Psychiatry

Table of Content

1 CHAPTER

BASICS OF PSYCHIATRY

The term "psychiatry" was coined by Johann Christian Reil. History-taking is the first step in evaluating a patient with a psychiatric disorder.

Informant: Individuals providing information about the patient and their illness are called 'informants'. Typically, informants include the patient themselves, as well as a close relative or friend who is knowledgeable about the patient and the illness.

Reliability of the informant: An informant is considered reliable if the following five parameters (5 C's) are met:

1. Consistency - The history provided by the informant to the final-year student and the consultant should remain the same.
2. Coherence - The first half of the information should be logically connected to the second half.
3. Chronological information - Information should be provided in chronological order.
4. Closeness with the patient - The informant should be close to the patient. For example, if the informant lives in another city, they cannot be considered reliable.
5. Concern for the patient - The informant should be genuinely concerned for the patient. For example, a wife who has filed a case against her husband is not a reliable informant for him.

Components of MSE (Mental Status Examination)

A. General Appearance and Behavior - The patient's appearance and behaviour can provide clues about their psychiatric disorder. For example, a patient comes to the OPD wearing a pink shirt, orange pants, goggles, a hat, and lots of makeup. This appearance itself suggests that the patient may have manic symptoms.

B. Speech - Evaluate the rate, tone, and volume of the patient's speech. For instance, a patient with mania may exhibit an increased rate, tone, and volume of speech.

C. Mood and Affect - Both terms reflect 'emotions'

Mood- Sustained (long-term) and internal emotional state

Affect- Short-lived and external expression of internal emotions that can be observed

The terms 'affect' and 'mood' are used interchangeably

Affect and mood are further described under the following heads:

1. Quality- Describes the predominant affective (or mood) state. Abnormalities include-

a. Elevation of mood

i. Euphoria- Excessive happiness without any reason (In mania/hypomania)

ii. Elation- Euphoria + increased psychomotor activity (PMA) (In mania)

iii. Exaltation- Euphoria + increased (PMA) + delusion of grandiosity (In mania)

iv. Ecstasy- State of extreme happiness/sense of bliss (In mania)

b. Dysphoria (dysphoric mood) - Irritability (In mania)

c. Depressed mood - Predominant sadness (In depression)

2. Fluctuations- Changes in mood/affect. Some level of fluctuation is normal; abnormalities of fluctuation include-

a. Labile mood or emotional lability - Excessive variations in the mood without any apparent reason. E.g.- A man starts crying and then starts laughing the next moment, without any apparent reason (In mania)

b. Affective flattening (flat affect, emotional blunting, blunt affect) - Lack of emotional response (In schizophrenia)

3. Appropriateness & Congruence

a. Appropriateness- Whether emotions are matching with the 'social situation'. A person starts laughing at a funeral (An example of inappropriate affect)

b. Congruence- Whether emotions are matching with the 'thought content'. A person starts laughing while discussing the 'death of mother' (an example of incongruent affect)

Inappropriate and Incongruent affect are features of Schizophrenia

Other disturbances of emotions-

1. Alexithymia- inability to understand the emotions of others and inability to express emotions of self.

2. Anhedonia- Loss of capacity to experience pleasure in activities that were previously pleasurable. Can be seen in depression, and schizophrenia.

Neuroanatomy of emotions

a. Generation- Limbic system (hippocampus, amygdala, hypothalamus, cingulate gyrus and related thalamic and cortical areas)

b. Control/regulation - Frontal lobe

D. Perception - Perception involves receiving information and processing it. Perceptual disturbances are common in psychiatric disorders. Two important disturbances of perception are:

- Illusions: 'False perception of a real object'. E.g, A man mistakes a rope for a snake and gets frightened.

- Hallucinations: 'False perception in the absence of any object or stimulus.' E.g. A man saw a snake on the ground when there was nothing there.

Properties of hallucinations:

- Occur in the absence of any sensory or perceptual stimulus.
- Are as vivid (clear or detailed) as true perceptions.
- Are experienced in the outer objective space. E.g. A patient with auditory hallucinations reported that the voices are coming from outside, such as from the wall or outside the house.
- Are not under the wilful control of the patient. The patient can neither start the hallucinations nor can he stop them.

