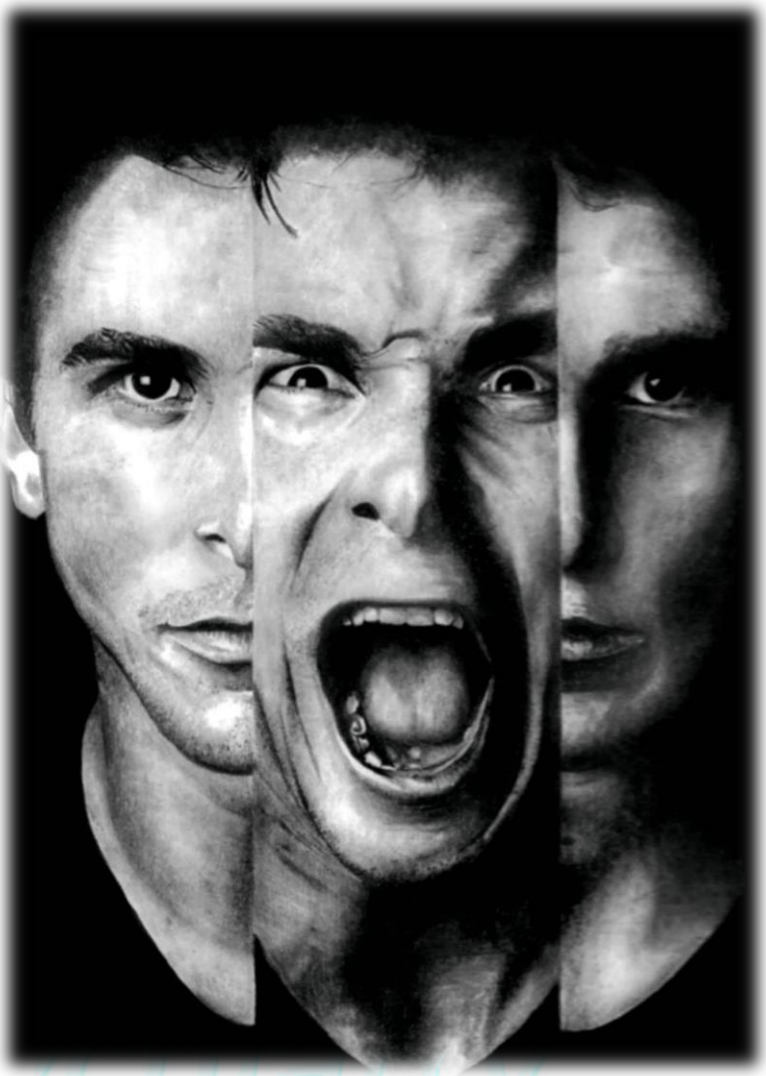

Schizophrenia

Psychiatry 4 3 2

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- **Important**
- **Additional information**
- **Male doctor's notes**
- **Female doctor's notes**

Objectives:

- ✓ To have the base knowledge about **Schizophrenia**.
- ✓ To be aware about **Schizophrenia**.
- ✓ To have skills to diagnose the disease.

Mind Map

First remember:

Delusions: are false fixed beliefs.

Hallucinations: are false abnormal perceptions.

Case of a schizophrenic patient

Mr. Schi 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 talks to himself and stares occasionally on the roof of his room**.

He **had two brief psychiatric hospitalizations in last 3 years that were precipitated by anger at his neighbor and voices commenting about his behavior.**

His personal history indicated that he was a healthy child, but his parents reported that he was a bed wetter and **seemed slower to develop than his brothers and sisters.**

Schi **smokes tobacco frequently to calm himself**. During his early adolescence he **used to smoke Hash heavily plus occasional use of amphetamine. He stopped both Hash and Amphetamine use 5 years ago**.

Notes:

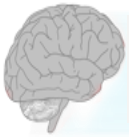
- Schizophrenia is different than "Dissociative identity disorder" or (multiple personality disorder) which is characterized by at least two distinct and relatively enduring identities or dissociated personality states.
- This disorder affects person's thoughts.
- Hallucinations 2 types **visual and auditory** .Usually patients have **auditory** hallucinations maybe (2nd person) or (3rd person sometimes "command").
- Persecutory delusions are the most common form of delusions in schizophrenia.
- Schizophrenics smoke more than any people because they have dopamine deficiency in the prefrontal cortex. So, Nicotine increases release of dopamine.
- Also, they have slow development in childhood.
- **Hash** is the highest risk factor of schizophrenia. Then, **amphetamine** comes after.

Schizophrenia

- It is not a single disease but a group of disorders with heterogeneous etiologies.
- Found in all societies and countries with equal prevalence & incidence worldwide (**not** related to culture).
- A life prevalence of 0.6 – 1.9 % (1%).
- Annual incidence of 0.5 – 5.0 per 10,000.
- Peak age of onset is 10-25 years for male & 25-35 years for female.
- Male: Female ratio = 1:1 <- females have better prognosis than male.

Note

#	Primary disorder	Secondary disorder
Etiology	Multifactorial.	Exact etiology.
Example	Schizophrenia.	Hyperglycemia secondary to steroids.



Etiology

Exact etiology is unknown.

Chronic relapsing disease

1- Stress-Diathesis Model:

- Integrates biological, psychosocial and environmental factors in the etiology of schizophrenia.
- Symptoms of schizophrenia develop when a person has **a specific vulnerability** that is acted on by a stressful influence.

