

# Psychosis

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## REVIEW ARTICLE



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## ABSTRACT

**PURPOSE OF REVIEW:** Psychosis is a psychiatric condition that has significant overlap with neurologic disease. This article is intended to educate the neurologist on the psychiatric manifestations of psychosis and its evaluation, diagnosis, and treatment. How to differentiate a primary psychiatric cause of psychosis from psychosis secondary to a medical or neurologic condition is also reviewed.

**RECENT FINDINGS:** Current research in psychotic disorders has focused increasingly on negative symptoms and cognitive impairment in psychotic illness, as it is now recognized that these cause the greatest impact on functional deficits for patients. A number of new medications have also been introduced to target negative symptoms and cognitive deficits in psychotic illness. These have new implications in terms of treatment overlap with medications being prescribed by providers in psychiatry, neurology, and general practice.

**SUMMARY:** This article discusses the current methods for evaluating, diagnosing, and treating psychosis. Psychosis as a primary mental health disorder is a diagnosis of exclusion, as psychosis can be a direct symptom of underlying medical or neurologic disease. Delirium and dementia are the two most important disorders to rule out. This article will help readers be more prepared to assess and treat the patient with psychosis.

## INTRODUCTION

Psychosis is a broad term that encompasses symptoms related to a change in perception of reality. Psychosis alone does not mean that a primary psychiatric disorder is present. In many cases, differentiating the origin of psychosis can be very difficult. This article discusses the psychiatric and medical manifestations of psychosis and reviews how to evaluate, diagnose, and treat the patient with psychosis. Some useful components of the examination are also addressed to help the clinician differentiate a primary psychiatric cause of psychosis versus psychosis secondary to a medical or neurologic condition.

## DEFINING PSYCHOSIS

In the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*, the chapter “Schizophrenia Spectrum and Other Psychotic Disorders” states that these disorders “are defined by abnormalities in one or more of the following five domains: delusions, hallucinations, disorganized thinking (speech), grossly disorganized or abnormal motor behavior (including catatonia), and negative

### CITE AS:

CONTINUUM (MINNEAP MINN)  
2018;24(3, BEHAVIORAL NEUROLOGY  
AND PSYCHIATRY):845-860.

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### RELATIONSHIP DISCLOSURE:

Drs Schrimpf and Aggarwal report no disclosures. Dr Lauriello has served as an advisor for Alkermes; Otsuka America Pharmaceutical, Inc; and Teva Pharmaceutical Industries Ltd and on the event monitoring board for Alkermes. Dr Lauriello has served on the editorial board of *Academic Psychiatry*. Dr Lauriello receives research/grant support from Florida Atlantic University/Otsuka America Pharmaceutical, Inc and the Missouri Foundation for Health and receives publishing royalties from Oxford University Press and UpToDate, Inc.

### UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:

Drs Schrimpf, Aggarwal, and Lauriello report no disclosures.

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symptoms.”<sup>1</sup> Defining and characterizing psychotic illness has been a continually evolving process. The early Greek physicians were the first to have documented delusions, paranoia, and changes in cognitive function and personality, and a number of other historical figures have offered unique ways of characterizing psychosis.<sup>2</sup> However, it was Emil Kraepelin and Eugen Bleuler, physicians trained in psychiatry and neurology, who provided what have become the dominant characterizations of a primary psychotic disorder. Kraepelin defined the disorder termed *dementia praecox* (an apparent decline in cognitive functioning at an early age) in contrast to Alzheimer dementia. Later, Bleuler coined the term *schizophrenia*, denoting a split between the content and processes of thought and the emotions expressed.<sup>3</sup> The patient’s feelings appear independent of the content of thought, leading to inappropriate emotional expression, such as flat affect when describing his or her depression. Over the years, the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* has modified how it characterizes and categorizes schizophrenia and the other disorders that manifest a significant level of psychosis. Affective disorders, such as major depressive disorder with psychotic features and bipolar I disorder, may manifest with psychosis but are categorized differently because the primary aberration is affective in nature, with different clinical features and prognosis.<sup>2</sup>

Although subtle changes have been made in the diagnostic criteria and categorization of psychotic illnesses, the basic components of psychosis have remained fairly stable since the early characterizations by the Greeks. The *DSM-5* diagnoses for schizophrenia spectrum and other psychotic disorders are listed in **TABLE 9-1**, and a general description of each diagnosis is reviewed later in this article. To diagnose patients with psychosis, it is important for clinicians to be able to evaluate and assess the five domains of psychotic illness: delusions,

