SCIENCE MAGAZINES

Issue 2: Disease State Schizophrenia

TABLE OF CONTENTS

SCHIZOPHRENIA	1
OVERVIEW	1
EPIDEMIOLOGY OF SCHIZOPHRENIA	2
CLINICAL DESCRIPTION OF SCHIZOPHRENIA	3
PATHOPHYSIOLOGY OF SCHIZOPHRENIA	5
MAJOR DOPAMINE PATHWAYS	6
DISEASE PRESENTATION	7
EFFECTS OF ANTIPSYCHOTIC AGENTS	8
DOPAMINE ANTAGONISM IN THE MESOLIMBIC PATHWAY	9
DOPAMINE ANTAGONISM IN THE MESOCORTICAL PATHWAY	10
NEUROCHEMISTRY AND SYMPTOMS	10
PARTIAL AGONIST ACTIVITY	11
CLINICAL ASSESSMENT	12
POSITIVE, NEGATIVE, AND COGNITIVE SYMPTOMS OF SCHIZOPHRENIA	13
DSM-5® CRITERIA FOR DIAGNOSIS OF SCHIZOPHRENIA	14
ADDITIONAL DSM-5® CRITERIA FOR DIAGNOSIS OF SCHIZOPHRENIA	15
DSM-5® CRITERIA FOR DIFFERENTIAL DIAGNOSIS OF SCHIZOPHRENIA	16
TREATMENT GOALS	17
TREATMENT STRATEGIES	18
PROGRESS CHECK QUESTIONS	19
PROGRESS CHECK ANSWERS	21
REFERENCES	22

SCHIZOPHRENIA

Schizophrenia is a chronic and severe disorder that affects how a person thinks, feels, and behaves. In this magazine, read how people with schizophrenia may seem like they have lost touch with reality, how disabling it can be, and the importance of ongoing care by healthcare professionals and family members.

OVERVIEW

We're going to talk about a subject that a lot of people don't understand. For some people, the term schizophrenia is associated with mystery, fear, and the mistaken impression that patients cannot be treated correctly. We need to move schizophrenia out of the realm of mystery and fear and on to hope and support. Although patients can clearly suffer with this disease, there are many types of support available, including therapeutic drugs, non-drug support, the help of family members and caregivers, support groups, and telephone support lines, to name a few.

Schizophrenia is a chronic and severe mental disorder that affects how a person thinks, feels, and behaves. People with schizophrenia may seem like they have lost touch with reality. Although schizophrenia is not as common as other mental disorders, the symptoms can be very disabling.⁶

ONE FACE OF SCHIZOPHRENIA

Functioning

Schizophrenia involves impairment in one or more major areas of functioning. The dysfunction persists for a substantial period during the course of the disorder and does not appear to be a direct result of any single feature. There is strong evidence of a relationship between cognitive impairment and functional impairment in individuals with schizophrenia.¹



Appearance

Individuals with schizophrenia may display inappropriate affect, depression, anxiety, or anger; a disturbed sleep pattern; and a lack of interest in eating or food refusal. Depersonalization, derealization, and being overly concerned about the body may occur and sometimes reach delusional proportions. Anxiety and phobias are common.¹

Performance

Cognitive deficits in schizophrenia are common and are strongly linked to vocational and functional impairments. These deficits can include memory problems, language function, and other executive functions, as well as slower processing speed. Abnormalities in sensory processing and inhibitory capacity, as well as reductions in attention, are also found.¹

The characteristic symptoms of schizophrenia involve a range of cognitive, behavioral, and emotional dysfunctions, but no single symptom is pathognomonic of the disorder. The diagnosis involves the recognition of a constellation of signs and symptoms associated with impaired occupational or social functioning. Individuals with the disorder will vary substantially on most features, as schizophrenia is a heterogeneous clinical syndrome.¹

EPIDEMIOLOGY OF SCHIZOPHRENIA

The point needs to be made again that schizophrenia is a serious mental illness that interferes with a person's ability to think clearly, manage emotions, make decisions and relate to others. Although this does not mean that these patients cannot get better, schizophrenia is a complex, long-term medical illness, affecting people of all backgrounds.⁷

According to the World Health Organization — WHO — schizophrenia is associated with considerable disability and may affect educational and occupational performance.⁷ The prevalence of schizophrenia is similar throughout the world. Internationally, it affects about 1% of the population — or about 21 million people.⁸ The 12-month prevalence of schizophrenia in the United States is 1.1% of the US adult population.⁹

