

Schizophrenia

- ① Schizophrenia literally means "Fragmented mind".
- ② Schizophrenia is one of the most complex chronic and challenging of psychiatric disorders that affects how a person thinks, feels, behaves.
- ③ It represents a heterogeneous syndrome of disorganized thoughts, delusions, hallucinations and impaired psychosocial functioning.

Etiology:

While many factors have been associated with developing schizophrenia - including genetics, early environment, neurobiology, and psychological and social process - the ~~exact~~ exact cause of the disease is unknown.

1. Viral Infections and Immune disorders:

Schizophrenia may be triggered by environmental events - such as viral infections are also at higher risk.

2. Genetics (Hereditry):

- ① Scientists recognize that the disorders tends to run in families and that a person inherits tendency to develop the disease, similar to some other genetically-related illnesses, schizophrenia may appear when the body undergoes hormonal and physical changes.
- ② The risk of developing schizophrenia is increases to approximately 10% if a first-degree relative has the illness and to 3% if a second degree relative has the

illness. If both parents have schizophrenia, the risk of producing a schizophrenic offspring increases of approx 40%.

Epidemiology:

- ① The prevalence of schizophrenia ranges from 0.6% to 1.0%, with an average of approximately 1%.
- ① Schizophrenia most commonly has its onset in late adolescence or early adulthood and barely occurs before adolescence or after the age of 40 years. The peak ages of onset 20-38 years for males and 26-32 years for females.
- ① Slightly more men are diagnosed with schizophrenia than women (on the order of 1.4:1) and women tend to be diagnosed later in life than men.

Types:

i) paranoid schizophrenia:

- ① common form of schizophrenia.
- ① prominent hallucinations and/or delusions.
- ① May develop at a later age than other types of schizophrenia.
- ① Speech and emotions may be unaffected.
- ① At risk for suicidal or violent behavior under influence of delusions.

i) Hebephrenic / Disorganized Schizophrenia:-

- ① Behavior is disorganised and without purpose.
- ① Thoughts are disorganised, difficult to understand by others.
- ① pranks, giggling, health complaints, grinning and mannerisms are common.
- ① Delusions and hallucinations are Fleeting.
- ① Usually develop between 15-25

iii) Catatonic Schizophrenia:

- ① Rarer than other types.
- ① At risk for malnutrition, exhaustion or self injury.
- ① unusual movements often switching between extremes of overactivity and stillness.
- ① unable to talk (catatonia)

iv) Undifferentiated Schizophrenia:

- ① Some characteristics of paranoid, hebephrenic or catatonic schizophrenia, but does not obviously fit one of these types.

v) Residual Schizophrenia:

- ① Past history of psychosis but only having negative symptoms.

Symptoms:

① positive symptoms:

① 'positive' refers to overt symptoms that should not be present. These include:

① Hallucinations:

It are sensations that appear to be real but are created within the mind.

Ex - Include seeing things that are not there hearing voices or other sounds, experiencing body sensation like crawling feelings on the skin, or smelling odors that are not there.

① Disorganized thoughts:

A disorder that affects a person's ability to think feel and behave clearly.

Symptoms: Disorganized behaviors.

Auditory hallucination.

Thought disorder.

① Negative symptoms:

① 'Negative' does not refer to a person's attitude, but instead to a lack of characteristics that should be present. These include -

① Reduced speech, even when encouraged to interact (alogia)

① Lack of emotional and facial expression (affective flattening)

Diminished ability to begin and sustain activities.
(avolition)

- ① Decreased ability to find pleasure in everyday (anhedonia)
- Social withdrawal (asociality)

Cognitive deficits:

Difficulties with following aspects of cognition can make it hard to live a normal life or earn a living:

- ① Memory
- ② Attention.

③ The Brain in Schizophrenia:

Many brain regions and systems operate abnormally in schizophrenia, including those highlighted below. Imbalances in the neurotransmitter dopamine were once thought to be the ~~primary~~ prime cause of schizophrenia, but new findings suggest that impoverished signaling by the more pervasive neurotransmitter glutamate.

- Basal ganglia
- Auditory system
- occipital lobe
- Hippocampus
- Frontal lobe.
- Limbic system.