TABLE 9-1

### DSM-5 Schizophrenia Spectrum and Other Psychotic Disorders<sup>a</sup>

- ◆ Schizotypal (personality) disorder
- ◆ Delusional disorder
- ◆ Brief psychotic disorder
- ◆ Schizophreniform disorder
- ◆ Schizophrenia
- ◆ Schizoaffective disorder
- ◆ Substance/medication-induced psychotic disorder
- ◆ Psychotic disorder due to another medical condition
- ◆ Catatonia associated with another mental disorder (catatonia specifier)
- ◆ Catatonic disorder due to another medical condition
- ◆ Unspecified catatonia
- ◆ Other specified schizophrenia spectrum and other psychotic disorder
- ◆ Unspecified schizophrenia spectrum and other psychotic disorder

*DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.*

<sup>a</sup> Data from American Psychiatric Association.<sup>1</sup> © 2013 American Psychiatric Association.

hallucinations, disorganized thinking (speech), grossly disorganized or abnormal motor behavior (including catatonia), and negative symptoms.

## Delusions

The *DSM-5* defines delusions as “fixed beliefs that are not amenable to change in light of conflicting evidence. Their content may include a variety of themes (eg, persecutory, referential, somatic, religious, grandiose).”<sup>1</sup>

**PERSECUTORY DELUSIONS.** Persecutory delusions are the most common type of delusion and involve a belief that someone is monitoring or trying to harm the patient. For example, patients may state that the Federal Bureau of Investigation (FBI) is monitoring them and has cameras in their home or may say “‘they’ are always watching me” or “‘they’ know everything I think.” When questioned further about these beliefs, the patient will not be able to reason through or accept any explanations that the beliefs are not factual. In fact, often the person trying to help the patient reason through the illogical beliefs will then become a part of the delusions, ie, that person may now be perceived as a member of the FBI sent to interrogate them.

**REFERENTIAL DELUSIONS.** Referential delusions involve the belief that subtle things occurring in an individual’s environment are cues that hold significant meaning. An example is a patient believing that the newscaster on the evening news is looking directly at him or her from inside the TV and has a special message embedded in the newscast that is meant specifically for the patient.

**SOMATIC DELUSIONS.** Somatic delusions involve irrational beliefs about a person’s body. A dramatic example would be a female patient believing she is pregnant, even though all logical evidence says otherwise. Somatic delusions can be subtle and lead to a number of unnecessary medical consultations, tests, and even operative procedures.

**RELIGIOUS DELUSIONS.** Religious delusions are also very common (eg, believing that one is God or an angel). A clear example one of the authors encountered involved a patient who believed he was Jesus Christ and had been crucified on the cross. The patient showed the scars from the nails on the palms of his hands, even though no imperfections of the skin were noted by others. With religious delusions, it is important to differentiate between culturally appropriate beliefs and delusions. For example, a patient may state he or she can talk to God. When the family is questioned about typical religious beliefs for the patient’s religious background, it may be discovered that talking directly to God or “speaking in tongues” is a belief in that religion and is thus culturally appropriate.

**GRANDIOSE DELUSIONS.** Grandiose delusions are exactly what they sound like: grandiose beliefs about oneself (eg, one’s own abilities, wealth, or fame). A patient with grandiose delusions may say that he or she flew a stealth bomber in the Iraq War and was the reason the war ended, even though he or she has no military experience and would have been too old to serve in the military during that time.

**OTHER DELUSIONS.** Other, less common, delusions patients may exhibit include erotomanic delusions (belief that a famous person is in love with them), nihilistic delusions (belief that a major catastrophe will occur), delusions of control (belief that a person’s will, thoughts, or feelings are under the control of external

## KEY POINTS

- The five domains of psychological functioning affected by schizophrenia and other psychotic disorders are delusions, hallucinations, disorganized thinking (speech), grossly disorganized or abnormal motor behavior (including catatonia), and negative symptoms.
- Delusions are fixed beliefs that a patient will maintain despite conflicting evidence offered by those around them. The delusions may be persecutory, referential, somatic, religious, or grandiose in nature.
- With religious delusions, it is important to differentiate between culturally appropriate beliefs and delusions.

## KEY POINTS

- Hallucinations are perceptual experiences that are very vivid and real to the individual experiencing them. They are not under voluntary control and can occur in any sensory modality.
- It is important to recognize that visual hallucinations can be a component of psychosis, but many times, especially if onset is acute, visual hallucinations are an indicator for delirium, dementia, or other neurologic disorders.
- Tactile, olfactory, and gustatory hallucinations are unusual in a primary psychotic disorder, and their presence suggests another underlying medical or neurologic cause.

forces), and delusions of mind reading (belief that people can read their mind or know their thoughts).