As for age of onset, most patients experience their first diagnosable symptoms during the years from late adolescence to early adulthood.⁸ Although it affects both men and women, slightly more men than women are affected, and schizophrenia in men carries a worse prognosis than in women.¹¹



Emergency Department Visits Related to Schizophrenia Among Adults Aged 18–64¹⁰

CLINICAL DESCRIPTION OF SCHIZOPHRENIA

Keep in mind that all symptoms are not present to the same degree in all patients, and that some patients may exhibit some, but not all, symptoms that are associated with schizophrenia. A patient must demonstrate a sufficient number of diagnostic criteria — but not necessarily all diagnostic criteria — to receive a diagnosis. This chart represents the PANSS, or the Positive and Negative Symptoms Scale.

POSITIVE AND NEGATIVE SYMPTOMS OF SCHIZOPHRENIA



Positive Symptoms¹²

In the evaluation of positive symptoms, the APA Guidelines include 7 items with a minimum score of 7 and maximum score of 49. The symptoms are:

- Delusions
- Conceptual disorganization
- Hallucinations

Negative Symptoms¹²

In the evaluation of negative symptoms, the APA Guidelines include 7 items with a minimum score of 7 and maximum score of 49. The symptoms are:

- Blunted affect
- Emotional withdrawal
- Poor rapport
- Lack of spontaneity and flow of conversation
- Stereotyped thinking
- Passive/apathetic social withdrawal

Hyperactivity

Grandiosity

 Difficulty in abstract thinking

General Psychopathology

The third part of the PANSS scale includes 16 items (minimum score = 16, maximum score = 112)¹²

- Somatic concern
- Anxiety
- Guilt feelings
- Tension
- Mannerisms and posturing
- Depression

- Motor retardation
- Uncooperativeness
 Unusual thought content
- Disorientation
- Poor attention
- Lack of judgment and insight

Suspiciousness/persecution

Hostility

- Disturbance of volition
- Poor impulse control
- Preoccupation
- Active social avoidance

Deeper Insight

People with mental disorders such as schizophrenia may appear to be completely normal when you encounter them. They may not show any signs of disturbed thinking and may be able to function normally, although some may feel that they can also recognize someone with schizophrenia. Do you think it is possible?

Even with these lists of positive and negative symptoms and a thorough interview by a psychiatrist, it may still be difficult to diagnose schizophrenia, especially in teens. This is because the first signs can include a change of friends, a drop in grades, sleep problems, and irritability—common and nonspecific adolescent behavior.

Can you tell which one of these people has been diagnosed with schizophrenia?



(Not real patients. Models used for illustrative purposes)

You can't, can you?

PATHOPHYSIOLOGY OF SCHIZOPHRENIA

Problems with certain brain chemicals, including neurotransmitters called dopamine and glutamate, may contribute to schizophrenia. Neurotransmitters allow brain cells to communicate with each other. Networks of neurons are likely involved as well.^{6,13}

PATHOPHYSIOLOGY AND PATHOLOGIC CIRCUITS¹³

One might wonder whether there is a pathologic circuit or a specific type of neurotransmitter abnormality that accounts for the symptoms that collectively lead to a diagnosis of schizophrenia. The answer isn't simple and it is important to keep in mind that the relationship between neurotransmitters, differences in levels of various neurotransmitters, and psychiatric disorders is complex and not completely understood. However, each psychiatric disorder, such as schizophrenia, may involve many neurotransmitter pathways, and most medications that act within the central nervous system affect multiple neurotransmitter systems.¹³

Ventral striatum

Part of the brain anatomy. The striatum is the collective name for the caudate nucleus and putamen that together with the globus pallidus or pallidum form the striate body. The ventral striatum refers to portions of the striatum located generally inferior to a plane representing the anterior commissure; includes the nucleus accumbens and some nuclei of the olfactory tubercle; may function in motor activities with emotional or motivational origins.¹⁴

Glu

Glu=glutamate. In neuroscience, glutamate generally refers to the anion of glutamic acid in its role as a neurotransmitter:

a chemical that nerve cells use to send signals to other cells. It is the most abundant neurotransmitter in the vertebrate nervous system. When glutamate is released from synaptic vesicles stored within glutamate neurons, it interacts with receptors in the synapse and is then taken up into neighboring glia by a reuptake pump known as an excitatory amino acid transporter.^{15, 17}