Pseudohallucinations fulfil the other criteria but are experienced in the 'inner and subjective space'. E.g. A patient with auditory pseudohallucinations reported that the voices are originating from within his mind and not from outside.

One-liners:

- Most common type of hallucination, overall: Auditory
- Most common type of hallucination associated with organic mental disorders: Visual hallucination.
- Cocaine intoxication: Tactile hallucination
- Olfactory and gustatory hallucination: Temporal lobe disorders (like temporal lobe epilepsy)

Specific hallucinations:

- Hypnagogic hallucination - While "going to sleep" (In narcolepsy)
- Hypnopompic hallucination - While getting up from sleep (In narcolepsy)
- Reflex hallucinations - Stimulus in one modality produces hallucinations in another modality. E.g. "Whenever I see a tube light (stimulus- visual modality), I start hearing the voice of Deepika Padukone" (hallucination- auditory modality). It's a morbid variety of synesthesia (syn=combination, aesthesia=sensations). Seen in cannabis and lysergic acid diethyl amide (LSD) intoxication.
- Functional hallucinations - Stimulus in one modality produces hallucinations in the same modality. E.g. "Whenever I hear the noise of an air conditioner (stimulus- auditory modality), I also start hearing the voice of Deepika Padukone (hallucination- auditory modality).

E. Thought

The terms "cognition" and "thought" are often used interchangeably. The disturbances of "thought" can be further subdivided into:

1. Disorders of the stream (flow) of thought: The stream of thought basically refers to the speed and continuity of thinking. The abnormalities include:

a. Flight of Ideas: Thoughts follow each other rapidly, and the connection between successive thoughts appears to be due to chance factors such as rhyming. For example, a patient said, "I live in Delhi, I like eating jelly, my cat has a big belly." This is seen in mania.

b. Circumstantiality: Thinking progresses slowly with the inclusion of unnecessary details and goes round and round before reaching the final goal. For example, a medical student was asked about his preferred branch in postgraduation, and he replied, "Sir, in the first year, I was very interested in physiology; however, in the second year, I started liking pathology. In my third year, ophthalmology was my favourite subject. However, in the final year, I realised that I have a lot of passion for orthopaedics, and I like putting casts and working with POP. I also think that after MBBS, one should get married as soon as possible and that no one should have more than two kids...Well, you see, I like paediatrics as a subject and want to do my postgraduation in paediatrics."

c. Perseveration: Repetition of the same response beyond the point of relevance. For example:

   i. Q: What is your name?

   ii. Ans: Mahesh Kumar

   iii. Q: Where do you live?

   iv. Ans: Mahesh Kumar

   v. Q: How many children do you have?

   vi. Ans: Mahesh Kumar

d. Thought block: The thought stream stops, leaving a blank, and a new thought begins.

2. Disorders of form: The form of thought refers to the organization of thinking/association between thoughts. In disorders of the form of thought or "formal thought disorders," there is a disturbance in the organization of thinking. The important formal thought disorders include:

   a. Derailment: Loss of connection between successive thoughts.

   b. Loosening of association: Loss of connection between components of the same thought.

   c. Incoherence (Word salad): Complete lack of organization that makes the thought incomprehensible and impossible to understand.

   d. Tangentiality: Thought is related to a goal in a distant way, but the goal is never reached. For example, a patient was asked about his favorite Indian actor. He replied, "Well, you see, the Indian movies are still male-centric and usually deal with relationship issues, whereas the Hollywood movies have lots of action and science fiction. I think the Indian Film Industry is growing rapidly, and it's a good medium for the entertainment of the masses." In this example, the patient never reached the final goal (never said who his favorite Indian actor is?)

   e. Neologism: Coining of a new word whose derivation cannot be understood. For example, a patient used the word "tintintapa" for a pen.

   f. Metonyms (word approximation): Old words used in a new or unconventional manner. For example, a

patient called a clock a "time regulatory mechanism."

g. Clanging (clang association): Words are associated with each other, as they sound similar, and there may be a lack of any meaningful connection. For example, A patient said, "I make sense out of non-sense, and nonsense is the essence of turbulence of life."

