Schizophrenia

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What is it?

- Schizophrenia is a chronic, severe, and disabling brain disease
- Approximately 1 percent
- Gender
- Onset age

What is it?

- Main symptom
- Outcome: 90% decline and 70% recovered
- Research is gradually leading to new and safer medications and unraveling the complex causes of the disease

General Considerations

- Emil Kraepelin : dementia praecox
- Eugen Bleuler: a more appropriate name than dementia praecox(autism, ambivalence, flat affect, and disturbance of volition)
- Kurt Schneider: first-rank symptoms (e.g., thought diffusion, thought insertion, voices arguing and commenting)

Criteria:

- The Diagnostic and Statistical Manual of Mental Disorder, 4th edition **(DSM-IV)**
- International Classification of Diseases **(ICD)**
- Chinese Classification and Diagnostic Criteria of Mental Disease, the third version **(CCMD-3)**

DSM-IV Diagnostic Criteria

A. Characteristic symptoms:

(l) Delusions

(2) Hallucinations

(3) disorganized speech (e.g., frequent derailment or incoherence)

(4) Grossly disorganized or catatonic behavior

(5) Negative symptoms, i.e., affective flattening, alogia, or avolition

B. Social/occupational dysfunction:

DSM-IV Diagnostic Criteria

C. Duration: Continuous signs of the disturbance persist for at least 6months.This 6 month period must include at least 1month of symptoms (or less if successfully treated)that meet Criterion A (i.e., active-phase symptoms)and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in CriterionA present in an attenuated form (eg , odd beliefs, unusual perceptual experience)

DSM-IV Diagnostic Criteria

D. Schizoaffective and mood disorder **exclusion:**

Schizoaffective disorder and mood disorder with psychotic features have been ruled out because either (1) no major depressive, manic, or mixed episodes have occurred concurrently with the active-phase symptoms, or (2)if mood episode have occurred during active-phase symptom, their total duration has been brief relative to the duration of the active and residual periods.

DSM-IV Diagnostic Criteria

E. Substance/general medical condition **exclusion:** The disturbance is not due to the direct physiological effect of a substance (e.g., a drug of abuse, a medication)or a general medical condition.

F. Relationship to a pervasive developmental disorder: If there is a history of autistic disorder or another pervasive developmental disorder, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated)

The three core syndromes

- **Positive symptoms:** delusions, hallucinations, and formal thought disorder.
- **Disorganization:** incoherence, loose associations, inappropriate affect, and poverty of thought content.
- **Negative symptoms:** affective flattening, loss of spontaneity, lack of initiative or willed action, anergia, and anhedonia.

Subtype in Schizophrenia

- **Paranoid schizophrenia:** prominent persecutor grandiose delusions.
- **Undifferentiated schizophrenia:**delusions and hallucinations are prominent, and are accompanied by incoherence disorganized behavior.
- **Disorganized schizophrenia:** absence of systematized delusions and the presence of incoherence and inappropriate affect.

Subtype in Schizophrenia

- **Residual schizophrenia:** in which positive symptoms are minimal and negative symptoms predominate.
- **Catatonic schizophrenia:** motor disturbance in the dominant feature, consisting of either agitated hyperactivity or decrease in gross motor activity with stupor, rigidity, or bizarre postures

Major Etiologic Theories

- Dopamine hypothesis
- Serotonin hypothesis
- Glutamate hypothesis
- Neurodevelopmental hypothesis

Major Etiologic Theories

- **Dopamine hypothesis**
  - The excess activity of DA in some brain area: eg, limbic, nucleus accumbens, stria terminalis, lateral septum and olfactory tubercle
  - Antipsychotics decreased DA activity by receptor blockade and depletion

Major Etiologic Theories

- **Serotonin hypothesis**
  - There are at least 15 types of 5-HT receptors; most of these relevant to schizophrenia are the 5-HT1, 5-HT1D, 5-HT2, 5-HT3, 5-HT6, and 5-HT7 receptors.
  - Schizophrenia was that it was due to an excess of brain serotonergic activity.
  - The potency of some agents as hallucinogens is highly correlated with their 5- HT2A-receptor antagonist affinity.
  - Newer antipsychotic drugs are potent antagonists of the 5-HT2A receptor.

Major Etiologic Theories

- **Glutamate hypothesis**
  - Decreased levels of glutamate in the CSF of patients with schizophrenia
  - Some antagonists of NMDA receptors can produce a range of positive and negative symptoms and cognitive dysfunction in normal control subjects and in schizophrenic patients.
  - Neuroleptics can block some of the clinical effects of PCP(a noncompetitive antagonists of NMDA receptors).

Major Etiologic Theories

- **Neurodevelopmental hypothesis**
  - Obstetric and perinatal complications.
  - Structural abnormalities based on in vivo brain imaging.
  - Postmortem studies.
  - Synaptic marker anomalies.
  - Adverse environmental events in uterus.
  - The absence of glia.
  - Congenital anomalies.
  - Developmental neurologic and biopsychosocial dysfunction.

