

# L3: Schizophrenia



## Editing file

Color index:

Main Text

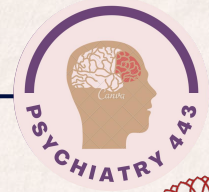
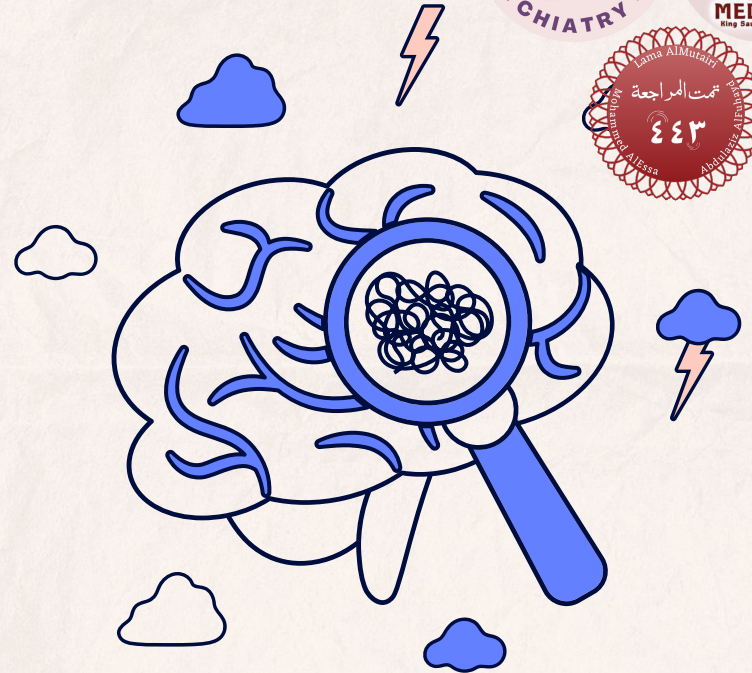
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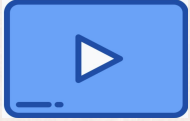
Male Slides

Female Slides

Doctor's Notes

Extra Info





# Objectives :



By the end of this lecture, a student should be able to:



- Appreciate that schizophrenia is a serious, brain illness that needs early intervention and comprehensive management approach.
- Enhance his knowledge of schizophrenia including epidemiology, etiology, diagnosis and management.
- Acquire preliminary skills to evaluate and intervene adequately to manage schizophrenic patients.



Keywords	Definition	Example
Delusions	Fixed, false beliefs that are not shared by the general population. Maintained in spite of proof to the contrary. Can be bizarre (ex. involving supernatural forces) or non-bizarre (ex. fear that organized crime is targeting someone in the family)	A man tells his doctor that his landlord is poisoning him with toxic gas.
Illusion	Misperception of real external stimuli.	An anxious woman interprets the sound of a door slamming as a shot being fired from a gun.
Hallucination	Perceptual abnormalities in which sensory experiences occur in the absence of external stimuli. Could be: visual, auditory, olfactory, tactile, gustatory.	A cocaine abuser feels bugs crawling under his skin (formication, or "cocaine bugs").
<b>frequent derailment</b>	frequent interruptions in thought and <b>jumping</b> from one idea to another unrelated or indirectly related idea.	تسألته سؤال ويجاوب ويروح موضوع ثاني وثالث بنفس السالفة.
<b>incoherence</b>	severe <b>lack of speech cohesion</b> at the basic level of syntax and/or semantics within sentences.	عندهم صعوبة في جمع أفكارهم بسرعة، لما تسألونهم ما يردون بسرعة وكان عندهم تأتأة وتردد بالكلام.
<b>catatonic behavior</b>	unusual behavioral and movement disturbances. manifest with slow or diminished movement (retarded or akinetic type), excess or agitated movement (excited type), or dangerous physiological changes (malignant type).	يسكتون، أو يحركون وجبههم بتعابير غريبة أو يقدون كلامك
<b>avolition</b>	a total <b>lack of motivation</b> that makes it hard to get anything done	الشخص يكون منطفي وما عنده رغبة بأي شي.

# Psychosis

**Psychosis**: Is an abnormal condition of the mind that results in difficulties determining what is real and what is not.