3. Disorders of content: Delusion is a disorder of the content of thought. Delusion is:

a. A false belief

b. Firm, fixed, and unshakeable (continues despite evidence against it)

c. Unexplained by social and cultural background

Types of delusions:

- Delusion of persecution: The most common type of delusion. The patient believes that he is being harmed. For example, "My family members want to kill me and take away my property."
- Delusion of reference: The patient believes that neutral events happening around him are somehow related to him. For example, "Doctor, the tube light in your room has a camera fitted which is recording me."
- Delusion of grandeur/grandiosity: The patient believes that he has some special power/role/identity. For example, "I am so powerful that I can push a train with my bare hands."
- Delusion of love (erotomania, de Clerembault syndrome, fantasy lover syndrome): Patients develop a false belief that someone is in love with them. For example, a rickshaw puller who had never left his town claimed that Katrina Kaif is in love with him and was forced to marry some other guy by big producers.
- Delusion of infidelity (morbid jealousy, pathological jealousy, Othello syndrome): The patient has a false belief that the partner/spouse is having an affair.
- Delusion of guilt: The patient develops guilt at a delusional level. The patient may claim that he is an evil person and has committed unpardonable sins. Usually seen in patients with severe depression.
- Nihilistic delusion (delusion of negation, Cotard syndrome): Patients may deny the existence of their body, their mind, or the world in general. For example, a patient with severe depression claimed that all his internal organs have rotted.
- Delusian of enormity: The patient believes that their action will cause a catastrophe. At times, patients with the delusion of negation also develop delusion of enormity. For example, a patient said, "I cannot urinate because if I urinate, there will be floods all around the world. If I sneeze, the world will blow away."
- Delusion of misidentification (misidentification syndrome):

a. Capgras syndrome (Delusion of doubles): The patient believes that a familiar person has been replaced by a "similar-looking stranger."

Close Person Got Replaced By A Stranger

b. Fregoli syndrome: The patient believes that a familiar person is changing the physical appearance and disguising as a stranger. And that multiple different appearances can be taken by this person. Familiar person giving goli

Bizarre vs. Non-bizarre delusions:

- Bizarre delusions: Scientifically impossible and culturally implausible (ununderstandable). For example, a patient claimed that aliens stole his heart and lungs, and now he is living without those organs.
- Non-bizarre delusions: False but possible. For example, a patient believed that a family member wants to hurt him and take away his property.

4. Disorders of Possession:

In disturbances of possession of thought, the patient may believe that someone is manipulating or interfering with their thoughts. Alternatively, they may feel that they have lost control over their thoughts.

- Thought insertion: "My neighbor is putting thoughts in my mind."
- Thought withdrawal: "My neighbor withdrew/stole thoughts from my mind."
- Thought broadcast: The patient experiences that thoughts are escaping his mind, and others can access them.
- Obsessions: A thought comes repeatedly into the patient's mind against his will.

F. Higher mental functions

1. Attention - Ability to attend to a specific stimulus without getting distracted.
   - Tested using the Digit Repetition Test (also known as the Digit Span Test).
   - During the test, the examiner recites a series of numbers, and the patient is required to repeat them back.
   - The test begins with a single digit and gradually progresses to longer sequences (e.g. two-digit, three-digit, etc.) until the patient is unable to accurately repeat the numbers.
   - An inability to repeat at least five digits indicates defective attention.
   - E.g. If the examiner says 1, 4, 2, 6, 9; the patient should be able to repeat and say 1, 4, 2, 6, 9.
   - A variation is the digit backward test, where if the examiner says 1, 4, 2, 6, 9; the patient is supposed to say 9, 6, 2, 4, 1, can also be used.
   - Digit repetition test (digit forward test) is preferred over digit backward test.
2. Concentration - Ability to sustain attention for a longer duration.
   - Tested using Serial Seven Subtraction Test in which the patient is asked to serially subtract 7s from 100 (100, 93, 86, 79....)