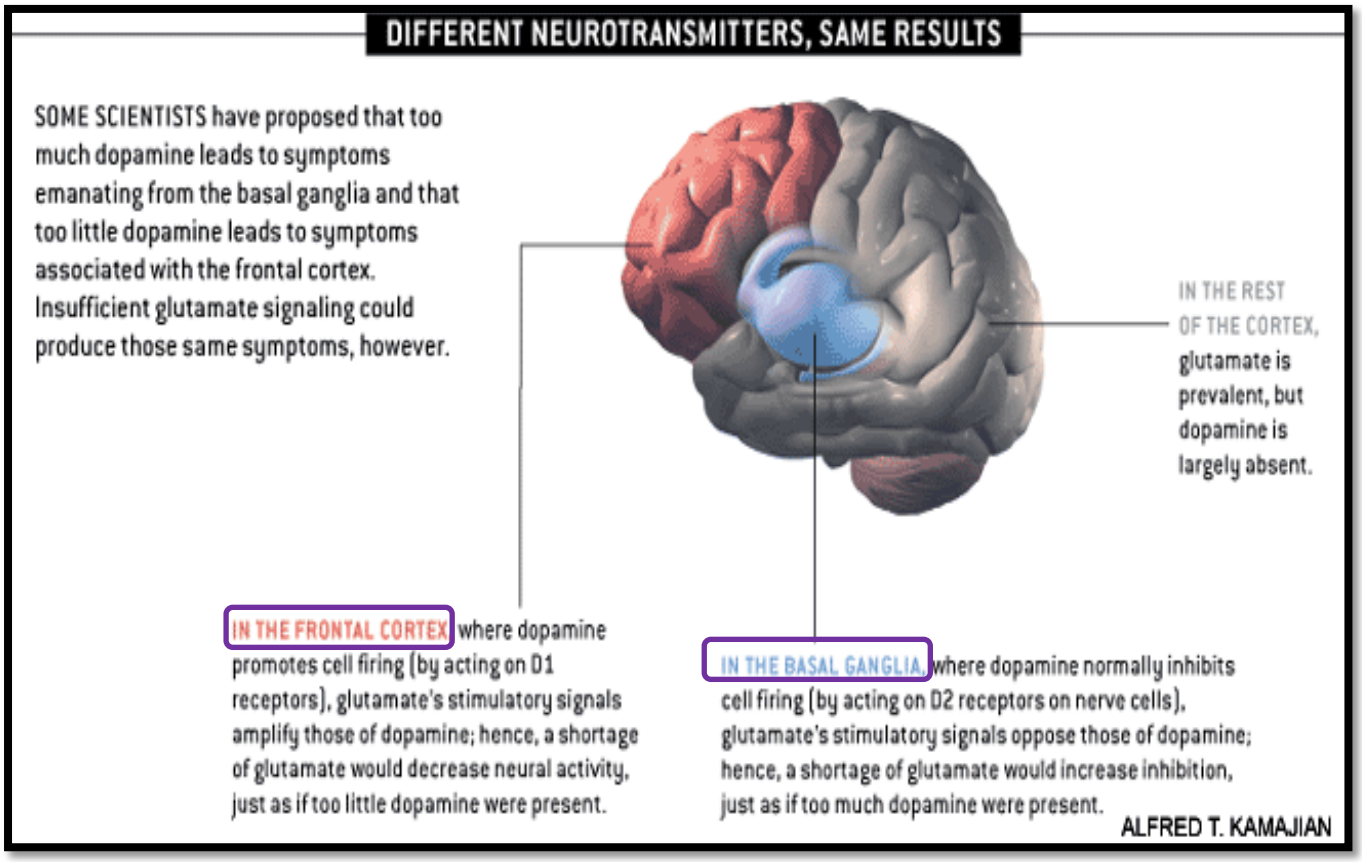
2- Neurobiology:

* Certain areas of the brain are involved in the pathophysiology of schizophrenia: **the limbic system "mesolimbic system", the frontal cortex, cerebellum, and the basal ganglia**.

A) Dopamine Hypothesis: "blind factor"