Symptoms	Causes
<ul style="list-style-type: none"> <li>● False unshakeable beliefs (Delusions) <small>ضلالات، مثلاً يشعر انه مراقب وفيه نوايا لقتله. مهما تحاول اقتاعه بغير ذلك لن يقتنع</small></li> <li>● Seeing or hearing things that others do not see or hear (hallucinations)</li> <li>● Incoherent speech &amp;/or behavior that is inappropriate for the situation</li> </ul> <p>Other symptoms:</p> <ul style="list-style-type: none"> <li>● There may be also be <b>social withdrawal, lack of motivation, &amp; difficulties carrying out daily activities (Negative symptoms)</b></li> </ul>	<ul style="list-style-type: none"> <li>● These include <b>mental illness</b>, such as <u>schizophrenia</u> or <u>bipolar disorder</u></li> <li>● Some <b>medical conditions</b> such as <u>Anti-NMDA receptor encephalitis</u>.</li> <li>● Certain <b>medications</b>, such high dose of <u>steroids</u>.</li> <li>● <b>Drugs/substance</b> such as <u>alcohol</u> , <u>stimulant</u> or <u>cannabis</u></li> </ul>

# Psychosis



## Case of Mr. M

### History of Present illness:

- Mr. M is a 28-year-old single male who was brought to emergency room by his family because of gradual changes in his behavior started 9 months ago.
- Since then, he became agitated; eat only canned food but not cooked food made by his family (afraid of being poisoned).
- He started to talk to himself and stare occasionally on the roof of his room.



### Past Psychiatric history:

- He had two brief psychiatric hospitalizations in last 3 years.
- Precipitated by anger at his neighbor and voices commenting about his behavior.

### Past personal history:

was a healthy child, but his parents report that he was a bed wetter and seemed slower to develop than his brothers and sisters.

# Schizophrenia

schizophrenia is not a single disease but a group of disorders with different presentations & with heterogeneous etiologies. Found in all societies and countries with equal prevalence & incidence worldwide.

1

A life prevalence of 0.6 – 1.9%

2

Annual incidence of 0.5 – 5.0 per 10,000

3

Peak age of onset are: 10 - 25 years for ♂ (males).  
25 - 35 years for ♀ (females).

## Etiology :



Exact etiology is unknown BUT There are many etiological theories trying to explain why some people develop schizophrenia.