3. Memory - Three different types of memory:

- Immediate memory/Working memory - For intervals of seconds. Tested using the digit repetition test or serial seven subtraction test.
- Recent memory - For minutes, hours or days. Tested using 24-hour recall method.
- Remote memory - For years, tested by asking for both personal information and historical events. E.g.: Which school did you go to? When did India win the world cup?

Clinical relevance- Dementia affects recent memory first and remote memory in later stages.

4. Intelligence: It is tested by asking questions about general information and assessing calculation skills.

5. Abstract thinking: Ability to form concepts and generalisations. Tests of abstract thinking-

a. Proverb testing- Here, the patient is asked to explain the meaning of proverbs, and the answer is evaluated.

b. Similarities testing: Here, the patient is asked to explain the similarities between two objects, e.g., 'What is the similarity between a chair and a table?' If the patient answers that 'both are pieces of furniture', it suggests the presence of abstract thinking; if the patient answers that 'both are kept on the floor', it suggests an absence of abstract thinking (known as concrete thinking).

6. Judgement: Ability to take the right decision according to the situation. Three types of judgments are there-

a. Test judgment: Here, a test situation is given, and the patient is asked to give the appropriate response in that situation. The commonly asked question is what would the patient do if he sees a "house on fire" and the response is evaluated.

b. Personal judgment: Here, the patient is asked about the plans for his future life, and the response is evaluated.

c. Social judgment: Here, the patient's ability to interact appropriately in social situations is evaluated.

7. Insight: Insight is defined as the 'awareness of the illness'.

Insight is rated on a five-point scale:

- Grade 1: Absent insight (e.g. I don't have any problem)
- Grade 2: Some awareness of being sick but denying it at the same time (e.g., At times, I hear some voices, but there is no illness)
- Grade 3: Awareness of being sick but attributing the symptoms to external or physical factors. (e.g., Yes, I hear voices, and it is because my neighbours have installed a hidden speaker to trouble me)
- Grade 4: Intellectual Insight, awareness of illness without any accompanying changes in behaviour. e.g., I know I have schizophrenia, but I don't want to take any medicines or treatments.
- Grade 5: Emotional Insight, awareness of illness along with the accompanying changes in the behaviour. It's the highest level of insight, e.g. I have schizophrenia, and I want to take regular medications to prevent any relapses.

Classifications:

Organic vs Functional (Nonorganic) mental disorders

Organic mental disorders: Disorders caused by demonstrable brain disturbances. E.g. delirium, dementia, etc.

Functional mental disorders: Disorders in which no demonstrable disturbance of brain parenchyma could be found, E.g. schizophrenia, mania, etc.

This classification is considered arbitrary.

Psychoses vs neuroses

	Psychoses	Neuroses
Insight	Absent	Present
Delusions/Hallucinations	Present	Absent
Reality Testing	Absent	Present

Classification systems

A. ICD-11 (International Classification of Diseases, 11th edition): Published by WHO

B. DSM-5-TR (Diagnostic and Statistical Manual of Mental Disorders, Text Revision): Published by American Psychiatric Association

C. RDoC (Research Domain Criterion): RDoC, funded by NIMH (National Institute of Mental Health, USA) aims to create new approaches for the investigation of mental disorders.

2 CHAPTER

SCHIZOPHRENIA AND OTHER PRIMARY PSYCHOTIC DISORDERS

HISTORY

- **Emil Kraepelin**

	Dementia Praecox	Manic depressive psychosis
Clinical features	Delusions & hallucinations	Distinct manic & depressive episodes
Course	Continuous & deteriorating	Episodic
Cognitive decline	Present	Absent
Current name	Schizophrenia	Bipolar disorder

