Psychotic disorders

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Schizophrenia

- Found in all societies and countries with equal prevalence & incidence worldwide.
- A life prevalence of 0.6 – 1.9 %
- Annual incidence of 0.5 – 5.0 per 10,000
- Peak age of onset are 10-25 years for ♂ & 25-35 years for ♀

Etiology

Exact etiology is unknown.

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, the frontal cortex, cerebellum, and the basal ganglia.

A. ***Dopamine Hypothesis***;

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

Other Neurotransmitters;

Serotonin, Norepinephrine, GABA, Glutamate & Neuropeptides

B. *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.

C. *Psychoneuroimmunology*;

↓ 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 ?

D. *Psychoneuroendocrinology*;

Abnormal dexamethasone-suppression test

↓ LH/FSH

A blunted release of prolactin and growth hormone on stimulation.

3- Genetic Factors

A wide range of genetic studies strongly suggest a genetic component

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

4- Psychosocial Factors:

no well-controlled evidence indicates specific family pattern plays a causative role in the development of schizophrenia.

High Expressed Emotion family: increase risk of relapse.

Diagnosis

DSM-5 Diagnostic Criteria for Schizophrenia:

A- ≥ two 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, Occupation 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 exclusion
E- The disturbance is not due to Substance or another medical condition.
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.
- ✓ Premorbid history includes schizoid or schizotypal personalities, few friends & exclusions of social activities.
- ✓ Prodromal features include obsessive compulsive behaviors, attenuated positive psychotic features.
- ✓ Picture of schizophrenia includes positive and negative symptoms.
- ✓ Positive symptoms like: delusions & hallucinations.
- ✓ Negative symptoms like: affective flattening or blunting, poverty of speech, poor grooming, lack of motivation, and social withdrawal.

Mental status examination

- Appearance & behavior (variable presentations)
- Mood, feelings & affect (reduced emotional responsiveness, inappropriate emotion)
- Perceptual disturbances (hallucinations, illusions)
- Thought: Thought content (delusions)
  Form of thought (looseness of association)
  Thought process (thought blocking, poverty of thought content, poor abstraction, perseveration)
- Impulsiveness, violence, suicide & homicide
- Cognitive functioning
- Poor insight and judgment

Course

Acute exacerbation with increased residual impairment
Full recovery: very rare
Longitudinal course: downhill

- **Differential Diagnosis**

<u>Secondary psychiatric disorders:</u>

Substance-induced disorders
Psychotic disorders due to another medical disorder :

- ✓ Epilepsy (complex partial)
- ✓ CNS diseases
- ✓ Trauma
- ✓ Others

Primary Psychiatric disorders:

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

Other Psychotic Disorders

- ✓ Psychotic Disorders due to another medical condition
- ✓ Substance-induced psychotic disorder
- ✓ Schizophreniform disorder;
- ✓ 1-6 month of disturbance
- ✓ Brief psychotic disorder:
- ✓ <1month of disturbance
- ✓ Delusional disorder (delusion only >1m)

- DSM-5 Diagnostic Criteria for Schizoaffective disorder
  1. An uninterrupted period of illness that includes either a major depressive disorder or a manic episode along with at least two active symptoms of schizophrenia (hallucinations, delusions, disorganized speech, severely disorganized or catatonic behaviors, negative symptoms like decreased emotional expression or movement)
  2. Delusions or hallucinations occur at least two weeks without major depressive or manic symptoms at some time during the illness.
  3. The major mood symptoms occur for most of the duration of the illness.
  4. The illness is not the result of a medical condition or the effects of alcohol, other drugs of abuse, or a medication.

- Substance-Induced psychiatric Disorder

Potentially severe, usually temporary.
Context of substances of abuse, medications, or toxins of any of the 10 classes of substances.
Clinically significant presentation of a secondary psychiatric disorder.

- ✓ Evidence in history, PE, MSE and labs of:
- ✓ Develop during or within 1 month of use
- ✓ Capable of producing mental disorder seen
- ✓ Not an independent mental disorder
  - Preceded onset of use
  - Persists for substantial time after use (more that a month after off of substance use)

Treatment

What are the indications for hospitalization?