NBM

NBM=nucleus basalis of Meynert. This is a region in the brain that is associated with cognitive function.¹⁶

DA

DA=dopamine. Dopamine is an intermediate in tyrosine metabolism and precursor of norepinephrine and epinephrine; this neurotransmitter can be found in the peripheral and central nervous systems.¹⁴

GABA

GABA=γ-aminobutyric acid. This is a constituent of the central nervous system; quantitatively, the principal inhibitory neurotransmitter. It is also used in the treatment of various neurologic disorders (e.g., epilepsy).¹⁴

MAJOR DOPAMINE PATHWAYS

Before you start reading about dopamine pathways, let's first talk a little about dopamine itself. What is it? Well, dopamine is a chemical in your brain that affects your emotions, movements, and your sensations of pleasure and pain. Dopamine neurotransmitters are located in the deep middle region of your brain called the substantia nigra. There are 5 dopamine receptors and several different pathways through which dopamine can act.³

The dopamine hypothesis is a theory espoused by some scientists working to understand the brain. According to the theory, a schizophrenic person is producing too much dopamine.³ It is not that simple, as you will find out, but the concept behind the dopamine hypothesis has been useful in directing scientists to certain areas of research that have been revealing.

MAJOR DOPAMINE PATHWAYS IN THE BRAIN

Abnormalities in the synaptic transmission of dopamine are thought to be involved in the pathogenesis of schizophrenia. As shown here, dopamine neurons are organized into 4 well-defined dopamine pathways.^{17,18}



MESOCORTICAL PATHWAY

Mesocortical pathway, which may play a role in mediating negative and cognitive symptoms of schizophrenia.¹⁷



TUBEROINFUNDIBULAR PATHWAY

Tuberoinfundibular pathway, which controls prolactin secretion.¹⁷



NIGROSTRIATAL PATHWAY

Nigrostriatal pathway, which is a part of the extrapyramidal nervous system and controls motor movements.¹⁷



MESOLIMBIC PATHWAY

Mesolimbic pathway, which is thought to have an important role in several emotional behaviors, including the positive symptoms of psychosis such as delusions and hallucinations; the mesolimbic pathway is also important for motivation, pleasure, and reward.¹⁷

DISEASE PRESENTATION

We previously discussed positive and negative symptoms of schizophrenia as hallmarks of the disease and how movement disorders and comorbidities may be part of the picture.^{12,13} Psychiatric comorbidities can include substance abuse; mood symptoms such as anxiety and depression; panic disorder; post-traumatic stress disorder (PTSD); and obsessive-compulsive disorder (OCD).¹⁹

Now that we have a better understanding of the neurotransmitter circuits and how they generally relate to symptoms, let's look at the relationship a little more closely. It is thought that in individuals with schizophrenia, excess dopamine is released in the mesolimbic pathway, which may be the cause of positive symptoms of psychosis.¹⁷

The therapeutic actions of first- and second-generation dopamine antagonists are thought to control this excess through the blockade of D_2 receptors. This blockade is thought to be responsible for reducing the hyperactivity in this pathway and thus symptoms of psychosis.¹⁷

EFFECTS OF ANTIPSYCHOTIC AGENTS

Because the causes of schizophrenia are still unknown, treatments focus on eliminating the symptoms of the disease. Treatments include a group of drugs called antipsychotic agents that are believed to work by altering certain chemical pathways in the brain. Antipsychotic medications are usually taken daily in pill or liquid form. Some antipsychotics are injections that are given once or twice a month. Some people have side effects when they start taking medications, but most side effects go away after a few days. Doctors and patients can work together to find the best medication or medication combination, and the right dose.⁶ Now that you know why we need to know about different pathways in the brain, let's take a closer look.