- **Eugen Bleuler**
  - Coined the term "schizophrenia"
  - Proposed fundamental (Primary) symptoms of schizophrenia (4 As of Bleuler)
    - Autistic thinking & behaviour (Autism) - Excessive fantasy thinking
    - Ambivalence (Inability to decide)
    - Affect disturbances (Disturbances of emotions)
    - Association disturbances (Formal thought disorders)
- **Kurt Schneider**
  - Described a list of 11 symptoms, Schneiderian First Rank Symptoms (SFRS)
  - Characteristic symptoms of schizophrenia
  - The SFRS are, however not exclusively seen in schizophrenia; they are not pathognomonic of schizophrenia either.
  - Include:
- Three thought phenomenon
  - Thought insertion
  - Thought withdrawal

- Thought broadcast
  - These three were already discussed in the first chapter

- Three made phenomenon
  - Made volition - Someone is controlling the actions
  - Made affect --Someone is controlling the emotions
  - Made impulse --Someone is controlling the impulses
- Three auditory hallucinations
  - Voices arguing or discussing about the patient - The patient reports hearing two or more voices (the term 'voices' is used to describe 'auditory hallucinations') which argue about or discuss the patient. The patient is usually referred to in the third person (hence called third-person auditory hallucination)
  - Voices giving running commentary - The patient hears voices that give a running commentary on the patient's activities
  - Audible thoughts (Thought echo) - The patient hears a voice that says the patient's thoughts aloud. The German word "Gedankenlautwerden" or the French word "echo de pensee" are used to describe audible thoughts.
- Delusional perception - A delusion is attached to a normal perception in an understandable manner. It is a type of primary delusion.
- Somatic Passivity - The patient experiences somatic sensations & blames an external agency for the same.

Primary delusions vs secondary delusions

Primary delusions- These arise directly due to an underlying disorder.

Secondary delusions- These arise as a result of some other symptoms. E.g.- A patient who was having threatening auditory hallucinations developed a delusion (secondary) that someone wants to harm him

Extra Edge

Concept of passivity

Passivity experiences are those in which the patient experiences that his thoughts, emotions, actions or sensations are controlled/influenced by others.

- **Ernst Kretschmer**
  - Studied the association of body types with psychiatric disorders
  - Described that schizophrenia is associated with asthenic (thin, less muscular) and less commonly athletic (muscular) body types
  - And bipolar disorder is associated with pyknic (short and stocky) body type
  - No longer accepted theory

EPIDEMIOLOGY

- Lifetime prevalence: 1%
- Equally prevalent in men and women; however, the onset of illness is earlier in males and later in females
- Age of onset- adolescence and young adulthood (15-24 years)
- Late-onset schizophrenia- If onset after 45 years
- More prevalent in lower socioeconomic status (Downward drift hypothesis- developing schizophrenia leads to migration to the lower socioeconomic class)

Prevalence in specific population

Population group	Prevalence
Monozygotic twin of patients with schizophrenia	47%
Non-twin siblings of patients with schizophrenia	12%
Non-twin siblings of patients with schizophrenia	8%
Children with one parent having schizophrenia	12%
Children with both parents having schizophrenia	40%

ETIOLOGY & PATHOGENESIS

- Neurotransmitter hypothesis
  - Dopamine hypothesis
    - Excessive levels of dopamine cause schizophrenia
  - Dopamine and serotonin hypothesis
    - Excessive levels of dopamine & serotonin cause schizophrenia
  - GABA, glutamate, ACh, and NE are also implicated.
- **Genetic factors**
  - Higher monozygotic concordance rate than dizygotic concordance rate
  - First-degree relatives of schizophrenia patients are more likely to develop schizophrenia than second-degree relatives, and the occurrence further drop in the third-degree relatives.
  - DiGeorge syndrome (22q11.2 deletion, velocardiofacial syndrome)
    - 30% develop schizophrenia by the time they reach adulthood
  - Candidate genes
    - DISC 1 (Disrupted in schizophrenia)
    - COMT (Catechol-o-methyl transferase)

- Neuroanatomical factors
  - Reduction in cortical grey matter volume and enlargement of ventricles (lateral and third)
  - Limbic system - Structural (smaller size) and functional abnormality in hippocampus and amygdala
  - Abnormalities in the prefrontal cortex, thalamus, basal ganglia and cerebellum
- Environmental factors
  - Pre and perinatal complications. More likely
  - Birth in late winter and spring. More likely. Hypothesis of maternal exposure to influenza and rubella.
  - Childhood risk factors- More likely to have poorer motor development, speech difficulties, delayed milestones and lower premorbid IQ.
  - Immigrants (second-generation > first-generation) are at higher risk
  - Urban birth and upbringing
  - Drug abuse, especially cannabis
  - Advanced paternal age