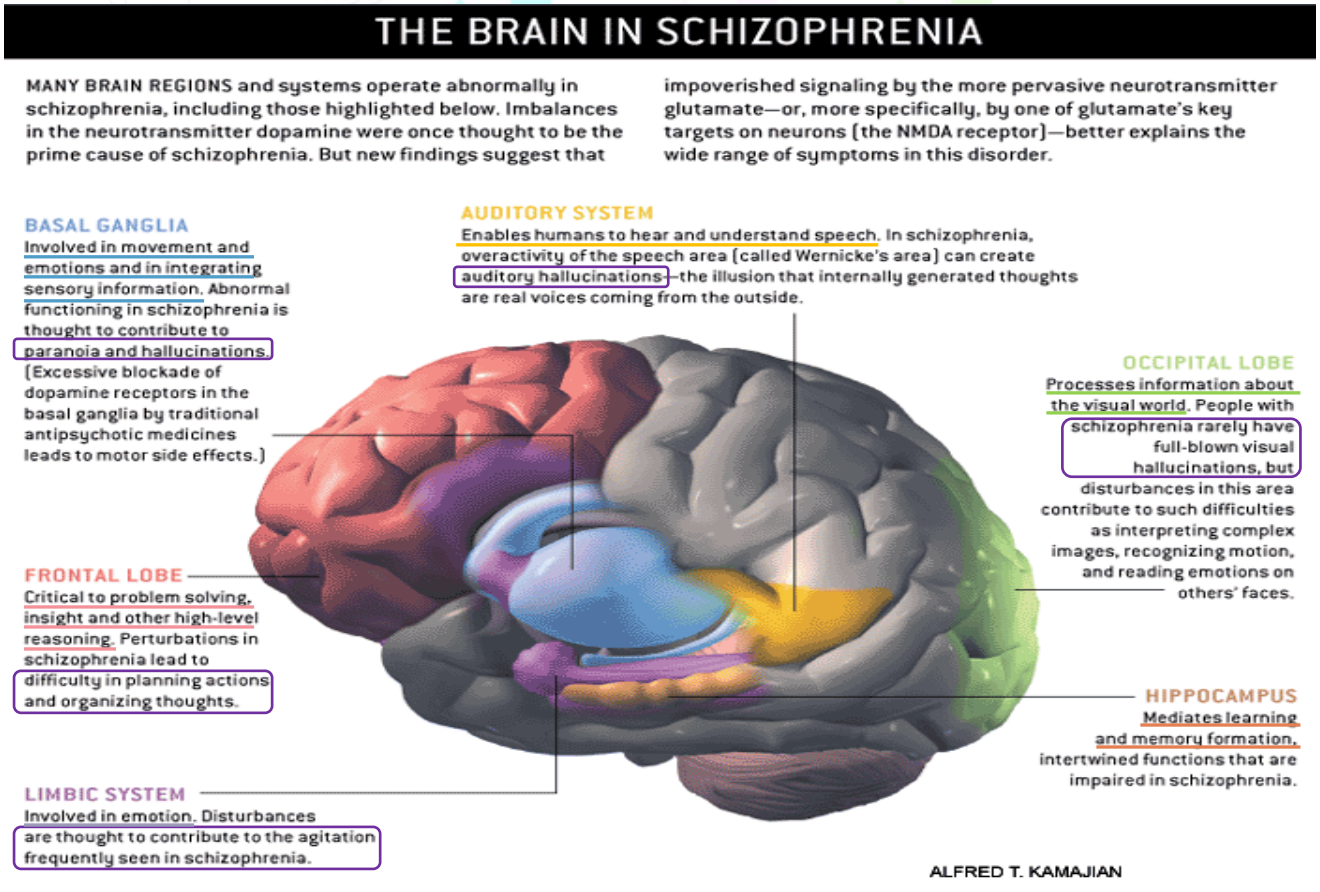
Too much dopaminergic activity (whether it is ↑ release of dopamine, ↑ dopamine receptors, hypersensitivity of dopamine receptors to dopamine, or combinations is not known).

B) Other Neurotransmitters; serotonin, Norepinephrine, GABA, Glutamate & Neuropeptides.

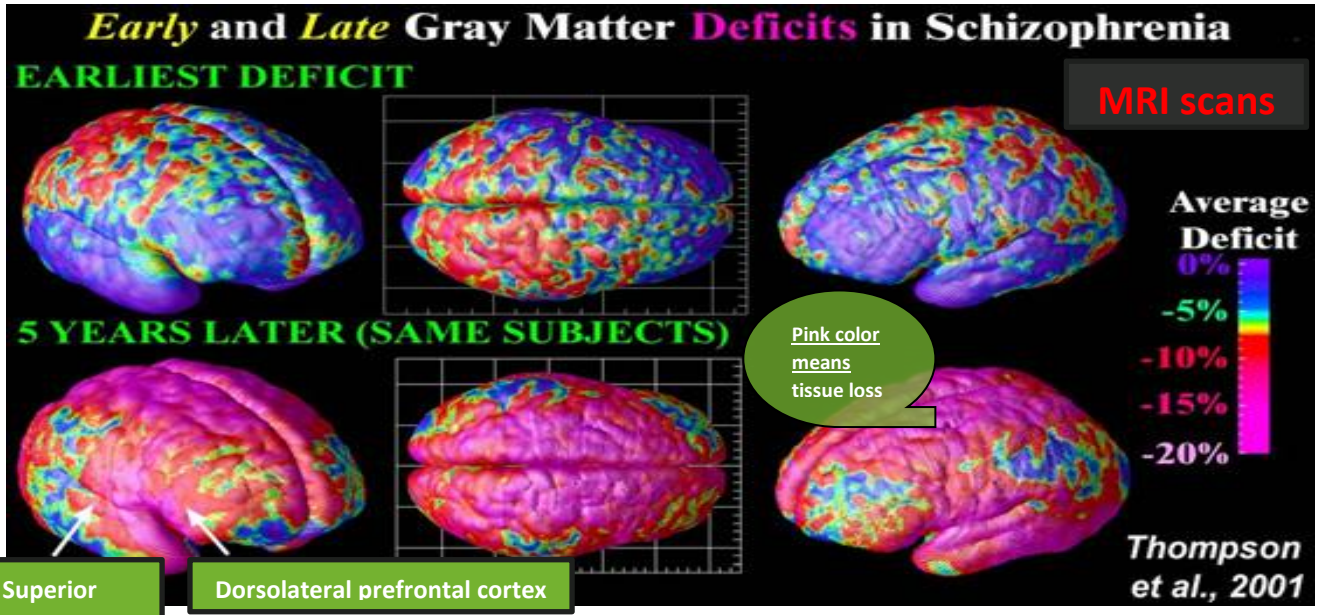


C) Neuropathology:

Neuropathological and neurochemical abnormalities have been reported in the brain particularly in the limbic system, basal ganglia and cerebellum, either in structures or connections.