Stress-Diathesis  
is  
Model

Neurobiology

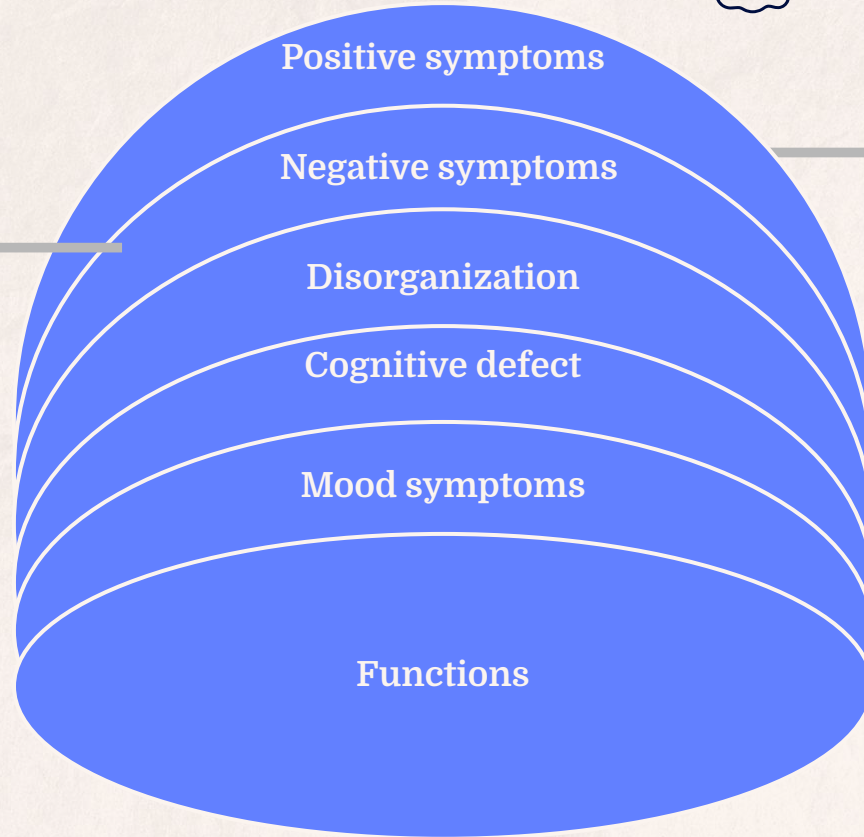
Neuroimaging and  
Neuropathy

Psychoneuroimmunology

Genetics  
factors

Psycho-neuroendocrinology

# Features of Schizophrenia



Positive symptoms

Negative symptoms

Disorganization

Cognitive defect

Mood symptoms

Functions

Feelings or behaviors that are usually **not present** in healthy individuals (eg. hallucinations)

**Negative symptoms**  
an absence or lack of normal mental function (eg. Social withdrawal, absence of pleasure)

Female slides only



# Theories about schizophrenia

Male slides only



## First theory (Stress-Diathesis Model)

1- Integrates biological, psychosocial and environmental factors in the etiology of schizophrenia.

2- Symptoms of schizophrenia developed when there is a stressful influence acted on a person with a specific vulnerability.

3- Such may include family dynamics, perinatal maternal factors and paternal age.

It does not necessarily mean that the stress is only psychological, but also other factors which are biological, psychosocial, and environmental such as usage of drugs or substances.







# Theories about schizophrenia

Male slides only

## Second theory (Neurobiology) <sup>141</sup>

1- Dopamine Hypothesis:	2- Serotonin hypothesis:		4- Glutamate hypothesis:	5- GABA hypothesis:
<p>Too much dopaminergic activity in mesolimbic area (whether it is ↑ release of dopamine, ↑ dopamine receptors, hypersensitivity of dopamine receptors to dopamine, or combinations is not known).</p>	<p>Abnormal serotonin metabolism in some patients.</p>	<p>3- Disturbed balance between dopamine and serotonin.</p>	<p><b>Glutamate hyperactivity</b> causes glutamate-induced neuro-toxicity. <b>Glutamate hypoactivity</b> It has been implicated because ingestion of phencyclidine (a glutamate antagonist) produces an acute syndrome similar to schizophrenia.</p>	<p>The loss of inhibitory GABAergic neurons. Could lead to the hyperactivity of dopaminergic neurons. Some patients with schizophrenia have a loss of GABAergic neurons in the hippocampus.</p>



# Theories about schizophrenia

Details found in Male slides only

## Third theory (Neuroimaging and Neuropathology)

{2} {3}

Neuropathological and neuroimaging abnormalities have been reported in the brain particularly in the limbic system, basal ganglia and cerebellum (Either in structures or connections).

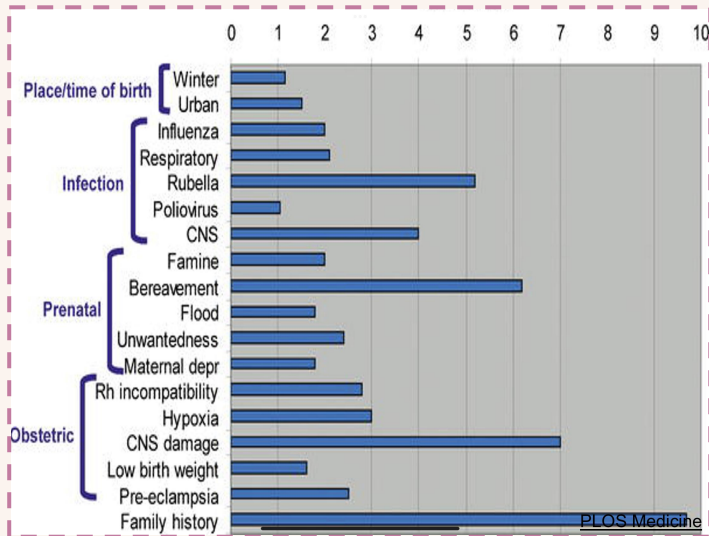
### CT scan studies showed:

- Cortical atrophy in 10 - 35% of schizophrenic patients.
- Enlargement of the lateral and third ventricles in 10 - 50% of schizophrenic patients.
- Findings correlate more with negative features and with cognitive impairments.