SYMPTOMS

- **Positive symptoms** (Or psychotic symptoms)
  - Delusions -- M/C is delusion of persecution
  - Hallucinations -- M/C - auditory hallucinations, 2nd M/C - visual hallucinations
  - If visual hallucinations are present, rule out organic brain disorder
- Both these positive symptoms respond well to medications
- Good prognostic factor
- Cause- Dopamine excess in the mesolimbic tract (ventral tegmental area to nucleus accumbens) leads to positive symptoms.
- **Negative symptoms (6As)**
  - Avolition - Loss of drive for goal-directed activities
  - Apathy - Lack of concern
  - Anhedonia - Lack of pleasure in previously pleasurable activities
  - Asociality - Lack of social interaction
  - Affective flattening (Or emotional blunting) - Lack of emotional response
  - Alogia - Decreased verbal communication

- Respond poorly to medications
- Poor prognostic factors
- Cause- Decreased dopamine in the mesocortical tract (Ventral tegmental area to the prefrontal cortex) results in negative symptoms.
- **Disorganization symptoms**
  - Disorganized behaviour (odd & socially inappropriate behaviour)
  - Disorganized speech and thinking (Formal Thought Disorders)
  - Inappropriate affect
- **Motor symptoms (Catatonic symptoms/symptoms of conation)**
- Term 'catatonia' was coined by 'Karl Kahlbaum'
- Motor symptoms include
  - Stupor - A state of extreme inactivity or immobility (akinesis) & minimal responsiveness.
  - Excitement - Extreme hyperactivity, which is non-goal-directed.
  - Posturing - Maintenance of a posture for a long period of time.
  - Catalepsy - When the examiner makes a passive movement on the patient, such as abduction at the shoulder joint, initially, no resistance is felt. Once the examiner stops the movement, the patient maintains the position they had reached during the movement. For instance, if the examiner had taken the shoulder to 45 degrees abduction and then stopped, the patient would maintain the 45-degree abduction position at the shoulder joint.
  - Waxy flexibility - It is the feeling of plastic resistance that the examiner experiences (similar to what is experienced while bending a wax candle) while making a passive movement on the patient.
  - Automatic obedience - Extreme cooperativeness despite unpleasant consequences.
  - Negativism - Purposeless refusal to follow the command
    - Passive negativism - Does not follow the command
    - Active negativism - Does the opposite of command
  - Echolalia - Repetition of speech
  - Echopraxia- Repetition of behaviour
  - Grimacing - Maintenance of odd facial expressions
  - Gagenhalten - Involuntary resistance offered by the patient in response to a passive movement. Equal and opposite to force applied.
  - Ambitendency - Inability to decide the motor movements
  - Stereotypy - Spontaneous, repetition of odd purposeless movements

- Mannerisms - Spontaneous repetition of semi-purposeful movements, done in an exaggerated manner.
- Perseveration - Induced movement, repeated beyond the point of relevance. It is suggestive of organic brain disorder. Two special types of perseveration
  - Palilalia - Patients repeats perseverated words with increasing frequency
  - Logoclonia - Last syllable of the last word is repeated. E.g. Today is tuesday-ay-ay-ay

- Suicide and violence
  - 10% of patients with schizophrenia die by suicide (DSM-5 figure: 5-6%)
  - 20%-50% of patients with schizophrenia attempt suicide
  - M/C cause of premature & unnatural death in schizophrenia

Risk factors for suicide in a patient with schizophrenia-

- Presence of a major depressive episode
- Increased symptoms (esp. command hallucinations, delusion of persecution)
- Early in course of illness, immediately after admission or discharge
- Young males, comorbid substance abuse, unemployed
- At times paradoxical (Fewer negative symptoms, less affect disturbances)

DIAGNOSIS

- According to DSM-5, for the diagnosis of schizophrenia, the total duration of illness should be at least **six months.**
- Out of these six months, for at least one month, the patient should have two or more of the following symptoms. At least one of these two symptoms should be (1), (2) or (3).