- ✓ **Every area of the brain may be affected by schizophrenia.**
- ✓ **Hippocampus involvement appears in advanced cases.**



- ✓ **There is no specific brain tissue loss in schizophrenia.**
- ✓ **There is brain loss, enlarged ventricle.**

D) Psychoneuroimmunology: "blind factor"
↓T-cell interlukeukin-2 & lymphocytes, abnormal cellular and humoral reactivity to neurons and presence of antibrain antibodies.

These changes are due to neurotoxic virus or endogenous autoimmune disorder.

E) Psychoneuroendocrinology: "blind factor"
Abnormal dexamethasone-suppression test.

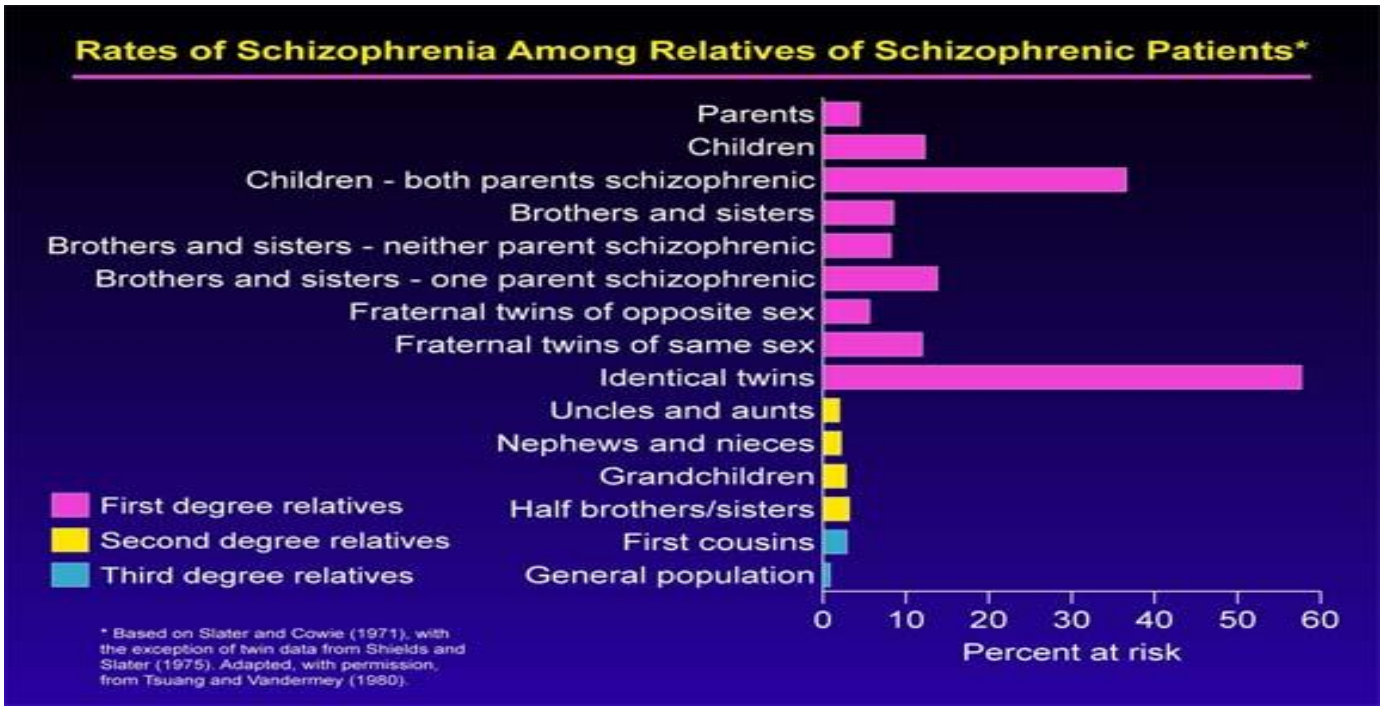
↓ LH/FSH

A blunted release of prolactin and growth hormone on stimulation.

3- Genetic Factors: **"The most important factor". (Important)**

- A wide range of genetic studies *strongly* suggest a genetic component to the inheritance of schizophrenia that out weights the environmental influence.

- These include: family studies, twin studies and chromosomal studies.



- **If only one parent is schizophrenic, the risk is 10 %**
- **If both parents are schizophrenics, the risk is 40%**
- **If there is a schizophrenic monozygotic twin, the risk is 50-60%**

Males Slides

❖ **Schizophrenia: 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.

There is also abnormal neurotransmission at glutamate synapses, possibly involving hypofunctional NMDA receptors.)

- There is no **only one gene** can cause schizophrenia.
- You don't have to remember these genes.

TABLE.
Susceptibility Genes for Schizophrenia

Dysbindin	Erb-B4
Neuregulin	FEZ1
DISC-1	MUTED
DAOA	MRDS1
DAAO	BDNF
RGS4	Nur77
COMT	MAO-A
CHRNA7	Spinophylin
GAD1	Calcyon
GRM3	Tyrosine hydroxylase
PPP3CC	$Dopamine_2$ receptor
PRODH2	$Dopamine_3$ receptor
AKT1	

DISC-1=disrupted in schizophrenia-1; DAOA=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 nictonic cholinergic receptor; GAD1=glutamic acid decarboxylase 1; GRM3=glutamate receptor, metabotropic 3; BDNF=brain derived neurotrophic factor; MAO-A=monoamine oxidase A.

Stahl SM. *CNS Spectr.* Vol 12, No 8. 2007.

