complications (hypoxia, maternal infections).
- Urban upbringing.
- Substance use (especially cannabis during adolescence).
- Psychosocial stressors.

Etiopathogenesis

Schizophrenia is a multifactorial disorder resulting from the interaction of genetic, neurobiological, and environmental factors.

Genetic Factors:

- High heritability (~80%).
- Polygenic inheritance with several risk genes implicated (e.g., DISC1, COMT, NRG1, DTNBP1).
- Monozygotic twin concordance: ~50%.

Neurodevelopmental Model:

- Abnormal brain development in utero or early life leads to altered brain connectivity.
- Evidence from MRI shows:
  - Enlarged ventricles.
  - Reduced grey matter in prefrontal cortex, hippocampus, thalamus.

Neurochemical Hypotheses:

- **Dopamine Hypothesis**: Overactivity of dopamine D2 receptors in mesolimbic pathway → positive symptoms.
- **Glutamate Hypothesis**: Hypofunction of NMDA receptors → negative and cognitive symptoms.
- **Serotonin Hypothesis**: 5-HT2A receptor dysregulation modulates dopamine and glutamate systems.
- **GABA Dysfunction**: Impaired inhibitory signaling contributes to cognitive deficits.

Environmental Factors:

- Urban environment.
- Childhood trauma.
- Cannabis use (especially in genetically vulnerable individuals).

Clinical Features / Symptoms

Symptoms are categorized into positive, negative, cognitive, and affective domains.

1. Positive Symptoms (Excess or distortion of normal functions):

- Delusions (fixed, false beliefs not amenable to logic).
- Hallucinations (mostly auditory – voices commenting or conversing).
- Disorganized speech (incoherence, tangentiality).
- Grossly disorganized or catatonic behavior.

2. Negative Symptoms (Loss of normal functions):

- Affective flattening (blunted emotional expression).
- Alogia (poverty of speech).
- Anhedonia (inability to experience pleasure).
- Avolition (lack of motivation).
- Social withdrawal.

3. Cognitive Symptoms:

- Impaired attention and concentration.
- Deficits in working memory.
- Impaired executive functioning.

4. Affective Symptoms:

- Depression.
- Anxiety.

- Mood lability (seen in schizoaffective disorder).

Diagnosis & Investigations

Diagnostic Criteria (DSM-5):

- Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one must be 1, 2, or 3:
  1. Delusions
  2. Hallucinations
  3. Disorganized speech
  4. Grossly disorganized or catatonic behavior
  5. Negative symptoms
- Duration of disturbance must persist for at least **6 months**, with at least **1 month of active-phase symptoms**.

Investigations:

- **Clinical evaluation** is the cornerstone (psychiatric interview).
- **Rule out organic causes**:
  - CBC, LFTs, RFTs.
  - Thyroid function tests.
  - B12, folate.
  - Urine toxicology (rule out substance-induced psychosis).
  - HIV, syphilis serology if indicated.
  - Brain imaging (CT/MRI) if focal neurological signs or atypical presentation.
  - EEG if seizure disorder suspected.

Treatment Goals / Therapeutic Objectives

- **Acute phase**: Rapid symptom control, reduce distress, ensure safety.
- **Stabilization phase**: Maintain symptom remission, prevent relapse.
- **Maintenance phase**: Improve functioning, minimize long-term disability.
- **Recovery**: Promote social, occupational integration; improve quality of life.

Non-Pharmacological Therapy

- **Psychoeducation**: For patient and family about illness nature, prognosis, adherence.
- **Cognitive Behavioral Therapy (CBT)**: Especially for treatment-resistant symptoms.
- **Social skills training**: Improve interpersonal functioning.
- **Cognitive remediation therapy**: For cognitive deficits.

- **Family therapy**: Reduce expressed emotion and relapse rates.
- **Supported employment and vocational rehabilitation**.
- **Assertive Community Treatment (ACT)** for frequent relapsers or non-adherent patients.

Pharmacological Therapy

First-Line Drugs

- **Atypical Antipsychotics (Second-Generation)** are first-line due to lower risk of extrapyramidal side effects (EPS):
  - **Risperidone** (2–6 mg/day)
  - **Olanzapine** (10–20 mg/day)
  - **Quetiapine** (300–800 mg/day)
  - **Aripiprazole** (10–30 mg/day)
  - **Amisulpride**, **Ziprasidone**, **Lurasidone**

Mechanism & Rationale

- Atypical antipsychotics block **D2 receptors** (moderate affinity) and **5-HT2A receptors**, modulating dopamine in mesolimbic and mesocortical pathways.
- They improve positive and, to a lesser extent, negative symptoms with reduced EPS.

Alternative Drugs / Special Cases

- **Clozapine**: For treatment-resistant schizophrenia (after 2 failed adequate antipsychotic trials).
- **Haloperidol**, **Fluphenazine** (typical antipsychotics): Less favored due to EPS but may be used in specific settings (acute agitation).

Duration of Treatment

- First episode: 1–2 years of maintenance post remission.
- Multiple episodes: At least 5 years or lifelong.
- Treatment-resistant: Often lifelong.

Individualized Patient-Specific Therapeutic Plan

1. Age:

- Adolescents: Use lowest effective dose, avoid sedating drugs.
- Elderly: Start low, go slow; monitor for orthostasis, anticholinergic effects.

2. Comorbidities:

- Diabetes/dyslipidemia: Avoid Olanzapine, Clozapine.
- Obesity: Prefer Aripiprazole or Ziprasidone.

- Cardiovascular disease: Avoid QT-prolonging agents.

3. Pregnancy:

- Use lowest effective dose.
- Preferred drugs: Haloperidol, Olanzapine (relatively safer).
- Avoid Clozapine (risk of agranulocytosis, sedation in neonate).

4. Renal/hepatic dysfunction:

- Dose adjustment may be needed.
- Avoid hepatically metabolized drugs in liver dysfunction (e.g., Olanzapine).

5. Allergies:

- Monitor for signs of drug allergy; switch class if needed.

Controversies / Special Considerations

- **Clozapine** remains underused despite being the gold standard for treatment-resistant schizophrenia due to monitoring requirements (agranulocytosis risk).
- **Long-acting injectables (LAIs)** are increasingly recommended for non-adherent patients.
- **Antipsychotics and mortality**: Debate on whether long-term antipsychotic use increases mortality.
- **Guidelines update**:
  - **NICE (2020)** and **APA (2020)** emphasize early intervention services and personalization of care.
  - Avoid polypharmacy unless evidence supports combination.

Monitoring Therapy

Clinical Parameters:

- Symptom reduction (PANSS, BPRS scales).
- Side effects (EPS, sedation, weight gain, prolactin elevation).
- Adherence.

Laboratory Monitoring:

- CBC (esp. for Clozapine: monitor ANC weekly initially).
- LFTs, lipid profile, blood glucose (metabolic monitoring).
- ECG (QT interval – especially for Ziprasidone, Haloperidol).

Time Course:

- Initial response: 1–2 weeks.
- Maximal response: 4–6 weeks.

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