

SCHIZOPHRENIA AND ASSOCIATED DISORDERS

- Schizophrenia is a psychotic mental disorder of unknown aetiology characterised by disturbances in thinking, mood and behaviour
 - Thinking disturbance is manifested by:
 - **Distortion of reality**
 - Sometimes with delusions and hallucinations
 - Fragmentation of associations that results in characteristic disturbance of speech
 - **Disturbance of mood:**
 - Ambivalence
 - Inappropriate or constricted affective responses
 - **Disturbance of behaviour:**
 - Apathetic withdrawal
 - Bizarre activity
- Patients may present with positive or negative symptoms:
 - **Positive symptoms:**
 - **Conceptual disorganisation**
 - **Delusions** (false belief, based on incorrect inference about external reality, not consistent with patient's intelligence and cultural background)
 - **Hallucinations** (false sensory perception not associated with real external stimuli)
 - In contrast to illusion which is a misperception or misinterpretation of real external sensory stimuli
 - **Negative symptoms:**
 - Predominate in one-third of patients
 - Associated with poor long-term outcome and poor response to drug treatment
 - Consist of:
 - Loss of function
 - Anhedonia
 - Decreased emotional expression
 - Impaired concentration
 - Diminished social engagement
 - The patient must have at least two of these for a 1-month period and continuous signs for six months to meet the formal diagnostic criteria

EPIDEMIOLOGY

- Lifetime prevalence of the disease is about 1%
- Equally prevalent between men and women
- Peak age of onset is between 15 and 35 (with 50% cases before age 25)
- Persons born in winter are more likely to develop the disease than those born in spring or summer

- There is an increased rate among babies born to mothers who have influenza during pregnancy
- There is a higher mortality rate from accidents and natural causes than in the general population
 - Leading cause of death in schizophrenic patients is suicide
 - Over 40% of schizophrenic patients abuse drugs and alcohol
- It is more common in lower rather than higher socio-economic groups

PATHOPHYSIOLOGY AND AETIOLOGY:

- The stress diathesis model is often used:
 - Person in whom schizophrenia develops has a specific biological vulnerability (*diathesis*) that is triggered by stress and leads to schizophrenic symptoms
- The stresses may be **genetic, biological, psychosocial or environmental:**
 - **GENETIC:**
 - Both single gene and polygenic theories have been put forward
 - Consanguinity:
 - Incidence in these families is higher than in the general population
 - Concordance is higher in MZ twin studies than DZ (45-50% vs 12-15%)
 - Adoption studies:
 - The prevalence of schizophrenia is greater in the biologic parents of schizophrenic adoptees than in adoptive parents
 - MZ twins raised apart have the same concordance rate as twins reared together
 - Rates of schizophrenia are not increased in children born to unaffected parents but raised by a schizophrenic parent
 - **BIOLOGICAL:**
 - **DOPAMINE HYPOTHESIS:**
 - The **mesolimbic** dopaminergic system has its origins in cell bodies of the **ventral tegmental area (VTA)**
 - These project to the limbic system, nucleus accumbens, ventral striatum and parts of the amygdala and hippocampus
 - **Overactivity** of this system accounts for the positive symptoms of schizophrenia:
 - The **mesocortical** dopaminergic system originates in VTA and projects to neocortex (particularly prefrontal)
 - Responsible for temporal organization of behaviour, motivation, planning, attention and social behaviour
 - **Underactivity** of this system accounts for the negative symptoms of schizophrenia
 - The theory is based upon the psychotogenic effects of drugs that increase dopamine levels (amphetamines and

cocaine) and the antipsychotic effects of dopamine receptor antagonists

- **NORADRENALINE HYPOTHESIS:**
 - Increased noradrenaline levels in schizophrenia lead to increased sensitisation to sensory input
- **GABA HYPOTHESIS:**
 - Decreased GABA activity increases dopamine activity
- **SEROTONIN HYPOTHESIS:**
 - Abnormalities in serotonin metabolism have been reported, with both high and low levels being found
 - Specifically, antagonism at the 5HT2 receptor has been emphasised as important in reducing psychotic symptoms
- **GLUTAMATE HYPOTHESIS:**
 - Hypofunction of NMDA receptor
- **NEURODEVELOPMENTAL THEORIES:**
 - Abnormal neuronal migration during the second trimester of foetal development
 - Abnormal neuronal functioning may lead to the emergence of symptoms during adolescence
- **PSYCHOSOCIAL AND ENVIRONMENTAL:**
 - Family factors:
 - Patients whose families have high levels of **expressed emotion** (EE – any overly involved, intrusive behaviour, be it hostile and critical or controlling and infantilising) have higher relapse rates
 - Relapse rates are lowered when behaviour is modified to lower EE
 - Most observers believe that family dysfunction is a consequence, rather than a cause, of schizophrenia
 - Other psychodynamic factors:
 - Knowing what psychological and environmental stresses are most likely to trigger psychotic decompensation in a patient helps the clinician address these issues supportively

DIAGNOSIS, SIGNS AND SYMPTOMS:

- DSM-IV criteria for schizophrenia:
 - **Characteristic symptoms** (two or more) are present for a significant portion of time during a 1-month period:
 - Delusions
 - Hallucinations (most frequently auditory)
 - Disorganised speech (frequent derailment or incoherence)
 - Grossly disorganised or catatonic behaviour
 - Negative symptoms (affective flattening, alogia or avolition)