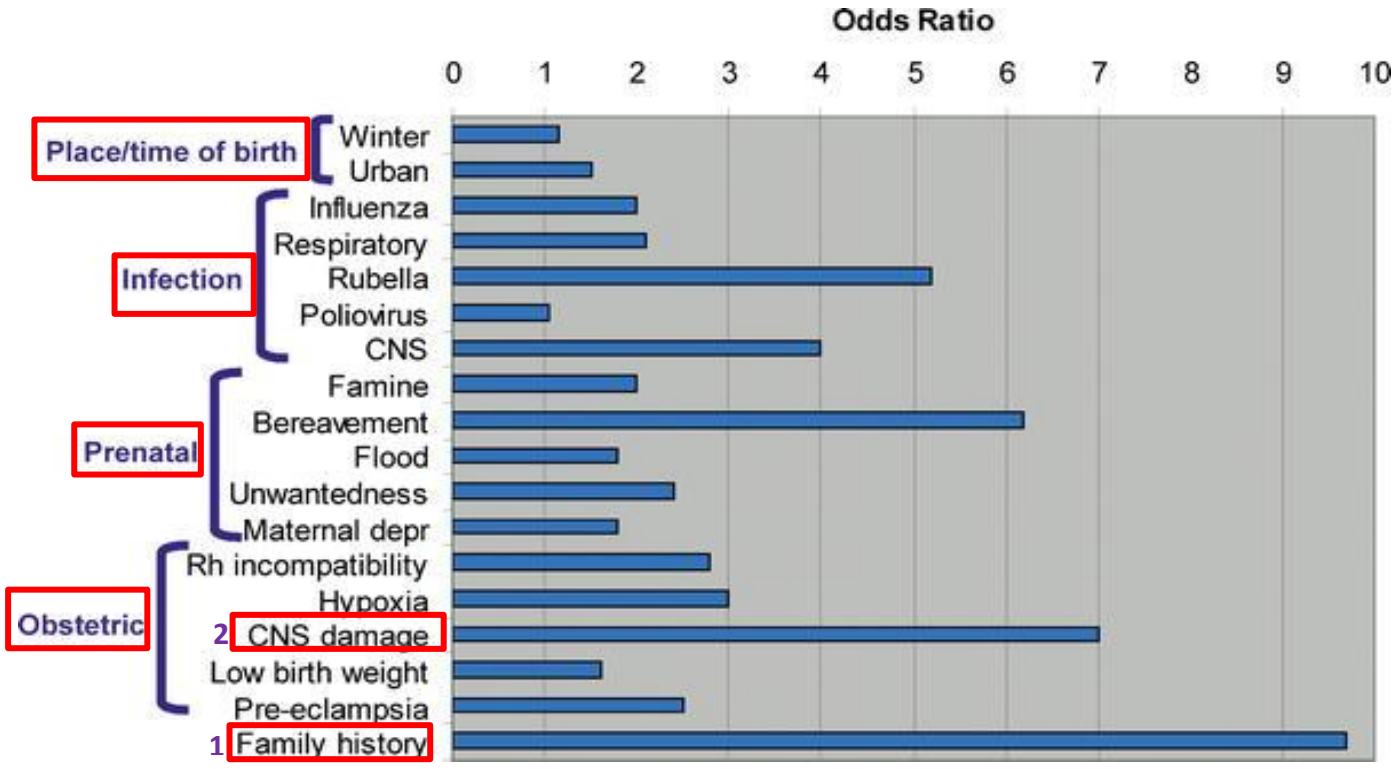
4- Psychosocial Factors:

- In family dynamics studies, **no** well-controlled **evidence** indicates specific family pattern plays a causative role in the development of schizophrenia (unless the boy already has schizophrenia → family dynamics in this case may affect the prognosis).

- **High Expressed Emotion family: increase risk of relapse**.

The increase is because the family expects a full recovery from the patient which in that case is very rare so that puts him in high stress.

"Weight of different risk factors"



Family history is the most risk factor of schizophrenia.

❖ Subtypes of Schizophrenia:

1. **Paranoid type:** (suspicious; e.g. he is followed by somebody…).
2. **Disorganized type:** Confused < ملخبط >&it's common in adolescents because personality, education, relationships not established yet.
3. **Catatonic type:** (unable to move his body; stupor & taking a certain position for long time).
4. **Undifferentiated type:** (can't distinguish among schizophrenia types).
5. **Residual type:** (after acute phase & after long time of disorder; after years the -ve symptoms appear) doesn't talk & runs away from home.يهرب من البيت.

Diagnosis

DSM-5 Diagnostic Criteria for Schizophrenia:

A- Two or more characteristic symptoms for one month, at least one of them is (1),(2) or (3):

1- Delusions "persecutory delusions." (Commonly seen in **Paranoid type**)

2- Hallucinations "auditory hallucinations."

3- Disorganized speech (frequent derailment or incoherence).

4- Grossly disorganized behavior or catatonic behavior.

(3 &4) Commonly seen in **disorganized type**

Grossly disorganized behavior: for example; confronting others without logical reason, wearing many layers of clothing on a warm day and having a very messy appearance.

Catatonic Behavior: characterized by muscular tightness or rigidity and lack of response to the environment.

5- Negative symptoms (diminished emotional expression or lack of drive. (Commonly seen in **Residual type**)

B- Social, Occupation or self-care dysfunction: Never diagnose an individual with Schizophrenia without the fact that there is a social/occupational 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 exclusion.

E- The disturbance is not due to Substance or another medical condition.

F- Relationship to pervasive developmental disorders.