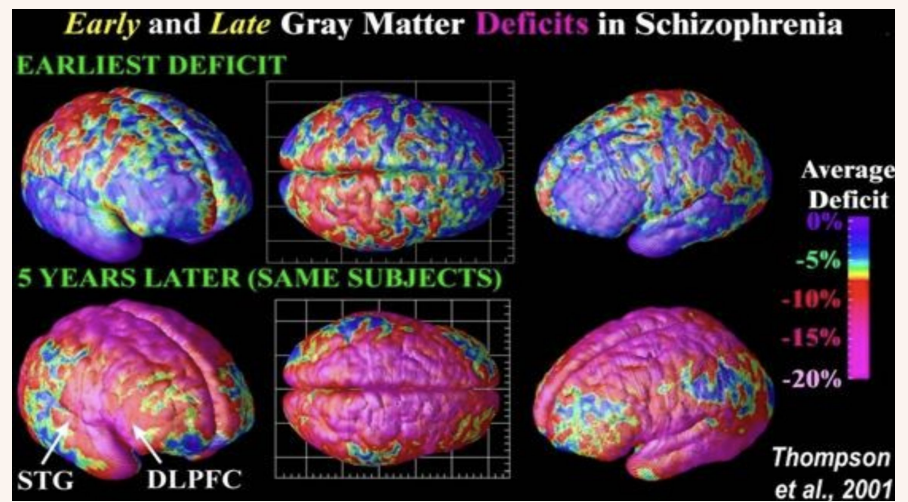
### MRI and PET (Positron Emission Tomography) studies showed:

Show Abnormal frontal, parietal, and temporal lobe structure and metabolism in some schizophrenic patients.

{1}



{2}



{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 prime cause of schizophrenia. But new findings suggest that

impoverished signaling by the more pervasive neurotransmitter glutamate—or, more specifically, by one of glutamate's key targets on neurons [the NMDA receptor]—better explains the wide range of symptoms in this disorder.

**BASAL GANGLIA**  
Involved in movement and emotions and in integrating sensory information. Abnormal functioning in schizophrenia is thought to contribute to paranoia and hallucinations. (Excessive blockade of dopamine receptors in the basal ganglia by traditional antipsychotic medicines leads to motor side effects.)

**AUDITORY SYSTEM**  
Enables humans to hear and understand speech. In schizophrenia, overactivity of the speech area (called Wernicke's area) can create auditory hallucinations—the illusion that internally generated thoughts are real voices coming from the outside.

**FRONTAL LOBE**  
Critical to problem solving, insight and other high-level reasoning. Perturbations in schizophrenia lead to difficulty in planning actions and organizing thoughts.

**OCCIPITAL LOBE**  
Processes information about the visual world. People with schizophrenia rarely have full-blown visual hallucinations, but disturbances in this area contribute to such difficulties as interpreting complex images, recognizing motion, and reading emotions on others' faces.

**LIMBIC SYSTEM**  
Involved in emotion. Disturbances are thought to contribute to the agitation frequently seen in schizophrenia.

**HIPPOCAMPUS**  
Mediates learning and memory formation, intertwined functions that are impaired in schizophrenia.

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{4}

### DIFFERENT NEUROTRANSMITTERS, SAME RESULTS

SOME SCIENTISTS have proposed that too much dopamine leads to symptoms emanating from the basal ganglia and that too little dopamine leads to symptoms associated with the frontal cortex. Insufficient glutamate signaling could produce those same symptoms, however.

**IN THE FRONTAL CORTEX**, where dopamine promotes cell firing (by acting on D1 receptors), glutamate's stimulatory signals amplify those of dopamine; hence, a shortage of glutamate would decrease neural activity, just as if too little dopamine were present.