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

Biological therapies

- ✓ Antipsychotic medications are the mainstay of the treatment of schizophrenia.
- ✓ Generally, they are remarkably safe.

Two major classes:

1. Dopamine receptor antagonists (haloperidol, chlorpromazine)
2. Serotonin-dopamine receptor antagonists (Risperidone, clozapine, olanzapine).

- ❖ Depot forms of antipsychotics eg. Risperidone Consta is indicated for poorly compliant patients.

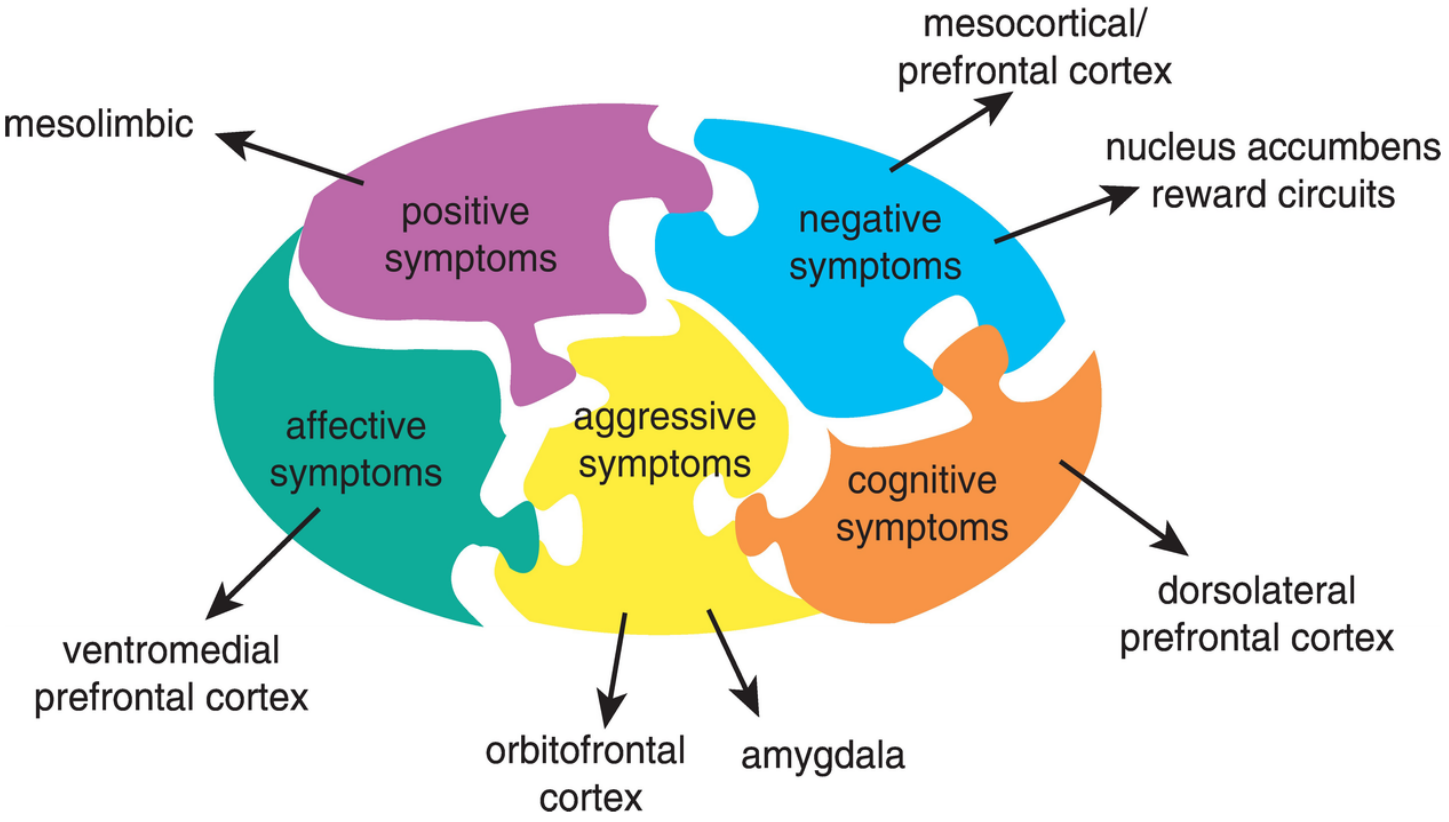
Electroconvulsive therapy (ECT) for catatonic or poorly responding patients to medications