NIGROSTRIATAL AND TUBEROINFUNDIBULAR PATHWAYS

Some antipsychotic drugs work by blocking receptors, the receiving units for dopamine and other neurotransmitters. When you block these receptors, it may help the patient's symptoms, but it can also cause side effects. Let's focus on what are called the D_2 receptors for just a moment.²⁰

D₂-receptor blockade in the nigrostriatal pathway is thought to lead to movement disorders. Since the nigrostriatal pathway is part of the extrapyramidal nervous system, the motor side effects associated with blocking D₂ receptors in this area are sometimes referred to as extrapyramidal symptoms or EPS. If D₂ receptors in the nigrostriatal pathway are chronically blocked, they can produce a hyperkinetic movement disorder known as tardive dyskinesia. This movement disorder causes facial and tongue movements such as constant chewing, tongue protrusions, and facial grimacing, as well as limb movements, which can be quick and jerky. It is thought that chronic dopamine blockade may mediate changes, sometimes irreversible, in the D₂ receptors in the nigrostriatal pathway, such as up-regulation or supersensitivity at the receptors.²⁰

 D_2 -receptor blockade in the tuberoinfundibular pathway can lead to increases in plasma prolactin levels and a condition called hyperprolactinemia. First- and second-generation antipsychotics antagonize D_2 receptors, whereas partial agonists bind to receptors and elicit only a partial response in this pathway. This is the rationale for using an agent that is a partial agonist — beneficial effects with a reduced risk of EPS and hyperprolactinemia.²⁰



What about serotonin? 5-HT_{2A}-receptor antagonists modulate dopaminergic activity and may be associated with modest improvement in cognition and a potential for antidepressive activity.^{21,22}

5-HT_{1A} agonism may be associated with anxiolytic properties and possible benefits for mood.²³ According to animal studies, D₂-receptor blockade along with 5-HT_{1A} agonism or 5-HT_{2A} antagonism is associated with possible improvement in working memory.²⁴

DOPAMINE ANTAGONISM IN THE MESOLIMBIC PATHWAY

Okay, we just talked about a couple of pathways in the brain that are involved in both the symptoms of schizophrenia and its treatment. There is another pathway — the mesolimbic pathway — that is thought to be very important. For example, blocking the effects of dopamine in this pathway may help to alleviate some of the patient's "positive symptoms." Let's see how this works.¹⁷

DOPAMINE ANTAGONISM IN THE MESOLIMBIC PATHWAY IMPROVES POSITIVE SYMPTOMS



It is thought that in individuals with schizophrenia, excess dopamine is released in the mesolimbic pathway, which may be the cause of positive symptoms of psychosis. The therapeutic actions of dopamine (D) antagonists are thought to control this excess through the blockade of D_2 receptors. This blockade is thought to be responsible for reducing the hyperactivity in this pathway and thus the positive symptoms of psychosis.^{17,25}

DOPAMINE ANTAGONISM IN THE MESOCORTICAL PATHWAY

One more pathway to take a closer look at — the mesocortical pathway.

DOPAMINE ANTAGONISM IN THE MESOCORTICAL PATHWAY MAY WORSEN NEGATIVE SYMPTOMS



It is thought that in patients with schizophrenia, there may be a hypodopaminergic state, or deficiency of dopamine, in the mesocortical pathway. Therefore, administration of a D₂ antagonist may exacerbate both negative and cognitive symptoms.^{17,25}

NEUROCHEMISTRY AND SYMPTOMS

The reason to learn about these pathways is that the way that neurotransmitters work — or don't work — in these pathways is thought to be related to symptoms that the patient experiences. First, we should review those categories of symptoms again, then check in on the patient.

Hallucinations. The apparent, often strong subjective perception of an external object or event when no such stimulus or situation is present; may be visual, auditory, olfactory, gustatory, or tactile.^{1,4}

Delusions. False beliefs or wrong judgments, sometimes associated with hallucinations, held with conviction despite evidence to the contrary.^{1,4}

Negative symptoms are symptoms of schizophrenia that follow from diminished volition and executive function including inertia, anergia, lack of involvement with the environment, poverty of thought, social withdrawal, and blunted affect.^{1,4}

Incoherence. Not coherent; disjointed; confused; denoting a lack of connectedness or organization of parts during verbal expression^{1,4}

PARTIAL AGONIST ACTIVITY

There is a group of drugs called partial agonists. The term "partial" is important and you will learn more about that a little later. But now, let's see what partial agonist activity looks like.²⁶:



Another strategy is partial dopamine agonism. A partial agonist at dopamine D₂ receptors therefore offers an attractive option for the treatment of schizophrenia. It should act as a functional antagonist in the mesolimbic dopamine pathway, where excessive dopamine activity is thought to cause positive symptoms, but show functional agonist activity in the mesocortical pathway, where reduced dopamine activity is thought to be associated with negative symptoms and cognitive impairment. In addition, it should avoid the complete blockade of the nigrostriatal or tuberoinfundibular pathways, associated with extrapyramidal symptoms (EPS) and elevated prolactin levels, respectively.²⁰