**IN THE REST OF THE CORTEX**, glutamate is prevalent, but dopamine is largely absent.

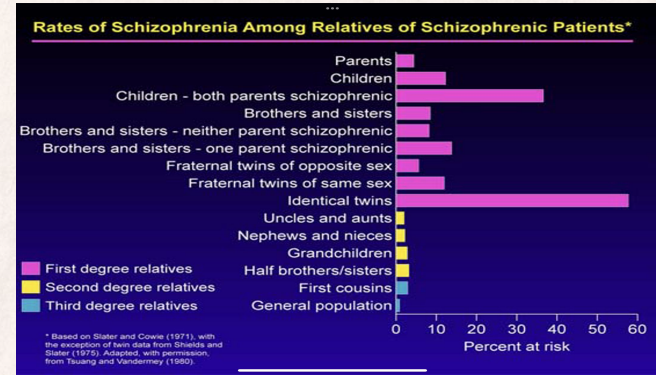
**IN THE BASAL GANGLIA**, where dopamine normally inhibits cell firing (by acting on D2 receptors on nerve cells), glutamate's stimulatory signals oppose those of dopamine; hence, a shortage of glutamate would increase inhibition, just as if too much dopamine were present.

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# Theories about schizophrenia

## Fourth theory (Genetic Factors):

A wide range of genetic studies strongly suggest a genetic component to the inheritance of schizophrenia that outweighs the environmental influence. Those genetic studies include: **Family studies, Twin studies, Chromosomal studies.**



**TABLE.**  
**Susceptibility Genes for Schizophrenia**

Dysbindin	Erb-B4
Neuregulin	FEZ1
DISC-1	MUTED
DAOA	MRDS1
DAAO	BDNF
RGS4	Nur77
COMT	MAO-A
CHRNA7	Spinophyllin
GAD1	Calcyon
GRM3	Tyrosine hydroxylase
PPP3CC	Dopamine <sub>2</sub> receptor
PRODH2	Dopamine <sub>3</sub> receptor
AKT1	

DISC-1=disrupted in schizophrenia-1; DAAO=D-amino acid oxidase activator (G72/G30); DAAO=D-amino acid oxidase; RGS4=regulator of G-protein signalling 4; COMT=catechol O methyl transferase; CHRNA7=α-7 nicotinic cholinergic receptor; GAD1=glutamic acid decarboxylase 1; GRM3=glutamate receptor, metabotropic 3; BDNF=brain derived neurotrophic factor; MAO-A=monoamine oxidase A.

Male slides only

Genes plus stressors

Schizophrenia is mostly caused by various possible combinations of many different genes (which are involved in neurodevelopment, neuronal connectivity and synaptogenesis) plus stressors from the environment conspiring to cause abnormal neurodevelopment.

# Diagnosis

## Diagnostic Criteria (DSM-5) for Schizophrenia:

A) Two or more of the following characteristic symptoms for one month at least one of them is 1, 2 or 3

1. Delusions.

2. Hallucinations.

3. Disorganized speech (frequent derailment or incoherence).

4. Grossly disorganized or catatonic behavior.

5. Negative symptoms (Diminished emotional expression or lack of drive (avolition)).

B) Social, Occupational or self-care dysfunction

C) Duration of at least 6 months of disturbance (Include at least one month of active symptoms that meet Criterion A; in addition of periods of prodromal and residual symptoms).

D) Schizoaffective, mood disorder, and other psychotic illnesses should be excluded

E) Disturbance is not due to substance or other medical conditions.

F) If there is history of autism spectrum disorder or a communication disorder of childhood onset, schizophrenia diagnosis is made only if delusion or hallucinations plus other criteria are present.

# Clinical features

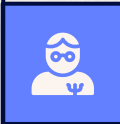


No single clinical sign or symptom is **pathognomonic** for schizophrenia

Patient's history & mental status examination are essential for diagnosis.



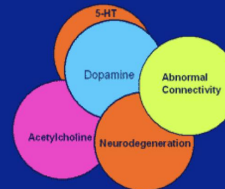
**Prodromal features** include obsessive compulsive behaviors, attenuated positive psychotic features.



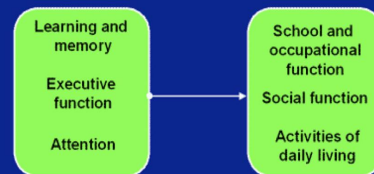
**Premorbid history** includes schizoid or schizotypal personalities, few friends & exclusion of social activities.