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Pathophysiology:

1. Dopamine Hypothesis:

- ① Numerous positron emission Tomography (PET) studies have shown dopaminergic hyperactivity in the nucleus accumbens and dopaminergic hypo function in the fronto temporal regions.
- ① PET studies using D_2 -specific ligands provide data suggesting increased densities of D_2 receptors in the nucleus accumbens.
- ① PET studies assessing D_1 function suggest that sub-populations of schizophrenics may have decreased densities of D_1 receptors in the prefrontal cortex.
- ① Thus positive symptoms are thought to result from overactivity in the mesolimbic dopaminergic pathway activating D_2 receptors whereas negative symptoms may result from a decreased activity in the mesocortical dopaminergic pathway where D_1 receptors predominate.

Dopamine tract	Origin	Innervation	Function.
Nigrostriatal	Substantia nigra	Striatum	Movement.
Mesolimbic	Ventral tegmentum. (Mid brain)	Nucleus Accumbens and Amygdala (Limbic system)	Arousal, stimulus processing, motivational behavior.
Mesocortical	Ventral tegmentum.	Frontal and prefrontal lobe cortex.	Cognition, communication, social function, response to stress.
Tuberohypophyseal	Hypothalamus	Pituitary gland	Inhibit prolactin release.



1. Glutamate Hypothesis:

- ① NMDA receptor hypofunction is thought to reduce the level of activity in mesocortical dopaminergic neurons. This would result in decrease in dopamine release in the prefrontal cortex and thus give rise to negative symptoms of schizophrenia.
- ① On the other hand NMDA receptor hypofunction is thought to enhance activity in the mesolimbic dopaminergic pathway perhaps because in this pathway the important NMDA receptors are those
- ① Thus NMDA receptor hypofunction would result in reduced GABAergic ~~inhibitions~~ inhibition of mesolimbic dopaminergic neurons and thus give rise to enhanced dopamine release in limbic areas such as the nucleus accumbens.

3. 5-HT Hypothesis:

- ① Serotonergic receptors are present on dopaminergic axons and it is known that stimulation of these receptors will decrease DA release in prefrontal cortex.
- ① Patients with schizophrenia with abnormal brain scans have higher whole blood 5-HT concentrations and these concentrations are correlated with increased ventricular size.
- ① Atypical antipsychotics with potent 5-HT₂ receptor antagonist effects reverse worsening of symptomatology induced by 5-HT agonists in patients with schizophrenia.

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Complication:

1. Depression:

Depression afflicts approximately half of schizophrenic patients. ~~So~~ Sadly, it is not always recognized or treated. It can significantly add to the suffering of the person. Additionally, comorbid ~~the~~ depression increases the risk of suicide in schizophrenic.

2. Anxiety:

Many individuals with schizophrenia also have an anxiety disorder, such as social anxiety disorders, PTSD, generalized anxiety disorders, OCD or panic disorders. In fact, ~~more~~ research suggests between 30% and 55% of people with schizophrenia have had an anxiety disorder at some point in time.

3. Suicide:

Suicide is one of the primary causes of death for individuals with schizophrenia. There are several factors which contribute to suicide risk in schizophrenia which include psychotic symptoms, such as voices telling the person to kill himself, substance abuse, recent diagnosis of schizophrenia and comorbid depression.

4. Substance Abuse and Smoking:

Substance abuse is a form of self-medication for many people with psychiatric disorders. Unfortunately, when patients use substances such as alcohol or street

as it can make their symptoms worse. They are also less likely to continue taking their medications when they abuse substances.

5. Violence:

While the media often depicts schizophrenic patient as violent, they are not necessarily more individuals with schizophrenia, such as delusions or command hallucinations a history of violent acts or using alcohol or drugs.

6. Self-Injury:

Self injury especially bizarre types of self mutilation is not uncommon with schizophrenia. Hallucinations and delusions can cause them to harm themselves in way which can be very serious, such as attempting to remove a finger or other body part.

Diagnosis:

① Diagnosis Criteria for schizophrenia:

It includes the criteria in the diagnostic and statistical manual of mental disorders published by the American psychiatric Association.

② Medical history:

A thorough medical history is the first step in the diagnosis of schizophrenia. This may be done to find other problems that could be causing symptoms and to check for any related complications.

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① Blood tests and Imaging: A complete blood count (C) test is helpful to monitor general health and rule out other conditions that may have been responsible for the symptoms. A blood test can provide accurate information about the involvement of recreational drugs. In some cases certain imaging techniques such as ~~mag~~ magnetic Resonance imaging or computed tomography (CT) scan may aid in the diagnosis.

