Beacon Clinical Topic: **Schizophrenia**

Schizophrenia was present at the birth of modern psychiatry. Our current nosology, the *DSM-5*, has its origins in the distinction made by the German psychiatrist Emil Kraepelin (1856-1926) between schizophrenia—which he termed Dementia Praecox—and bipolar disorder—which he called manic depressive illness in his 1899 textbook.

1. DEFINITION

The *DSM-5* has substituted the classic schizophrenia subtypes, i.e. paranoid, disorganized, catatonic and undifferentiated, for a severity assessment of the primary symptoms of psychosis.

a. Epidemiology: The lifetime prevalence of schizophrenia varies from 0.3% to 0.7% across regions, migrant status, and race/ethnicity (APA, 2013). There is a male to female rate ratio of 1.4:1. Onset is also earlier in males. Persons with schizophrenia have a standardized mortality ratio of 2.6—indicating a much higher than expected risk of dying and leading to shorter life expectancy; and a suicide rate of 4.9%, which is much higher than the average risk.

b. Risk factors and comorbidities: There has been a classic finding of a season-of-birth effect; those with schizophrenia are more likely to have been born in late winter or early spring (APA, 2013) while those with the Deficit Syndrome subtype have a summer seasonality. Advanced Paternal Age (APA) is another risk factor for schizophrenia. Comorbid substance use disorders are common among those with schizophrenia, with more than half having tobacco use disorder. Rates of OCD and panic disorder are also elevated.

2. DIAGNOSIS

The *DSM-5* introduced a few but significant changes in the diagnosis of schizophrenia: first, the elimination of special status to bizarre delusions and Schneiderian first-rank symptoms, and second, the addition of the requirement that at least one of the two Criterion A symptoms be delusions, hallucinations, or disorganized speech.

a. Two (or more) of the following each present for a significant portion of time during a one-month period (or less if successfully treated). At least one of these must be 1., 2. or 3. below:
   1. Delusions
   2. Hallucinations
   3. Disorganized speech
   4. Grossly disorganized or catatonic behavior
   5. Negative symptoms

b. For a significant portion of the time since the onset, level of functioning in one or more major area is markedly lower.

c. Continuous signs of the disturbance for at least six months

d. Schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out.

e. The disturbance is not attributable to the use of a substance or to another medical condition.

f. If there is a history of autism spectrum or a communication disorder with childhood onset, the additional diagnosis of schizophrenia is to be made only if prominent delusions or hallucinations, in addition to the other requirements, are present for at least one month.

Specify whether:

- First episode, currently in acute episode
- First episode, currently in partial remission
- First episode, currently in full remission
- Multiple episodes, currently in acute episode
- Multiple episodes, currently in partial remission
- Multiple episodes, currently in full remission
- Continuous
- With catatonia

3. TREATMENT

a. Psychopharmacology: Antipsychotics are the cornerstone of the pharmacological treatment of schizophrenia and have evolved so far in two generations. First-generation antipsychotics are usually classified as high potency—i.e., haloperidol, dose range from 6-20 mg/day—versus low potency—i.e., chlorpromazine doses ranging from 300-800 mg/day. Second-generation agents may be classified by mechanism, such as D2, 5-HT2 antagonists, including Olanzapine, Iloperidone, Lurazidone, and Ziprasidone; D2, 5-HT2, and NE alpha-2 antagonists, such as Risperidone and Asenapine; D2, 5-HT1A partial agonists, such as Aripiprazole and Brexpiprazole. A few of these medications are available for use in long-acting injection form. Clozapine is a highly effective antipsychotic that requires close monitoring for its risk of a serious side effect—agranulocytosis—and, as such, is reserved for treatment-resistant presentation despite its efficacy. Antipsychotics

should be used with care given the many side effects requiring monitoring and management. Some of the common side effects of antipsychotics are extra-pyramidal side effects (EPS), prolactin elevation, weight gain, glucose abnormalities, lipid abnormalities, QTc prolongation, sedation, hypotension, and anticholinergic side effects.

b. Psychotherapy: **Emotional support** in dealing with a disabling illness, enhancement of **coping strategies** to promote functional recovery, and **alteration of underlying pathophysiology and processes of illness** are the three elements of psychotherapy interventions for schizophrenia. Psychotherapeutic interventions for schizophrenia include Cognitive Behavioral Therapy (CBT), Personal Therapy (PT), Compliance Therapy (usually during an acute episode), Acceptance and Commitment Therapy (ACT), and Supportive Therapy. The RAISE study has proposed Individual Resilience Therapy for First Episode Psychosis patients.

c. Other psychosocial interventions: Family psychoeducation has been shown to improve outcome and treatment adherence in schizophrenia. Supported employment has been shown to help those individuals with schizophrenia obtain competitive jobs as well as work and earn more.

d. ECT: This treatment is for individuals with schizophrenia who have persistent severe psychosis and/or suicidal ideation or behaviors and for whom prior treatments, including clozapine, have failed. ECT should also be considered for individuals with prominent catatonic features who have not responded to an acute trial of lorazepam.

4. PROGNOSIS

Since the outcomes in schizophrenia can be variable, several predictors of good and poor prognosis have been identified. See table below from *Goodwin and Guze's Psychiatric Diagnosis*. One important modifiable risk factor to improve outcomes is decreasing the Duration of Untreated Psychosis (DUP).

5. SUMMARY AND TAKEAWAYS

	Good Prognosis	Poor Prognosis
Mode of onset	Acute	Insidious
Precipitating events	Frequently reported	Usually not reported
Pre-psychotic history	Good	Poor—frequent history of "schizoid" traits
Confusion	Often present	Usually absent
Affective symptoms	Often present and prominent	Absent or minimal; affective response usually blunted or flat
Marital status	Usually married	Often single, specially males
Family history of affective disorders	Often present	Less likely
Family history of schizophrenia	Absent or rare	Increased

Our understanding of schizophrenia, along with its treatment options, have improved tremendously over the last 50 years. Instead of "schizophrenic reactions," we now see a neurodevelopmental brain disease whose underpinnings will lead us to ways to minimize its effects and manage psychotic symptoms. What used to be voices of demons—or your super-ego—are now malfunctioning neuro-networks in need of modulation. These findings have revolutionized our understanding, but we still have a long way to reach widespread clinical practice and availability.

6. THREE QUESTIONS FOR CLINICAL TEAM DISCUSSION

a. How do we best help families with psychoeducation about schizophrenia?

b. What are the reasons for poor adherence to treatment recommendations?

c. How do we reduce the suicide risk in schizophrenia?

7. KEY REFERENCES AND RESOURCES FOR FURTHER INFORMATION

There are practice guidelines for the assessment and management of schizophrenia by the APA—along with a quick reference guide—and the NHS/NICE. The 2009 Schizophrenia Patient Outcomes Research Team (PORT) recommendations are here, and here are the 2002 Mount Sinai Conference recommendations. Schizophrenia is an area of active and fascinating research efforts. Two good places to keep up are here and here.

References

APA. (2013). *DSM-5*. Washington, DC: American Psychiatric Association Press.