## Cognitive deficits in schizophrenia

Multiple Mechanisms for Cognitive Dysfunction in Schizophrenia



Cognitive Deficits Predict Functional Outcomes



Male slides only

# Clinical features



## Positive symptoms

- Delusions \*
- Hallucinations \*\*

Picture of schizophrenia includes **positive** and **negative** symptoms

## Negative symptoms

- Affective flattening or blunting
- Poverty of speech
- Poor grooming
- Lack of motivation
- Social withdrawal

\*= Delusions are False fixed beliefs (مثلا يكون معتقد اعتقاد جازم ان الدكتور رح يعطيه سم بدل العلاج)

\*\*= Hallucinations are False perception of objects or events involving your 5 senses (مثلا يسمع احد يناديه باسمه بس بالواقع ما فيه احد)





# Mental Status Examination



01

Appearance & behavior (Variable presentations) (Poor self care)

02

Mood, feelings & affect (Reduced emotional responsiveness, inappropriate emotion) (No reactions)

03

Thought Process/form (Looseness of association, thought blocking, poverty of thought content, perseveration) (كلامه غير مترابط)

04

Perceptual disturbances (Hallucinations, illusions)

05

Thought content (Delusions, violence, suicide, & homicide)

06

Cognitive functioning (Poor abstraction)

07

Poor insight and judgment



# Illness course:

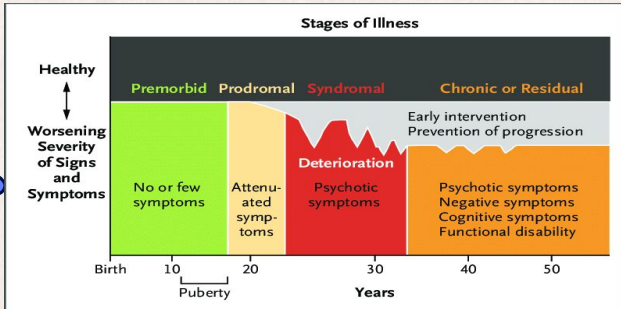
Male slides

## Common illness Course:

- Chronic Illness
- **Acute exacerbation** with **increased** residual impairment
- **Full recovery: very rare**
- Longitudinal course: **downhill**

## Illness course:

- **Link to prognostic risk factors**



# Prognostic risk factors

## **Good** Prognostic factors

- **Late** age of onset
- **Female**
- **Acute** onset
- Obvious precipitating factors
- **Few** relapses
- Presence of mood component
- Good response to Tx
- Good supportive system

## **Poor** Prognostic factors

- **Young** age of onset
- **Male**
- Insidious onset
- Lack of precipitating factors
- **Multiple** relapses
- **Low IQ**
- No Remission in 3 years
- Poor compliance
- Poor premorbid personality
- Negative symptom
- Positive family history



# Management of schizophrenia

Male slides

Schizophrenia

Chronic illness

When patients stable they treated and seen frequently at:

outpatient clinic

In relapse, they should be admitted to:

psychiatric inpatient unit

Treatment include:

- Biological therapies
- Psychosocial therapies
- Biopsychosocial approach**

## Indications for hospitalization

- Patient & other's safety
- Can't take care of himself/herself
- Initiating or stabilizing medications
- Diagnostic purpose
- Establishing an effective association between patient & community supportive systems



Antipsychotic medications are the mainstay of the treatment.

## Types

**Typical:** Dopamine receptors antagonists

**Atypical:** Serotonin-dopamine receptor antagonists

## Side Effects

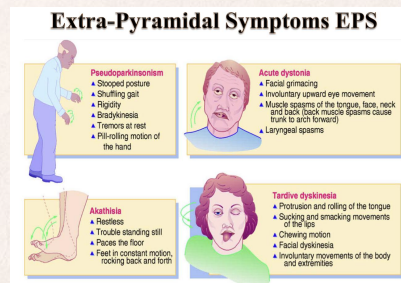
- Stiffness and shakiness, like Parkinson's' disease (**Dystonia**).
- Uncomfortable restlessness (**Akathisia**).
- Long-term use can produce movements of the face (**tardive dyskinesia**) and rarely, of the arms or legs.
- Feeling sluggish, slow in thinking, apathy, low motivation (**Negative symptoms**).
- Problems with breast swelling or tenderness and (**Galactorrhea**).
- Some can affect blood pressure and make patient feel dizzy.
- Decrease Libido.