- NB only one of these symptoms are required if delusions are bizarre or hallucinations consist of voice keeping running commentary of person's actions
 - **Social or occupational dysfunction** (compared to the period prior to onset)
 - **Duration.** Needs to be continuous of disturbance for at least six months
 - **Schizoaffective and mood disorder exclusion:**
 - No major manic, depressive or mixed episodes have occurred concurrently with the active-phase symptoms
 - **Substance/general medical condition exclusion**
- **Otherwise:**
 - Affect is abnormal (blunted, flat, labile, inappropriate)
 - Sense of self is disturbed
 - Interpersonal functioning is impaired:
 - Social withdrawal
 - Emotional detachment
 - Aggressiveness
 - Sexual inappropriateness
 - Cognition is impaired:
 - Inattention
 - Impaired information processing

DIFFERENTIAL DIAGNOSIS:

- **MEDICAL AND NEUROLOGIC DISORDERS:**
 - Substance intoxication (particularly cocaine and phenylcyclidine)
 - CNS infections
 - SLE
 - Temporal lobe epilepsy
 - Degenerative disease (e.g. Huntingtons)
- **SCHIZOPHRENIFORM DISORDER:**
 - Symptoms may be identical to those of schizophrenia but last for less than six months
 - Deterioration is less pronounced and prognosis is better
- **BRIEF PSYCHOTIC DISORDER:**
 - Symptoms last for less than one month and proceed from a clearly defined psychosocial stress
- **MOOD DISORDER:**
 - Both manic episodes and major depressive episodes of bipolar I disorder and major depressive disorder may present with psychotic features
 - This differential diagnosis is particularly important because of the availability of specific and effective treatments for the mood disorders
- **SCHIZOAFFECTIVE DISORDER:**
 - Mood symptoms develop concurrently with symptoms of schizophrenia, but delusions or hallucinations must be present for 2 weeks in the absence of prominent mood symptoms during some stage of the illness

- **DELUSIONAL DISORDER:**
 - Relatively intact, well functioning personality
- **PERSONALITY DISORDER:**
 - Generally no psychotic features (may be transient)
- **FACTITIOUS OR MALINGERING DISORDER:**
 - Patient is feigning the symptoms
 - Clear secondary gain (malingering)
 - Deep psychological motivation (factitious)

TREATMENT:

- **PHARMACOLOGIC:**
 - Choice of drug is important:
 - **Dopamine receptor antagonists (typical antipsychotics):**
 - Effective in treatment of positive symptoms:
 - High potency agents (e.g. haloperidol) are most likely to cause EPS:
 - Akathisia
 - Acute dystonia
 - Pseudoparkinsonism
 - Low potency agents (e.g. chlorpromazine) are more sedating, hypotensive and anticholinergic
 - These agents (collectively) can cause **tardive dyskinesia** at rate of 5% per year of exposure
 - A significant portion of patients are either unresponsive to or intolerant of these drugs
 - As a result, the newer, second generation antipsychotic agents are usually employed as first line agents
 - **Serotonin-dopamine antagonists (atypical, novel or second-generation antipsychotics):**
 - Provide potent 5-HT₂-receptor blockade and varying degrees of D₂ blockade.
 - In comparison with dopamine receptor antagonists, these drugs improve two classes of disabilities typical of schizophrenia:
 - **Positive AND negative symptoms**
 - Cause fewer EPS
 - Do not elevate prolactin levels
 - Less likely to cause tardive dyskinesia
 - Can be highly sedating and cause weight gain
 - Included amongst this group:
 - **Risperidone**
 - **Olanzapine**
 - **Clozapine** (1% risk of agranulocytosis)
 - **Maintenance:**

- Long-term treatment with antipsychotic medication is usually required to decrease the risk for relapse
 - If the patient has been stable for one year, the dose can be decreased to the minimum effective dosage
- **ELECTROCONVULSIVE THERAPY (ECT):**
 - Can be effective for acute psychosis and catatonic subtype
 - Also promising for refractory positive symptoms
- **PSYCHOSOCIAL TREATMENTS:**
 - Antipsychotic medication alone is not sufficient in treating schizophrenic patients
 - **Behaviour therapy:**
 - Desired behaviour is positively reinforced with rewards
 - **Group therapy:**
 - Focus is on support and social skills development (ADLs etc)
 - Helpful in decreasing isolation and increasing reality testing
 - **Family therapy:**
 - High EE family interactions can be diminished through family therapy, thereby decreasing relapse rates
 - **Supportive psychotherapy:**
 - Traditional, insight-oriented therapy is not recommended, as egos of patients are too fragile.
 - Supportive therapy may include:
 - Advice
 - Reassurance
 - Education
 - Modelling
 - Limit setting
 - Reality testing
 - **Social skills training:**
 - **Case management:**
 - Responsible for the patient's concrete needs and coordination of care
 - Participate in treatment planning and communication between various providers
 - Help patients:
 - Make appointments
 - Obtain housing
 - Obtain financial benefits
 - Navigate the health care system (advocacy)
 - **Support groups**