CLINICAL ASSESSMENT

CLINICAL ASSESSMENT AND COLLATERAL INFORMATION^{4,27,28}



Clinical Assessment

- Exclude other causes
- No symptom or group of symptoms is pathognomonic for schizophrenia
- Water for "hallmark symptoms"
- Diagnostic interview



Collateral Information

- Interviews with family
- Interview with caregivers
- Medical records

The diagnosis of schizophrenia is frequently made only after other causes of symptoms have been ruled out. Hallucinations and delusions are often considered characteristic of the illness, as you learned when we talked about specific types of hallucinations and delusions. These symptoms, which are known as "hallmark symptoms," are present in 75% of schizophrenia patients at some point from the first hospitalization when followed for a 20-year period.⁴ They include delusional perceptions, auditory hallucinations experienced as voices speaking one's thoughts, voices arguing, and voices commenting on one's actions, and 7 types of delusions including somatic passivity, thought withdrawal, thought broadcasting, thought insertion, belief that one's emotions are not one's own, belief that impulses are controlled by an outside force, and belief that actions are controlled by an outside force.⁴

Keep in mind that although there are no laboratory or physical examination findings or other biomarkers that can establish a diagnosis, physical and laboratory assessments may help to rule out other medical causes of psychosis.

A diagnostic interview with a patient is typically supplemented by information from family members or caregivers, who may be able to provide useful information about a patient's behavior outside the clinic or hospital. Medical records can also give useful supplemental information.^{27,28}

POSITIVE, NEGATIVE, AND COGNITIVE SYMPTOMS OF SCHIZOPHRENIA

We talked about positive, negative, and cognitive symptoms earlier. Let's take a closer look at what the patient actually experiences. Keep these in the back of your mind because they will come up again and again, especially when you begin to read about specific classes of drugs and what they do.



Positive Symptoms

- Hallucinations
 - Auditory
 - Visual
 - Somatic
- Delusions



Negative Symptoms

- Affective flattening
- Poverty of speech
- Apathy
- Asociality/anhedonia



Cognitive Symptoms

- Attention
- Language
- Memory
- Processing speed

Positive symptoms of schizophrenia include auditory, visual, and somatic hallucinations as well as delusions. Negative symptoms account for a substantial portion of the morbidity associated with schizophrenia and include affective flattening, poverty of speech, apathy, and asociality and anhedonia.¹ Cognitive symptoms are also an important part of the patient's symptom complex.²⁸

DSM-5® CRITERIA FOR DIAGNOSIS OF SCHIZOPHRENIA

Criterion 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 $3.^1$

- 1. Delusions bizarre delusions alone are sufficient
- 2. Hallucinations a voice commenting or voices conversing is sufficient
- 3. Disorganized speech for example, frequent derailment or incoherence
- 4. Grossly disorganized or catatonic behavior
- 5. Negative symptoms for example, diminished emotional expression or avolition



Criterion B

For a significant portion of the time since the onset of the disturbance, level of functioning in one or more major areas, such as work, interpersonal relations, or self-care, is markedly below the level achieved prior to the onset — or when the onset is in childhood or adolescence, there is failure to achieve the expected level of interpersonal, academic, or occupational functioning.¹

Criterion C

Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 Criterion A symptom, present in an attenuated form — for example, odd beliefs, or unusual perceptual experiences.¹

ADDITIONAL DSM-5® CRITERIA FOR DIAGNOSIS OF SCHIZOPHRENIA

What else does the psychiatrist use to make a diagnosis? There are several additional criteria that may be helpful.

CLINICAL EVALUATION INVOLVES CONSIDERATIONS AND EXCLUSIONS

Criterion D

Schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out, because either 1) no major depressive or manic episodes have occurred concurrently with the activephase symptoms, or 2) if mood episodes have occurred during active-phase symptoms, they have been present for a minority of the total duration of the active and residual periods of the illness.¹

Criterion E

The disturbance is not attributable to the direct physiological effects of a substance (eg, a drug of abuse, a medication) or another medical condition.¹



Criterion F

If there is a history of autism spectrum disorder or a communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations, in addition to the other required symptoms of schizophrenia, are also present for at least 1 month (or less if successfully treated).¹

DSM-5[®] CRITERIA FOR DIFFERENTIAL DIAGNOSIS OF SCHIZOPHRENIA

Not real patients. Models used for illustrative purposes.