1. Delusions
2. Hallucinations
3. Disorganised speech (which is a result of formal thought disorders)
4. Disorganised behaviour or catatonic behaviour (symptoms)
5. Negative symptoms (i.e., diminished emotional expression or avolition)

- The ICD-11 also uses similar symptom criteria for the diagnosis of schizophrenia; however, the duration criterion of ICD-11 is one month and not six months.

In older classifications, the subtypes of schizophrenia were defined according to the symptomatology however, in both DSM-5 and ICD-11, such subtypes have been removed.

Also

In both, DSM-5 and ICD-11, catatonia has been made a separate diagnosis.

Miscellaneous points

- Pfropf schizophrenia - Schizophrenia in a patient with mental retardation
- Van Gogh syndrome - Self-mutilation in a patient with schizophrenia
- Substances causing schizophrenia like symptoms -- Phencyclidine, amphetamines, cocaine, other hallucinogens, cannabis

TREATMENT

- Antipsychotics are the mainstay of treatment in schizophrenia **(in catatonia, the first line treatment is i.v lorazepam and electroconvulsive therapy)**
- Typical antipsychotics and atypical antipsychotics

	Typical (FGA)	Atypical (SGA)
Mechanism	D2 antagonism	D2 and 5HT2 antagonism
Effective against	Positive symptoms	Positive and negative symptoms
Extrapyramidal symptoms & hyperprolactinemia	More	Less
Metabolic side effects	Less	More

Typical antipsychotics (First generation antipsychotics)- Classification according to chemical groups-

- Phenothiazines- Chlorpromazine, trifluoperazine, thioridazine, prochlorperazine, triflupromazine, fluphenazine, perphenazine
- Thioxanthenes- Thiothixene, flupenthixol
- Butyrophenones- Haloperidol, droperidol, penfluridol
- Miscellaneous- Pimozide, loxapine, molindone

Low potency & High potency

- Low potency - Chlorpromazine, thioridazine
- High potency - Haloperidol, fluphenazine

Side effects

A. Movement disorders (or extrapyramidal side effects or EPS)

- Caused by the blockade of dopamine receptors in the nigrostriatal tract (neural pathway from substantia nigra to striatum)
- More common with typical antipsychotics than atypical antipsychotics
- More common with high potency antipsychotics than low potency antipsychotics
- More common with parenteral administration than oral administration

- Drug-induced parkinsonism
  - Symptoms - Tremors (3-6 Hz), Rigidity, Bradykinesia
  - Prophylaxis - Anticholinergics (E.g. trihexyphenidyl, diphenhydramine etc)
  - Treatment - Anticholinergics (E.g. trihexyphenidyl, diphenhydramine etc), shift to second generation antipsychotics
- Acute dystonia
  - Symptoms - Sudden contraction of a muscle group resulting in symptoms like torticollis, trismus (contraction of jaw muscles), deviation of eyeballs (oculogyric crisis due to contraction of extraocular muscles), laryngospasm, etc
  - Earliest side effect of antipsychotics
  - More common in young males
  - Treatment - Parenteral anticholinergics (e.g. i.m. promethazine)
  - Prophylaxis - Anticholinergics (E.g. trihexyphenidyl, diphenhydramine etc)
- Acute akathisia
  - Commonest side effect of antipsychotics
  - Characterised by an inner sense of restlessness along with objective signs of restlessness such as fidgeting of legs, pacing around, and inability to sit or stand in one place for a long time
  - DOC - Propranolol
  - Anticholinergics, benzodiazepines can also be used
- Tardive dyskinesia
  - The term 'tardive' means long-term and dyskinesia means abnormal movements
  - Develops after long-term treatment with antipsychotics
  - Can present with involuntary movement of jaw (chewing movements), lips (pouting, puckering, smacking) or extremities
  - Choreiform (rapid, jerky, nonrepetitive) or athetoid movement (slow, sinusoid)
  - Rabbit syndrome - Rhythmic motions of the mouth along a vertical plane
  - Cause - Long term use of antipsychotics and accompanying blockade of D2 receptors results in D2 receptors up-regulation along with postsynaptic dopamine receptor supersensitivity.
  - Treatment - Shift to second generation antipsychotics, Use of Valbenazine, Tetrabenazine, and Deutetrabenazine.
- Neuroleptic malignant syndrome
  - Symptoms - Muscle rigidity, elevated temperature (greater than 38°C), and increased CPK (creatine

phosphokinase) levels.