Males Slides

G- 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

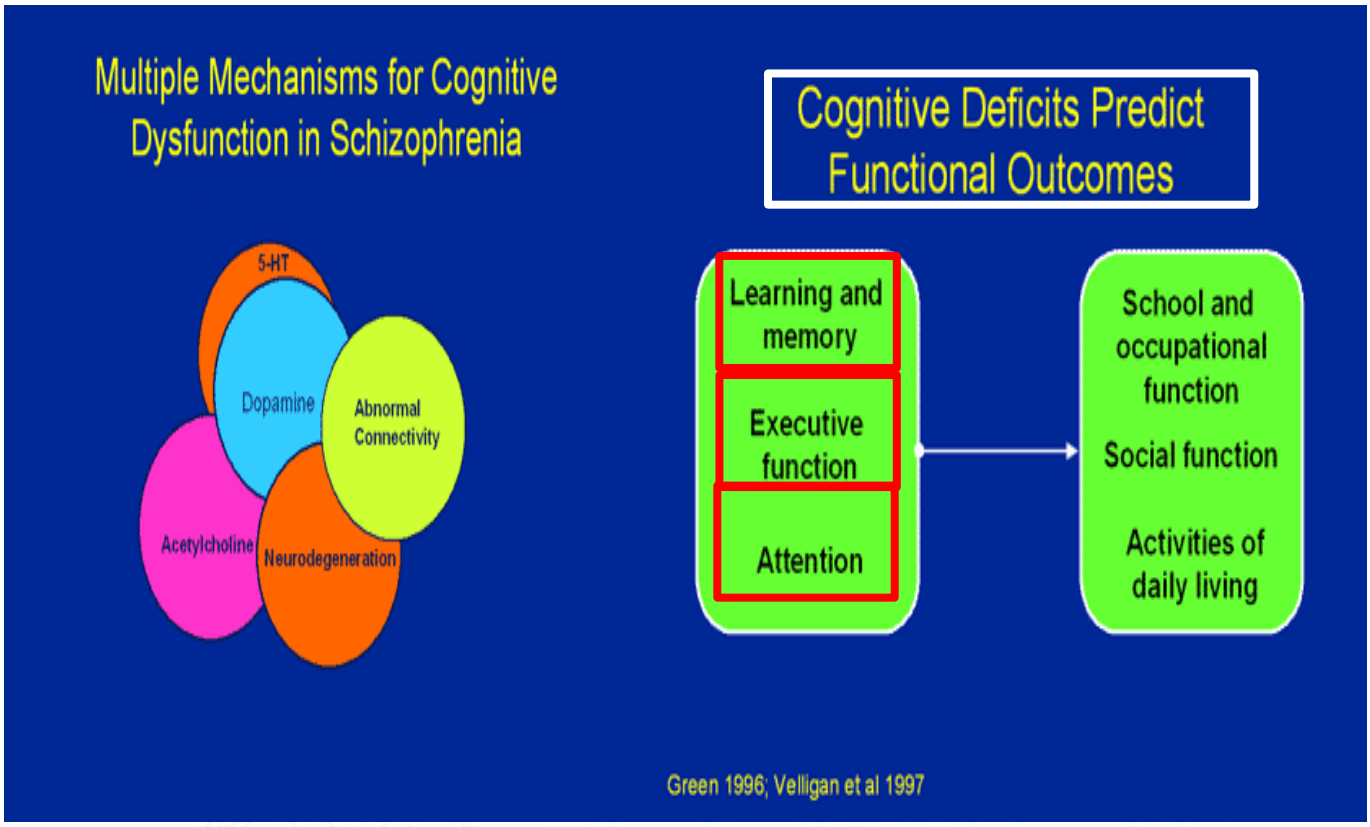
- **No single clinical sign or symptom is pathognomonic for schizophrenia.**
- Patient's history & mental status examination are **essential** for diagnosis.
- Premorbid history includes **schizoid** (the patient isolates himself from any social activity & interacts with things like computers…) or **schizotypal** (unusual clothes or personality unexpected from him in a certain situation) personalities, few friends & exclusion of social activities.
- Prodromal features (precursor) include obsessive compulsive behaviors which are bizarre (e.g. the patient feels oil in his hand & it will inter his body), attenuated positive psychotic features.

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

❖

- **Positive symptoms like: delusions & hallucinations.**
- Positive symptoms mean excess or distortion of normal functions.
- **Negative symptoms like: affective flattening or blunting (deficit in feeling; بليد), poverty of speech, poor grooming (cleaning & maintaining appearance), lack of motivation, and social withdrawal (e.g. occupational & functional).**
- Negative symptoms mean a diminishment or absence of characteristics of normal function.