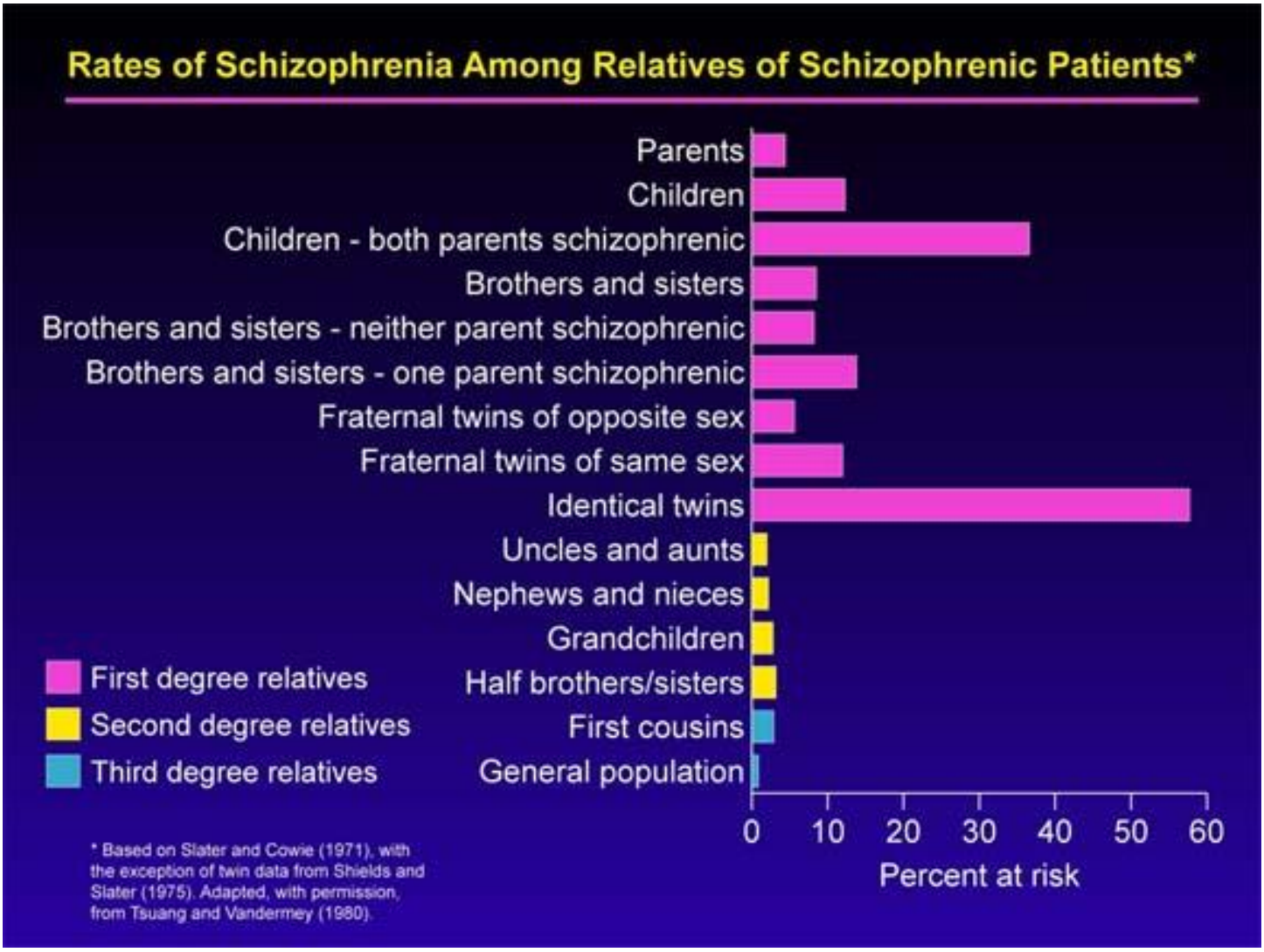
Psychosocial therapies