Epidemiology

- **Schizophrenia affects 1%** of the adult population. The incidence is comparable in all societies.
- **Lower income**:
- **Gender**: slightly more common in males than in females
- **Age at onset**:
  - The mean age for female patients is 25 years with a range of 15- 30 years.
  - For male patients, the mean age is 20 years with a range of 10-24 years.

Genetics

- Complex mode of inheritance
- Inheritance: 60-80%
- Candidate gene:DR,5-HTR,NGF,NT-3
- Linkage study: chromosome6, 11, 22,1

Clinic Findings

- Obtain as much information as possible:
  - medical and psychiatric history, mental status examination, family and social history, other pertinent information from family and friends.
- Progressive behavioral disturbances in childhood and adolescence:
  - social withdrawal and academic and personal problems

Clinic Findings

- Early findings:
  - Personality changes, withdrawal, decreased academic performance, less interest, obsessive-compulsive, ritualistic behavior, poor hygiene, moodiness, flat affect, magical thinking, aggressiveness.

Clinic Findings

- Schizophrenic patients may appear disheveled:
  - Thoughts loosen, delusion, hallucination,
  - Behavior: stereotyped behavior, repeat various functions or gestures.
    - Echopraxia: They may imitate others' movements.
    - Negativism: refuse to cooperate
    - Catatonic stupor: remain motionless for a long time
    - Waxy flexibility or catalepsy: and maintain their limbs or trunks in unusual positions for various lengths of time

Clinic Findings

- Cognitive dysfunction:
  - The intelligence quotient (IQ)
  - Characteristic:
    - It is based on diffuse rather than localized brain disease.
    - Treatment might improve slightly.
    - It is independent of three core syndromes.
    - Small percentage of patient reach to severe level.

Treatment

- **Pharmacological Treatments:**
- **Electroconvulsive (ECT) Treatment**
- **Psychosocial Treatment**:

Treatment

- **Pharmacologic Treatments:**
  - **Initiation of treatment**
    - Generally low dosage at beginning
    - Dosage raising gradually
    - Rapidly dosage raising induce side effects
  - **Typical antipsychotic drugs**
  - **Atypical antipsychotics**

Commonly used antipsychotic drugs

Class and Drug Name	Dosage Range (mg}	Approximate Oral Dose Equivalents (mg)	Parenteral Dosage(mg)
Conventional Drugs			
Butymphenone			
Haloperidol(Haldol)	**5-30**	**2**	**5-10**
Haloperidol decanoate (Haldol-D)	**NA**	**NA**	**25-100 every,1-4 weeks**
Dibenzoxazepine			
Loxapine succinate (Loxitane)	**40-100**	**15**	**25**
Diphenylbutylpiperidine			
Pimozide (Orap)	**2-6**	**1**	**NA**
Molindone hydrochloride (Moban)	**50-225**	**10**	**NA**

Phenothiazines			
chlorpromazine (Thorazine)	200-800	100	25-50
Thioridazine (MeHaril)	150-800	100	NA
Mesoridazine (Serentil)	75-300	50	25
perphenazine (Thrilafon)	8-32	10	5-10
Trioperazine(Stelazine)	5-20	5	1-2
Fluphenazine hydmchloride (PmHxin)	2-60	2	1.25-2.5
Fluphenazine decanoate (Prolixin-D)	NA	NA	12.5-50 every 1-4weeks
Fluphenazine enanthate (Prdixin-E)	NA	NA	12.5-50every 1-4weeks
Thioxanthenes			
Thiothixene hydmchbride (Navane)	5-30	5	24

Atypical Drugs			
Benzisothiazolyl piperazine			
Zipmsidone (Zeldox)	40-160	40	10
Benzisoxazole			
Risperidone (Risperdale)	4-8	1	NA
Quetiapine fumarate (Seroquel)	150-600	100	NA
Dibenzodiazepine			
Clozapine(Clozaril) Imidazolidinone	100-900	50	NA
sertindole(Serleet)	12-24	4	NA
Thienobenzodiazepine			
Olanzapine(Zyprexa)	10-20	4	NA

Treatment

- **Pharmacological Treatments:**
  - Initiation of treatment
  - Typical antipsychotic drugs
  - Atypical antipsychotics

Treatment

- **Electroconvulsive (ECT) Treatment**

ECT is used today in the need for maintenance treatment, which is difficult to provide on an outpatient. A short course of ECT is 6-12 treatments.

Treatment

- **Psychosocial Treatment**:

  Besides the treatment of antipsychotic drugs, Psychosocial treatment is also important, especially for the patients in convalescence.

Prognosis & Course of Illness

- Age at onset, socioeconomic status, occupational record, family history of mental illness, length of course, clinic symptoms, treatment
  - Relapse rate more than 50% if no any therapy
  - Relapse reduce to 30% with continuing antipsychotic drugs
  - Relapse reduce to 10% with both continuing antipsychotic drugs and psycho-social rehabilitation.

Summary:

- What is it
- Clinic symptoms
- Etiology
  - Genetics
  - Some hypothesis
- Treatment
  - Typical and atypical antipsychotics
  - Psychosocial treatment
- Prognosis

Thanks