Cognitive deficits in schizophrenia



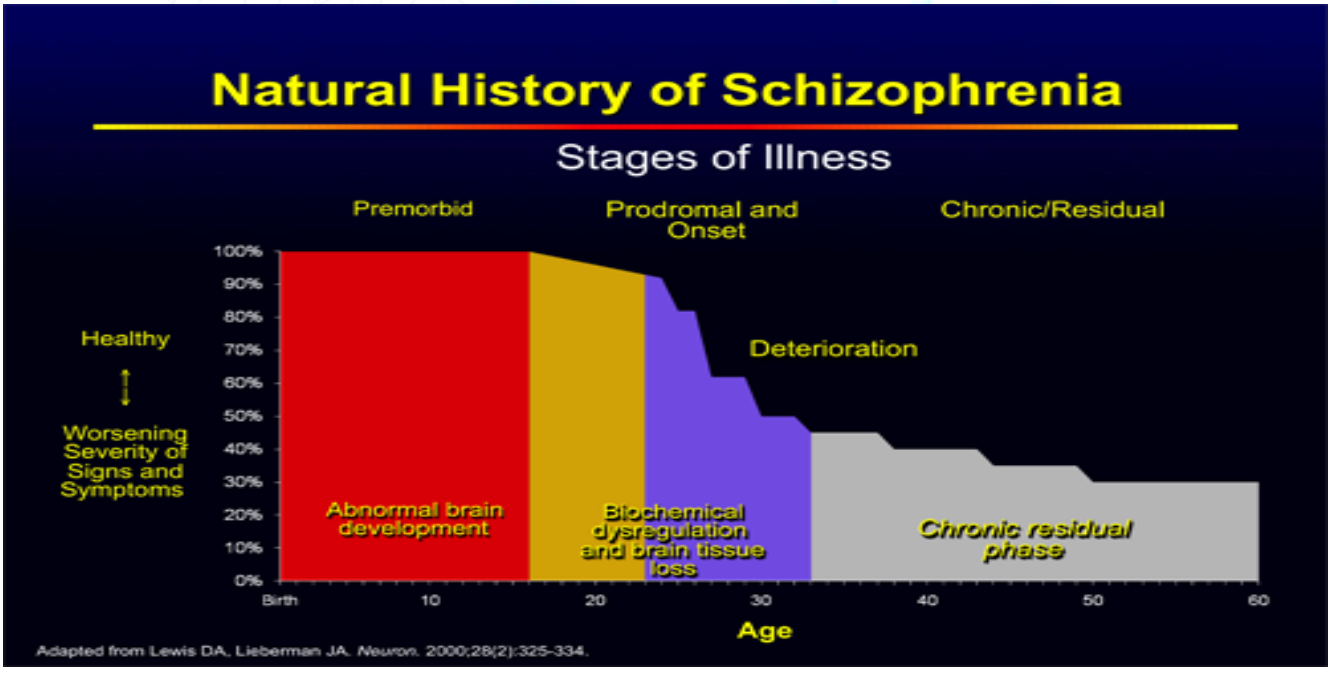
Mental Status Examination:

Appearance & behavior	Variable presentations.
Mood, feelings & affect	Reduced emotional responsiveness, inappropriate emotion.
Perceptual disturbances	Hallucinations, illusions.
Thought	- Thought content (delusions) "persecutory". - Form of thought (looseness of association). - Thought process (thought blocking, poverty of thought content, poor abstraction, and perseveration).
Impulsiveness, violence, suicide & homicide.	- Suicide: killing self. - Homicide: killing others.
Cognitive functioning	Poor.
Insight and judgment	Poor.

Course

- Acute exacerbation with increased residual impairment.
- Full recovery: very rare.
- Longitudinal course: downhill (they are treated for life time).
- 5% of patients have major Deterioration, no medication response and may end up to be admitted to hospital for long time.
- 15% of patients have excellent prognosis and may take one year of disturbance or less.
- 30 % of patients have relapses from time to time.
- 50 % of patients have many relapses, but they don't need to be admitted to hospital.

Males Slides



1. Premorbid phase --> abnormal brain development
2. Prodromal phase --> biochemical dysregulation and brain tissue loss
   Prodromal = early symptom indicating the onset of an attack or a disease
3. Deterioration phase --> relapses begins
4. Chronic residual phase.

Prognosis:

Good Prognosis factors	Poor Prognosis factors
1. Late age of onset. Females have better prognosis **2. Acute onset.** 3. Obvious precipitating factors. 4. Presence of mood component. 5. Good response to Treatment. 6. Good supportive system.	**1. Young age of onset.** **2. Insidious onset (gradual).** 3. Lack of P.F. 4. Multiple relapses. 5. Low IQ. 6. Poor premorbid personality. 7. Negative symptom. 8. Positive family history.

Differential Diagnosis	
Secondary psychiatric disorders (Non-psychiatric)	**Primary Psychiatric disorders**
1- **Substance-induced disorders** e.g.: Hash + **amphetamine**. 2- **Psychotic disorders due to another medical disorder**: • Epilepsy (complex partial) & in TLE = temporal lobe epilepsy. • CNS diseases. • Trauma. • Others.	• **Schizophreniform disorder** → better prognosis. • Brief psychotic disorder. • Delusional disorder. • Schizoaffective disorder. • Mood disorders. • Personality disorders (schizoid, schizotypal & borderline personality). • Factitious disorder. • Malingering.

Criteria of other Psychotic Disorders

- Psychotic Disorders due to another medical condition
- Substance-induced psychotic disorder
- **Schizophreniform disorder:**

  1-6 month of disturbance " Very important "
- **Brief psychotic disorder:**

  < 1 month of disturbance.
- **Delusional disorder (delusion only > 1 month).**
- **Schizoaffective disorder: (**An uninterrupted period of illness during which there is a major mood episode (major depressive or manic) concurrent with Criterion A of schizophrenia. There is Delusions or hallucinations for 2 or more weeks in the absence of a major mood episode during the illness course.**)**

Treatment

The indications for hospitalization:

- Diagnostic purpose.
- Patient & other's safety.
- Initiating or stabilizing medications.
- Establishing an effective association between patient & community supportive systems.

A- Biological therapies:

- **Antipsychotic medications** are the mainstay of the treatment of schizophrenia.
  - Generally, they are remarkably safe.
  - Two major classes:

1- **Dopamine receptor antagonists** (Typical or Conventional), (1st generation) e.g. haloperidol, chlorpromazine.

2- **Serotonin-dopamine receptor antagonists** (Atypical), (2nd generation) e.g. Risperidone, clozapine, olanzapine).