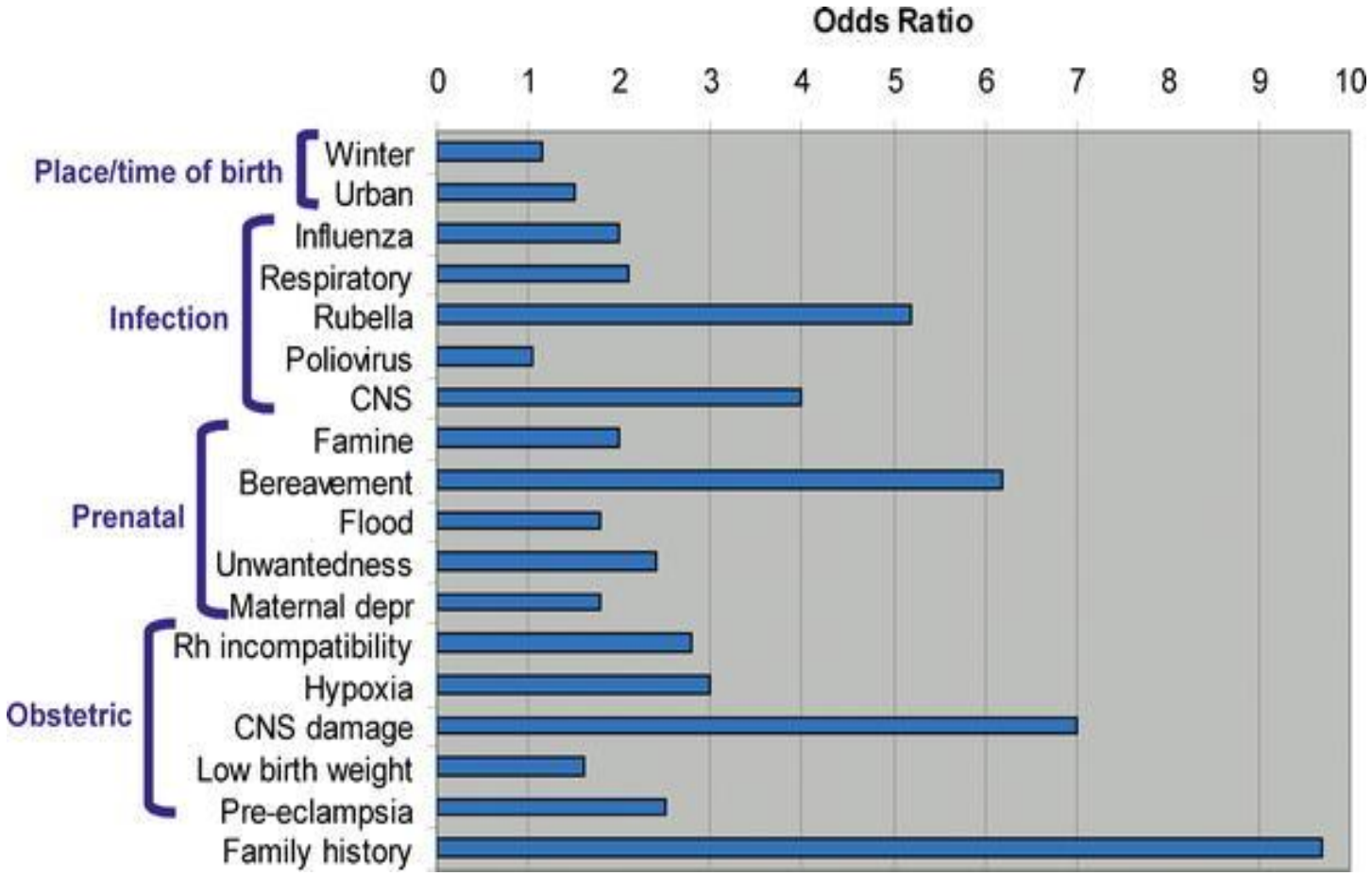
- ➢ Social skills training
- ➢ Family oriented therapies