Major depressive or bipolar disorder with psychotic or catatonic features

The distinction between schizophrenia and major depressive or bipolar disorder with psychotic features or with catatonia depends on the temporal relationship between the mood disturbance and the psychosis, and on the severity of the depressive or manic symptoms. If delusions or hallucinations occur exclusively during a major depressive or manic episode, the diagnosis is depressive or bipolar disorder with psychotic features.



Schizoaffective disorder

A diagnosis of schizoaffective disorder requires that a major depressive or manic episode occur concurrently with the active-phase symptoms and that the mood symptoms be present for a majority of the total duration of the active periods.



Schizophreniform disorder and brief psychotic disorder

These disorders are of shorter duration than schizophrenia as specified in Criterion C, which requires 6 months of symptoms. In schizophreniform disorder, the disturbance is present less than 6 months, and in brief psychotic disorder, symptoms are present at least 1 day but less than 1 month.



Delusional disorder

Delusional disorder can be distinguished from schizophrenia by the absence of the other symptoms characteristic of schizophrenia.



Schizotypal personality disorder

Schizotypal personality disorder may be distinguished from schizophrenia by subthreshold symptoms that are associated with persistent personality features.



Obsessive-compulsive disorder and body dysmorphic disorder

Individuals with obsessive-compulsive disorder and body dysmorphic disorder may present with poor or absent insight, and the preoccupations may reach delusional proportions. But these disorders are distinguished from schizophrenia by their prominent obsessions, compulsions, preoccupations with appearance or body odor, hoarding, or body-focused repetitive behaviors.



Posttraumatic stress disorder

Posttraumatic stress disorder may include flashbacks that have a hallucinatory quality, and hypervigilance may reach paranoid proportions. But a traumatic event and characteristic symptom features relating to reliving or reacting to the event are required to make the diagnosis.



Autism spectrum disorder or communication disorders

These disorders may also have symptoms resembling a psychotic episode but are distinguished by their respective deficits in social interaction with repetitive and restricted behaviors and other cognitive and communication deficits. An individual with autism spectrum disorder or communication disorder must have symptoms that meet full criteria for schizophrenia, with prominent hallucinations or delusions for at least 1 month, to be diagnosed with schizophrenia as a comorbid condition.

Other mental disorders associated with a psychotic episode



The diagnosis of schizophrenia is made only when the psychotic episode is persistent and not attributable to the physiological effects of a substance or another medical condition. Individuals with a delirium or major or minor neurocognitive disorder may present with psychotic symptoms, but these would have a temporal relationship to the onset of cognitive changes consistent with those disorders. Individuals with

substance/medication-induced psychotic disorder may present with symptoms characteristic of Criterion A for schizophrenia, but the substance/medication-induced psychotic disorder can usually be distinguished by the chronological relationship of substance use to the onset and remission of the psychosis in the absence of substance use.

TREATMENT GOALS

The goals of treatment include short-term goals and long-term goals.

TREATMENT GOALS FOR SCHIZOPHRENIA²⁹

Overall Goals	Immediate Goals Acute Phase	Long-term Goals Maintenance
Few and/or stable symptomsAvoid hospitalization	Reduce agitated, disorganized, or hostile behavior	Avoid adverse events and metabolic consequences
 Improved quality of life based on patient's functioning and personal goals 	 Decrease impact of hallucinations Improve organization of thought processes (cognitive processes) Reduce social withdrawal Limit risk of side effects 	• Enhance treatment acceptability to help improve adherence
		Help to avoid relapse
		 Maintain and enhance acute- phase therapeutic gains
		Maintain or enhance cognitive function

The overarching goals of therapy relate mostly to helping patients live as independently as possible by stabilizing symptoms, avoiding hospitalization, and improving quality of life based on patients' functioning. This looks great on paper, but effective, long-lasting treatment of schizophrenia is associated with many challenges. Let's look at some of them now.⁵

TREATMENT STRATEGIES

Treatment strategies focus on a combination of medication, psychotherapy, and psychosocial interventions. It is important to treat the whole patient through the use of medication, psychotherapy, and psychosocial intervention.