- Depot forms of antipsychotics e.g. Risperidone Consta is indicated for poorly compliant patients.

- **Other drugs:**
  1- Anticonvulsants
  2- Lithium
  3- Benzodiazepines

- **Electroconvulsive therapy (ECT) for catatonic or poorly responding patients to medications.**

- **Side effects of antipsychotics:**

TABLE
RECEPTOR BLOCKADE AND ANTIPSYCHOTIC SIDE EFFECTS[2]

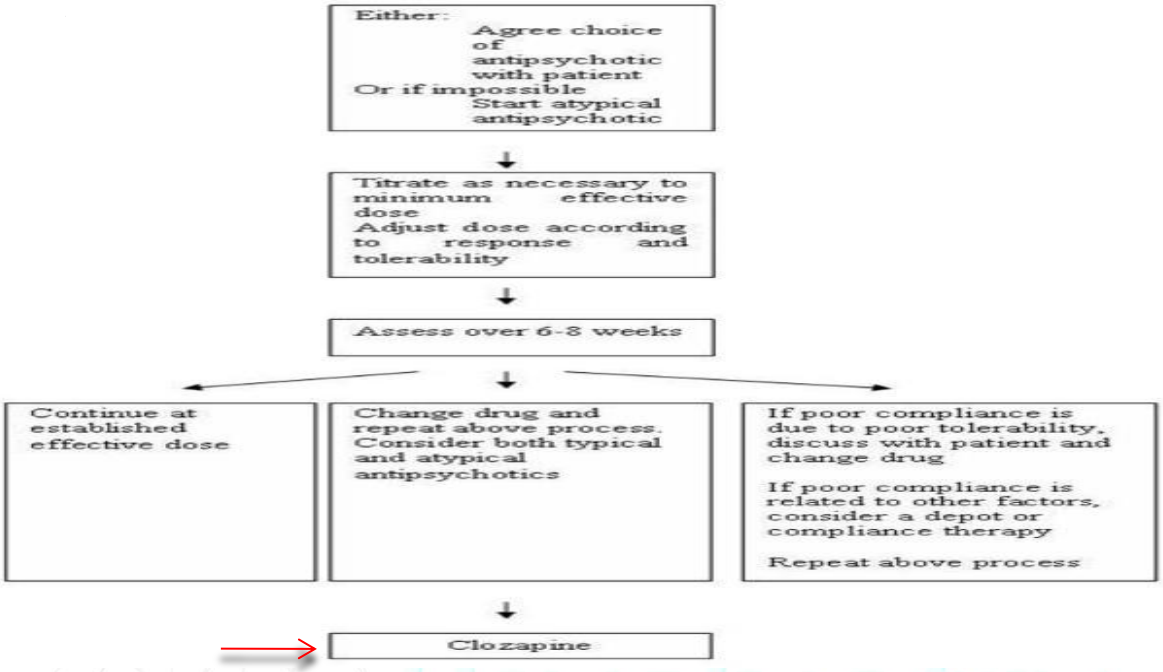
Receptor Type	*Side Effects*
D_2	EPS, prolactin elevation
M_1	Cognitive deficits, dry mouth, constipation, increased heart rate, urinary retention, blurred vision
H_1	Sedation, weight gain, dizziness
α_1	Hypotension
$5\text{-}HT_{2A}$	Anti-EPS (?)
$5\text{-}HT_{2C}$	Satiety blockade

D=dopamine; EPS=extrapyramidal symptoms; M=muscarine; H=histamine; 5-HT=serotonin.

Robinson DS. *Primary Psychiatry.* Vol 14, No 10. 2007.

- **High Potency typical antipsychotics: Neurological side effects.**
- **Low Potency typical and atypical antipsychotics: many other side effects.**

❖ Pharmacological Treatment



The last choice of the treatment of schizophrenia is **Clozapine**

Clozapine has serious side effects:

Agranulocytosis (↓WBC count) & reduced seizures threshold.

Common side effects of antipsychotic medication:

First generation antipsychotics	*Second generation antipsychotics*	*Clozapine*
Extrapyramidal effects Dystonia Pseudoparkinsonism Akathisia Tardive dyskinesia	Olanzapine Weight gain Sedation Glucose intolerance and frank diabetes mellitus Hypotension	Sedation
Sedation		Hypersalivation
Hyperprolactinaemia	Risperidone Hyperprolactinaemia Hypotension EPS at higher doses Sexual dysfunction	Constipation
Reduced seizure threshold		Reduced seizure threshold
Postural hypotension	Amisulpiride Hyperprolactinaemia Insomnia Extrapyramidal effects	Hypo & hypertension
Anticholinergic effects Blurred vision Dry Mouth Urinary Retention	Quetiapine Hypotension Dyspepsia Drowsiness	Tachycardia
Neuroleptic malignant syndrome		Pyrexia
Weight gain		Weight gain
Sexual dysfunction		Glucose intolerance and diabetes mellitus
Cardio-toxicity (including prolonged QTc)		Nocturnal enuresis
		Rare serious side effects Neutropaenia 3% Agranulocytosis 0.8% Thromboembolism Cardiomyopathy Myocarditis Aspiration pneumonia

B- Psychosocial therapies:

A. Social skills training.
B. Family oriented therapies. (For High Expressed Emotion family).
C. Group therapy.
D. Individual psychotherapy.
E. Assertive community treatment.
F. Vocational therapy. "Occupational therapy"

For any questions, suggestions or problems, please contact us

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Good Luck!