- Group therapy
- Individual psychotherapy
- Assertive community treatment
- Vocational therapy

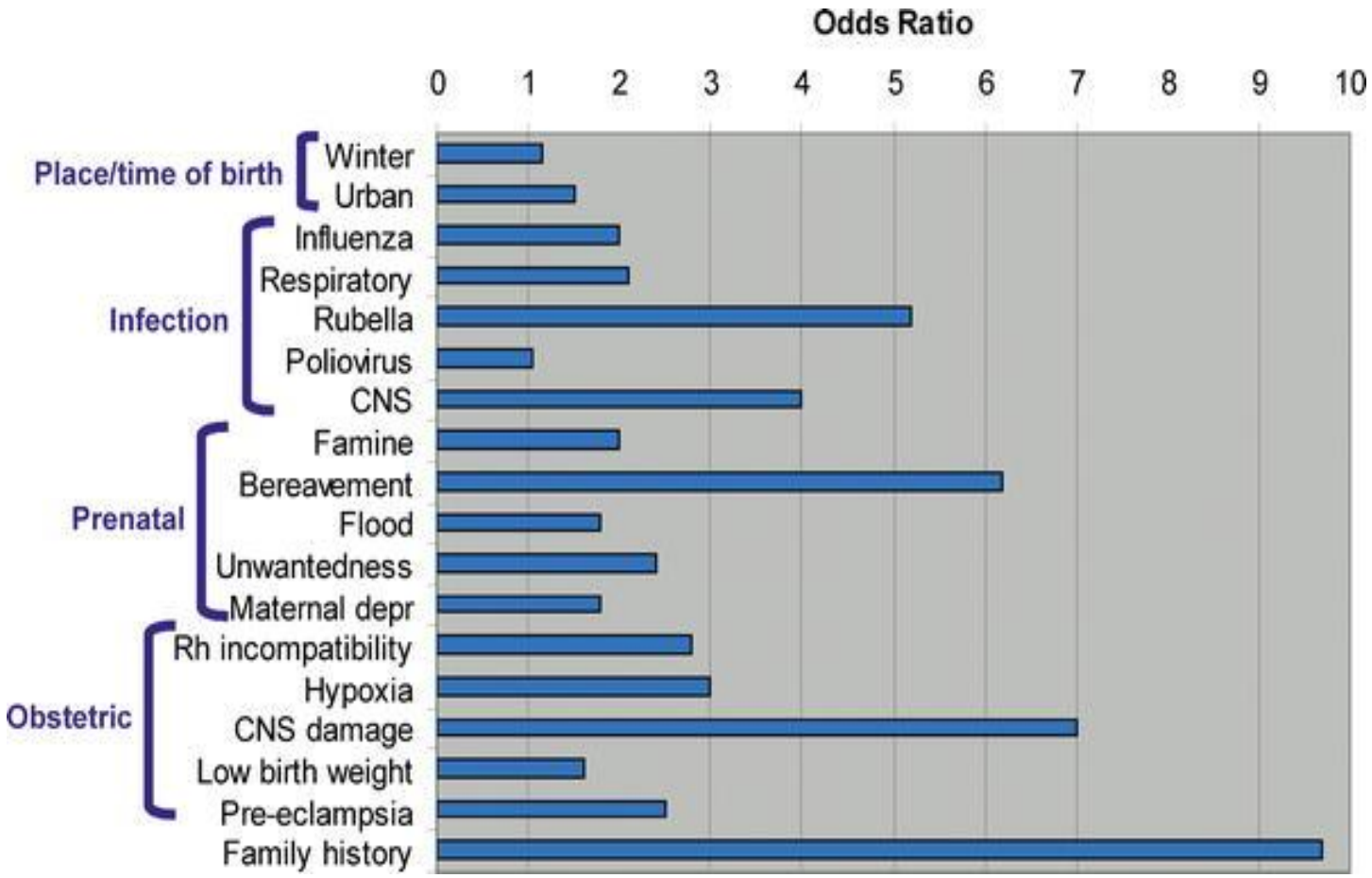
Match Each Symptom to Hypothetically Malfunctioning Brain Circuits