Strategies for treating patients in the acute phase and managing them in the stabilization phase are in line with the treatment goals outlined earlier in this module.²⁶

TREATMENT STRATEGIES FOR SCHIZOPHRENIA²⁶

Acute Phase

- Prevent harm
- Control disturbed behavior
- Reduce the severity of psychosis and associated symptoms (eg, agitation, aggression, negative symptoms, affective symptoms)
- · Determine and address the factors that led to the occurrence of the acute episode
- Effect a rapid return to the best level of functioning
- Develop an alliance with the patient and family
- · Formulate short- and long-term treatment plans
- · Connect the patient with appropriate aftercare in the community

Stabilization Phase

- Reduce stress on the patient
- Provide support to minimize the likelihood of relapse
- Enhance the patient's adaptation to life in the community
- Facilitate continued reduction in symptoms and consolidation of remission
- Promote the process of recovery

During the maintenance phase, medication regimens can be continued if effective or modified, if needed, to maintain or enhance control of psychotic symptoms.²⁶

PROGRESS CHECK QUESTIONS

Answers to these questions can be found on page 21.

Question 1

Which of the following is the most common period during which schizophrenia typically appears clinically?

- A. Childhood
- B. At puberty
- C. Late adolescence to mid-30s
- D. Mid-30s to mid-40s

Question 2

Which of the following are positive symptoms? (More than one answer may be correct)

- A. Delusions
- B. Conceptual disorganization
- C. Hallucinations
- D. Emotional withdrawal

Question 3

Which of the following pathway(s) is/are thought to be most closely related to the appearance of negative symptoms?

- A. Mesocortical pathway
- B. Tuberoinfundibular pathway
- C. Nigrostriatal pathway
- D. Mesolimbic pathway

Question 4

Which of the following pathway(s) is/are thought to be most closely related to the appearance of positive symptoms?

- A. Mesocortical pathway
- B. Tuberoinfundibular pathway
- C. Nigrostriatal pathway
- D. Mesolimbic pathway

Question 5

Using the DSM-5[®] criteria for the diagnosis of schizophrenia, if a patient presented with grossly disorganized behavior and diminished emotional expression for the last two months, can you make a diagnosis of schizophrenia?

- A. Yes
- B. No

Question 6

- Using the DSM-5[®] criteria for the diagnosis of schizophrenia, if an untreated patient presented with bizarre delusions, hallucinations and catatonic behavior that appeared on a total of 4 days during the last 2 weeks, can you make a diagnosis of schizophrenia?
- A. Yes
- B. No