- Sleepiness and slowness.
- **Weight gain.**
- Increased chance of developing **diabetes** and **metabolic syndrome**
- Decrease Libido
- Some can affect blood pressure and make patient feel dizzy.
- In high doses, some have the same EPS and Parkinsonian side-effects as the older medications (stiffness of the limbs) but less than typical.
- Problems with breast swelling or tenderness and **galactorrhea** but less than typical

TO BE CONTINUED

## Side Effects

- High Potency typical antipsychotics: **Neurological** side effects.
- Low Potency typical and atypical antipsychotics: many other side effects.
- Extrapyramidal symptoms (EPS):
  - Acute Dystonia (hours)
  - Akathisia (days)
  - Pseudo-parkinsonism (weeks)
  - Tardive Dyskinesia (years)
- Acute and Chronic EPS



**Maximum**

**Minimum**

← HIGH POTENCY FGAs

RISPERIDONE

OLANZAPINE

PALIPERIDONE  
(DOSE-RELATED)

→ CLOZAPINE  
ZIPRASIDONE  
QUETIAPINE  
ARIPIPRAZOLE\*

## Other types of biological therapy:


Male slides

- Depot forms of antipsychotics (can be an injection given every week or month)
  - Risperidone Consta is indicated for poorly compliant patients
- Electroconvulsive therapy (ECT) for catatonic or poorly responding patients to medications

## Antipsychotic Medications

Conventional Antipsychotics	Atypical Antipsychotics
Chlorpromazine	Aripiprazole
Fluphenazine	Clozapine
Haloperidol	Olanzapine
Loxapine	Paliperidone
Molindone	Quetiapine
Perphenazine	Risperidone
Pimozide	Ziprasidone
Prochlorperazine	
Thiothixene	
Thioridazine	
Trifluoperazine	

# Neuroleptic malignant syndrome (NMS)

- 
- 1 — Can conceptually be characterized as “severe EPS (i.e., extreme rigidity) with fever”
  - 2 — Possibly secondary to dopaminergic receptor blockade in the Substantia Nigra producing rigidity and fever
  - 3 — Can develop with any antipsychotic medication.
  - 4 — Presents with symptoms easily recalled with the acronym (**F + ARGO**):
    - **F**ever
    - **A**utonomic dysregulation (e.g., hypertension, tachycardia, urinary incontinence).
    - **R**igidity (“lead-pipe”).
    - **G**ranulocytosis (as well as increased lactic dehydrogenase, liver function tests, creatinine phosphokinase [CPK], and myoglobinuria)
    - **O**rientation changes (confusion, coma).
    - Can additionally present with acute renal failure (due to myoglobinuria), proteinuria, deep vein thrombosis, respiratory distress, and dehydration.

# Other Psychotic Disorders

## Primary disorders

- Schizophreniform disorder
- Brief psychotic disorder
- Delusional disorder
- Schizoaffective disorder
- Mood disorders
- Personality disorders
- (schizoid, schizotypal & borderline personality)
- Factitious disorder
- Malingering



## Secondary disorders


- Substance-induced disorders
- Psychotic disorders due to another medical disorder :
  - Epilepsy ( complex partial)
  - CNS disease
  - Trauma
  - Others

# Psychosocial Therapies


- Social skills training.
- Family oriented therapies.
- Group therapy.
- Individual psychotherapy.
- Assertive community treatment.
- Vocational therapy.

## Criteria of other Psychotic Disorders

- Schizoaffective Disorder
  - Brief Psychotic Disorder (<1 month of disturbance)
  - Schizophreniform Disorder (1-<6 months of disturbance)
  - Delusional Disorder (delusion only > 1 month)
  - Substance/medication-Induced Psychotic Disorder
  - Psychotic Disorder Due to Another Medical condition
- نفس الأعراض، الفرق بالمدة




## Team Leaders :



**Reema alzughaibi**

**Marwan almalki**



## Team Members:

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