Rates of Schizophrenia Among Relatives of Schizophrenic Patients*
Parents
Children
Children - both parents schizophrenic
Brothers and sisters
Brothers and sisters - neither parent schizophrenic
Brothers and sisters - one parent schizophrenic
Fraternal twins of opposite sex
Fraternal twins of same sex
Identical twins
Uncles and aunts
Nephews and nieces
Grandchildren
Half brothers/sisters
First cousins
General population
First degree relatives
Second degree relatives
Third degree relatives
0
10
20
30
40
50
60
Percent at risk
* Based on Slater and Cowie (1971), with the exception of twin data from Shields and Slater (1975). Adapted, with permission, from Tsuang and Vandermey (1980).



Odds Ratio
0
1
2
3
4
5
6
7
8
9
10
Place/time of birth
Winter
Urban
Infection
Influenza
Respiratory
Rubella
Poliovirus
CNS
Prenatal
Famine
Bereavement
Flood
Unwantedness
Maternal depr
Obstetric
Rh incompatibility
Hypoxia
CNS damage
Low birth weight
Pre-eclampsia
Family history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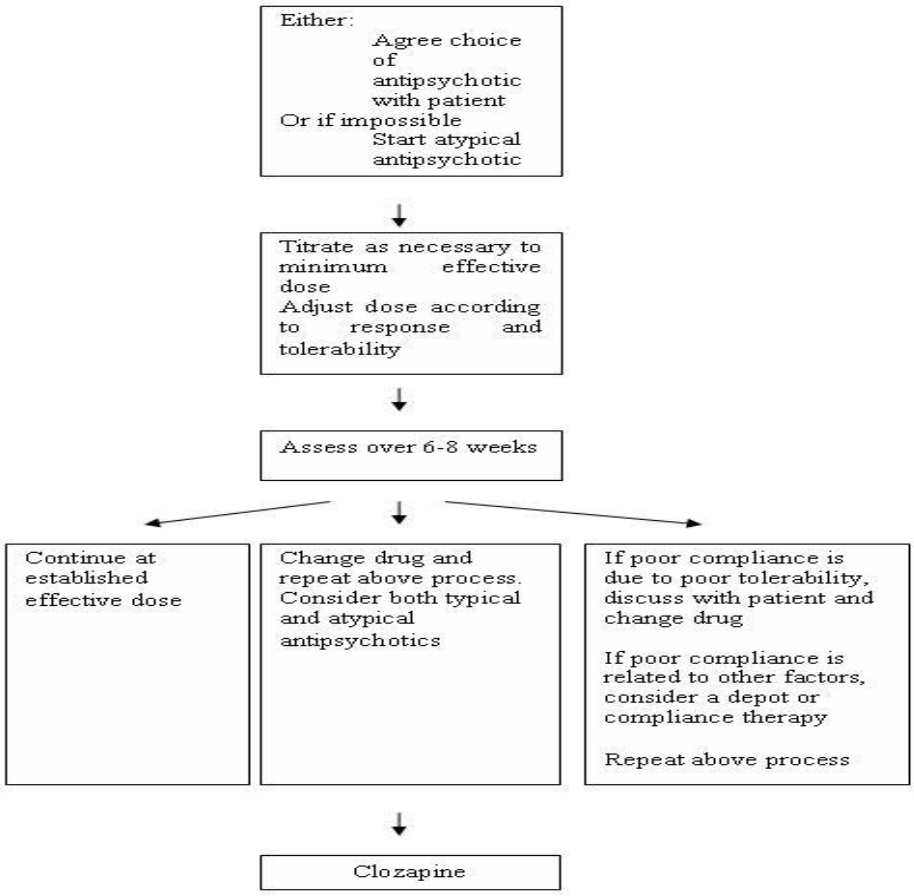
Antipsychotic Medications