Psychiatric Evaluation:

A doctor or mental health professional checks mental status by observing appearance, demeanor and asking about thoughts, moods and awareness. A person may be diagnosed if they at least 2 of the symptoms usually over a month —

- i) Delusions.
- ii) Hallucinations.
- iii) Disorganised behaviour.
- iv) Disorganised speech and thought process.
- v) catatonic behaviour presenting as staring daze or hyperactivity.
- vi) Negative symptoms, impaired normal function.

Management hospitalization:

① During ~~and~~ crisis periods or time of severe symptoms hospitalization may be necessary to ensure safety proper nutrition adequate sleep and basic hygiene.

Individual therapy: psychotherapy may help to normalize thought patterns. Also, learning to cope with stress and identify early warning signs of relapse can help people to manage their illness.

① Social skills training:

This focuses on improving communication, social interactions and improving the ability to participate in daily activities.

① Family therapy:

This provides support and education to patient families.

① Vocational rehabilitation and supported employment:

This focuses on helping people with schizophrenia prepare for, find and keep jobs.

Electroconvulsive therapy:

① For adults with schizophrenia who do not respond to drug therapy, electroconvulsive therapy may be considered. ECT may be helpful for someone who also has depression.

① The indications for ECT in schizophrenia are -
catatonic stupor and uncontrolled catatonic excitement
Acute exacerbations not controlled with drugs.
Risk of suicide homicide or danger of physical assault.

① Cognitive behavioural therapy:

① CBT aims to help to identify the thinking patterns that are causing to have unwanted feelings and behaviour and learn to replace this thinking with more realistic and

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useful last for about an hour.

Clinical Management:

- ① The APA guidelines treatment recommendations for patient with schizophrenia divided the treatment into 3 phase -
1. Acute phase (Initial presentation) 4 to 8 weeks: Defined by acute psychotic episode.
 2. Stabilization phase (Early Symptom remission) as long as 3 months.

constitutes a time-limited transition to continuing treatment.

3. Stable phase (Maintenance treatment): Involves stable treatment.

① APA guideline refers to the American psychiatric Association

Antipsychotic / Neuroleptic / Ataractic / Major Tranquillizer:

Typical or classical or 1st generation antipsychotics.

A. phenothiazines -

1. with aliphatic amine side chain: chlorpromazine, Trifluorpromazine.

2. with piperidine side chain: Thioridazine.

3. with piperazine side chain: Trifluoperazine, fluphenazine.

B. Butyrophenones: Haloperidol, Trifluoperidol, penfluridol.

C. Thioxanones: Flupenthixol, Thiothixene.

D. other heterocycles: pimozide, Loxapine.

typical or Novel or 2nd generation antipsychotics:

- ① clozapine
- ① olanzapine.
- ① Quetiapine.
- ① Aripiprazole
- ① Risperidone
- ① Amisulpride.
- ① Ziprasidone.

Drug	Daily dosage
Amisulpride	400 - 800
Aripiprazole	10 - 30
Olanzapine	10 - 20
Quetiapine	250 - 600
Risperidone	4 - 6
Sentindole	16 - 24
Ziprasidone	120 - 160

Typical antipsychotic:

- ① All anti psychotics have potent dopamine D_2 receptor blocking action.
- ① Antipsychotic action of typical neuroleptic is believed to be produced by competitive blockade of postsynaptic D_2 receptors in mesolimbic system.
- ① Initially D_2 presynaptic receptors are also blocked, which increases synthesis and release of dopamine, so its metabolites like HVA and DopAc level is increased in blood and urine.
- ① But on prolonged use, there is a feedback inhibition of DA release, due to increased DA concentration in synaptic cleft, which results in decreased turnover and release.
- ① A typical neuroleptic drug also blocks D_2 receptors in nigrostriatal pathway and explains the unwanted

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Extrapyramidal side effects.

Blockage of D_2 receptor in CTZ is responsible for antiemetic effects.

- ① Neuroleptics consistently increased prolactin release by blocking activity: chlorpromazine: $\alpha_1 = 5-HT_2 > D_2 = D_4 > D_1 > M_1$ thioridazine: $\alpha_1 > D_2 > M_1 = 5-HT_2 > D_1$
Haloperidole $D_2 > \alpha_1 > D_4 > 5-HT_2 > D_1$ Pimozide: $D_2 > 5-HT_2 > D_4$
- ② These drugs produce hypotension due to high α blocking property.
- ③ chlorpromazine potent a local anaesthetic as procaine but is not used for this purpose because irritant action.