- Other symptoms - diaphoresis, tremors, confusion, autonomic disturbances, liver enzyme elevation and leukocytosis.
- Pathophysiology - D2 blockade in-
  - Corpus striatum causes muscle rigidity that generates heat
  - Hypothalamus interferes with heat regulation
  - Spinal neurons causes autonomic disturbances
  - Muscle injury causes an increase in CPK levels
  - Continuing muscle damage can cause myoglobinuria and renal failure
- Treatment- Withdraw antipsychotic, adequate hydration, dantrolene is the drug of choice, dopamine agonists like bromocriptine and amantadine can be used too.
- How to restart the antipsychotics? - Keep the patient antipsychotic-free for 2 weeks, then start with second-generation antipsychotics.

B. Endocrine side effects

- Blockade of dopamine receptors in the tuberoinfundibular tract causes hyperprolactinemia (remember dopamine inhibits prolactin secretion)
- Symptoms- Galactorrhoea, menstrual disturbances in females, Sexual dysfunction, low libido in males

C. Sedation, anticholinergic side effects, orthostatic hypotension (mostly with low potency antipsychotics)

Atypical antipsychotics (Second generation antipsychotics)

- Clozapine, olanzapine
- Risperidone, paliperidone, iloperidone
- Quetiapine, ziprasidone, aripiprazole
- Sertindole, zotepine, lurasidone
- Asenapine, amisulpride
- Newer ones - Brexpiprazole, cariprazine, pimavanserin

Side effects of atypical antipsychotics

- Movement disorders (Extrapyramidal symptoms): Less likely than typical antipsychotics
- Endocrine side effects: Less likely than typical antipsychotics (except risperidone and amisulpride, which have a comparatively higher incidence)
- Metabolic side effects: More common than typical antipsychotics. Amongst atypicals, clozapine and

olanzapine have the highest incidence of metabolic side effects.

- Sedation, QTc prolongation & seizures

Clozapine

- **Treatment-resistant schizophrenia (TRS)-** Lack of response to at least two different antipsychotics, including at least one second-generation antipsychotic, given in adequate dosage and for an adequate duration (at least 4-6 weeks).
- Clozapine is the drug of choice (DOC) in TRS.
- Unique mechanism of action- More affinity for D4 than D2, hence causes **minimal EPS.**
- Antipsychotic that causes **max weight gain.**
- Clozapine is the only antipsychotic with **antisuicide property.**

Side effects of clozapine

- Life-threatening: Agranulocytosis (idiosyncratic), myocarditis (idiosyncratic), seizures (dose-dependent)
- Sedation (most common), sialorrhea
- Syncope, hypotension, tachycardia, nausea, vomiting
- Weight gain, anticholinergic side effects

Due to the possibility of agranulocytosis, when a patient is on clozapine, **ANC and TLC monitoring** is required. The regime of monitoring-

  - First 6 months- Once a week
  - Next 6 months- Once in two weeks
  - After 1 year- Once in four weeks, till clozapine is continued
- Stop clozapine, if WBC < 3000/dl or ANC < 1500/dl
- Contraindications for clozapine use
  - WBC < 3500/dl
  - History of agranulocytosis on clozapine
  - Use of other bone marrow suppressants like carbamazepine

Long-acting injectable antipsychotics (Depot antipsychotics)

- Used in cases of poor compliance with antipsychotics
- Intramuscular injections of antipsychotics are typically given once a month or once a fortnight
- Z-track technique is used to give the intramuscular injection