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


Either:
Agree choice of antipsychotic with patient
Or if impossible
Start atypical antipsychotic
Titrate as necessary to minimum effective dose
Adjust dose according to response and tolerability
Assess over 6-8 weeks
Continue at established effective dose
Change drug and repeat above process. Consider both typical and atypical antipsychotics
If poor compliance is due to poor tolerability, discuss with patient and change drug
If poor compliance is related to other factors, consider a depot or compliance therapy
Repeat above process
Clozapine

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

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.

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Table 2

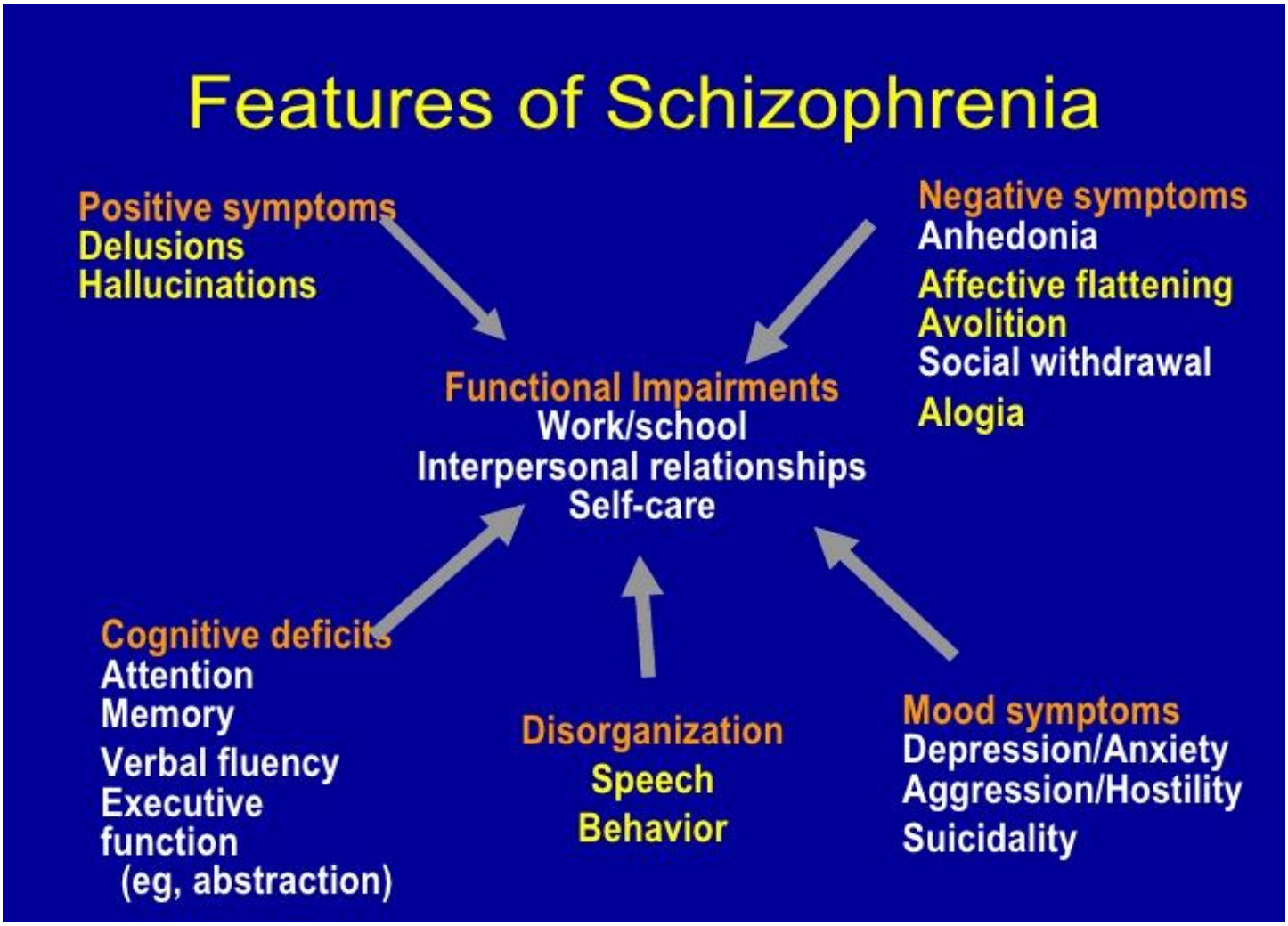
Relative Adverse Effect Incidence of Antipsychotics