PROGRESS CHECK ANSWERS

- 1. C
- 2. A, B, C
- 3. A
- 4. D
- 5. B
- 6. B

REFERENCES

- 1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association; 2013.
- 2. Road to Recovery: Employment and Mental Illness. National Alliance on Mental Illness 2014 Web site. https://www.nami.org/work. Accessed September 21, 2017.
- 3. Sorenson B. What Is dopamine responsible for? Livestrong.com Web site. http://www.livestrong.com/article/208418-what-is-dopamine-responsible-for/. Updated August 14, 2017. Accessed September 21, 2017.
- Rosen C, Grossman LS, Harrow M, Bonner-Jackson A, Faull R. Diagnostic and prognostic significance of Schneiderian first-rank symptoms: a 20-year longitudinal study of schizophrenia and bipolar disorder. *Compr Psychiatry*. 2011;52(2):126-131.
- Meyer JM. Pharmacotherapy of psychosis and mania. In: Brunton LL, Chabner BA, Knollmann BC, eds. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 12th ed. New York, NY: McGraw-Hill; 2011. http://accesspharmacy.mhmedical.com/content.aspx?bookid=1613§ionid=102158680. Accessed September 21, 2017.
- 6. National Institute of Mental Health. Schizophrenia. https://www.nimh.nih.gov/health/topics/schizophrenia/index.shtml. Updated February 2016. Accessed September 22, 2017.
- 7. World Health Organization. Schizophrenia Fact Sheet. July 2016. Web site. http://www.who.int/mediacentre/factsheets/fs397/en/ Accessed September 21, 2017
- 8. World Health Organization. Schizophrenia: what is schizophrenia? http://www.who.int/mental_health/management/schizophrenia/en/. Updated 2017. Accessed September 21, 2017.
- 9. National Institute of Mental Health. Schizophrenia: prevalence http://www.nimh.nih.gov/health/statistics/prevalence/schizophrenia.shtml. Accessed September 21, 2017.
- 10. Emergency Department Visits Related to Schizophrenia Among Adults Aged 18-64: United States, 2009-2011. Web site https://www.cdc.gov/nchs/products/databriefs/db215.htm. Accessed September 21, 2017.
- 11. Burden of mental illness. Centers for Disease Control and Prevention Web site. http://www.cdc.gov/mentalhealth/basics/burden.htm. Updated October 24, 2015. Accessed September 21, 2017.
- 12. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull*. 1987;13(2):261-76.
- 13. Coyle JT, Balu D, Benneyworth M, Basu A, Roseman A. Beyond the dopamine receptor: novel therapeutic targets for treating schizophrenia. *Dialogues Clin Neurosci*. 2010;12(3):359-82.
- 14. Stedman's Online Dictionary. http://stedmansonline.com/index. Accessed September 22, 2017.
- 15. Meldrum BS. Glutamate as a neurotransmitter in the brain: review of physiology and pathology. *J Nutr*. 2000;130(4S Suppl):1007S-1015S.
- 16. Liu AK, Chang RC, Pearce RK, Gentleman SM. Nucleus basalis of Meynert revisited: anatomy, history and differential involvement in Alzheimer's and Parkinson's disease. *Acta Neuropathol.* 2015;129(4):527-540.
- 17. Stahl SM. Chapter 4 Psychosis and schizophrenia. In: *Stahl's Essential Psychopharmacology*. 4th ed. New York, NY: Cambridge University Press; 2013. Web site: http://stahlonline.cambridge.org/essential_4th.jsf
- 18. Black DW, Andreasen NC. Schizophrenia and the psychotic disorders. In: Black DW, Andreasen NC, eds. *Introductory Textbook of Psychiatry*. 5th ed. Washington, DC: American Psychiatric Publishing; 2011; 107-139.
- 19. Buckley PF, Miller BJ, Lehrer DS, Castle DJ. Psychiatric comorbidities and schizophrenia. *Schizophr Bull*. 2009.;35(2):383-402.
- 20. Lieberman JA. Dopamine partial agonists: a new class of antipsychotic. CNS Drugs. 2004;18(4):251-267.

- 21. Roth BL, Hanizavareh SM, Blum AE. Serotonin receptors represent highly favorable molecular targets for cognitive enhancement in schizophrenia and other disorders. *Psychopharmacology (Berl)*. 2004;174(1):17-24.
- 22. Roth BL, Shapiro DA. Insights into the structure and function of 5-HT(2) family serotonin receptors reveal novel strategies for therapeutic target development. *Expert Opin Ther Targets*. 2001;5(6):685-695.
- 23. Millan MJ. Improving the treatment of schizophrenia: focus on serotonin (5-HT)(1A) receptors. *J Pharmacol Exp Ther*. 2000;295(3):853-861.
- 24. Abi-Dargham A, Moore H. Prefrontal DA transmission at D1 receptors and the pathology of schizophrenia. *Neuroscientist.* 2003;9(5):404-416.
- Tortora GJ, Derrickson B. Nervous tissue. In: Tortora GJ, Derrickson B, eds. *Principles of Anatomy and Physiology*. 12th ed. Hoboken, NJ: John Wiley & Sons; 2009:447-491.
- 26. Lehman AF, Lieberman JA, Dixon LB, et al; Work Group on Schizophrenia. *Practice Guideline for the Treatment of Patients With Schizophrenia.* 2nd ed. American Psychiatric Association; 2010.
- Fischer BA, Buchanan RW. Schizophrenia: clinical manifestations, course, assessment, and diagnosis. UpToDate Web site. http://www.uptodate.com/contents/schizophrenia-in-adults-clinical-manifestations-course-assessment-anddiagnosis?source=search_result&search=Schizophrenia%3A+Clinical+manifestations%2C+course%2C+assessment %2C+and+diagnosis&selectedTitle=1%7E150. Accessed September 21. 2017.
- 28. Miller B, Bucklet P. Schizophrenia, Chapter 10. In Conn H, Bope E. eds. *Conn's Current Therapy.* Philadelphia, PA: Elsevier; 2017.
- 29. Frankenberg FR. Schizophrenia. Medscape Web site. http://emedicine.medscape.com/article/288259-overview. Updated December 22, 2014. Accessed September 21, 2017.