	Sedation	EPS	Anticholinergic	Orthostasis	Seizures	Prolactin Elevation	Weight Gain
Typical Low Potency							
Chlorpromazine	High	Moderate	Moderate	High	Moderate	Moderate	Low
Thioridazine	High	Low	High	High	Low	Very high	Moderate
Typical High Potency							
Trifluoperazine	Low	High	Low	Low	Moderate	Moderate	Low
Fluphenazine	Low	Very high	Low	Low	Low	Moderate	Low
Thiothixene	Low	High	Low	Low	Low	Moderate	Low
Haloperidol	Very low	Very high	Very low	Very low	Low	Moderate	Low
Loxapine	Moderate	High	Low	Moderate	Low	Moderate	Very low
Molindone	Very low	High	Low	Low	Low	Moderate	Very low
Atypicals							
Clozapine	High	Very low	High	High	High	0	High
Risperidone	Moderate	Very low*	Low	Moderate	Low	0 to moderate††	Low
Olanzapine	Moderate	Very low†	Moderate	Low	Low	Very low	Moderate
Quetiapine	Moderate	Very low	Low	Low	Low	0	Low
Ziprasidone	Low	Very low	Low	Low	Low	0	Very low
Aripiprazole	Low	Very low	Low	Low	Low	0	Very low

** Very low dosages (<8 mg/day); † With dosages <20 mg/day; †† Dose related. EPS: extrapyramidal symptoms.*

Box 4.6 Neuroleptic Malignant Syndrome (NMS) (2, 47, 48)

- Uncommon but potentially fatal complication of antipsychotic therapy
- Typically occurs soon after an antipsychotic is started or dose is increased but may occur late
- Risk factors include depot antipsychotics, intramuscular administration, rapid increase in dose of antipsychotics, high doses of antipsychotics, dehydration, malnutrition, iron deficiency, underlying brain abnormalities, and agitation.
- Diagnostic triad – fever ≥38° C (100.4° F), muscle rigidity, mental status changes
- Autonomic instability and hyperthermia are the major causes of morbidity and mortality.
- Common lab abnormalities include ↑CPK or myoglobinuria, ↑WBC, metabolic acidosis
- Ensure other medical causes have been excluded.
- Management includes discontinuing antipsychotic(s), lithium, and dopamine blocking antiemetic agents and providing supportive care, most commonly in an ICU. Although older references recommend use of bromocriptine or dantrolene, more recent references show no advantage for these agents.


Features of Schizophrenia
Positive symptoms
Delusions
Hallucinations
Negative symptoms
Anhedonia
Affective flattening
Avolition
Social withdrawal
Alogia
Functional Impairments
Work/school
Interpersonal relationships
Self-care
Cognitive deficits
Attention
Memory
Verbal fluency
Executive function
(eg, abstraction)
Disorganization
Speech
Behavior
Mood symptoms
Depression/Anxiety
Aggression/Hostility
Suicidality