### Hallucinations

According to *DSM-5*, “Hallucinations are perception-like experiences that occur without an external stimulus. They are vivid and clear, with the full force and impact of normal perceptions, and not under voluntary control. They may occur in any sensory modality, but auditory hallucinations are the most common in schizophrenia and related disorders.”<sup>1</sup>

**AUDITORY HALLUCINATIONS.** Typically, auditory hallucinations involve hearing voices, either the familiar voices of people the patient knows or unfamiliar voices. The patient may hear one voice or multiple voices, either talking to the patient or talking to each other. The voices may say derogatory things about the patient, such as “You’re worthless” or “You’re a failure,” or the voices may tell the patient to do things. These are termed *command hallucinations* (eg, “Kill yourself” or “Kill your boyfriend; he’s going to hurt you”). Musical hallucinations are another form of auditory hallucination and necessitate an audiologic evaluation before other etiologies are investigated, as hypoacusis is the most prevalent etiology.<sup>4</sup>

**VISUAL HALLUCINATIONS.** Visual hallucinations are another common hallucination observed in primary psychosis. Patients may say they can see dead family members or individuals/faces unknown to them. However, visual hallucinations can also be a sign of delirium or dementia, especially if they are acute in onset,<sup>5</sup> and can also occur in other neurologic disorders. Patients may note insects crawling around the room or strange fantasy figures when they are delirious from an infection, intoxicated, or withdrawing from substances.

**TACTILE, OLFACTORY, AND GUSTATORY HALLUCINATIONS.** Tactile, olfactory, and gustatory hallucinations are unusual in a primary psychotic disorder, and their presence suggests a differential diagnosis of other underlying medical or neurologic causes.<sup>3</sup> A sensation of bugs crawling on the skin can be a common manifestation of delirium. Olfactory hallucinations of burning or unpleasant smells may be a sign of mesial temporal lobe seizures. Fifteen percent of patients with seizures from a temporal lobe tumor will have olfactory or gustatory auras.<sup>6</sup> Hallucinations that occur while falling asleep (hypnagogic) or waking up (hypnopompic) may be a symptom of narcolepsy, but from a psychiatric standpoint, they are usually considered to be within the normal range of experience.<sup>1</sup>

### Disorganized Thinking (Speech)

Disorganized thinking is assessed by a person’s speech patterns and is indicative of a formal thought disorder.<sup>1</sup> Different patterns of disruption of speech can occur. Patients could be described as having thought blocking if they are speaking and stop in the middle of a sentence and pause for a prolonged period. When they resume talking, they do not acknowledge the pause and will start speaking about something completely unrelated to what they were talking about previously.

**TABLE 9-2** lists formal thought disorders and associated speech patterns.

### Grossly Disorganized or Abnormal Motor Behavior (Including Catatonia)

Disorganized behavior is observed in the patient’s inability to complete goal-directed activities. Disorganized patients may appear disheveled and

malnourished, typically dressed inappropriately for the weather. They may also be observed talking to themselves and can become agitated in an unpredictable manner.<sup>1</sup> Disorganized behavior can also be seen as inappropriate laughing or childlike behavior. Catatonia is an extreme form of abnormal motor behavior in which a patient can assume a rigid, inappropriate, or bizarre posture. Patients may also cease any verbal or motor responses to their environment; these are termed *mutism* and *stupor*, respectively. Catatonic excitement is the opposite of stupor and involves excessive motor activity with no obvious cause. Other symptoms included in this category are repeated stereotyped movements, staring, grimacing, and echoing of speech.<sup>1</sup>

### Negative Symptoms

Negative symptoms are most often seen in schizophrenia versus other psychotic disorders. Negative symptoms include diminished emotional expression, avolition (a lack of motivation), alogia (poverty of speech), anhedonia (lack of the ability to experience pleasure), and asociality. Negative symptoms have been the target of novel drug development for many drug companies, because it is now recognized that negative symptoms gravely impair an individual's ability to function productively in society.

### Cognitive Symptoms

Cognitive symptoms are not listed in *DSM-5* as one of the five domains in psychotic illness but are included here as they are the most related to level of functioning in schizophrenia. Three outcome domains exist in schizophrenia: functional

## Formal Thought Disorders<sup>a</sup>

TABLE 9-2

Thought Disorder	Associated Speech Pattern
<b>Circumstantiality</b>	Overinclusion of trivial or irrelevant details that impede the sense of getting to the point
<b>Clang associations</b>	Thoughts are associated by the sound of words rather than by their meaning (eg, through rhyming or assonance)
<b>Derailment (synonymous with loose associations)</b>	A breakdown in both the logical connection between ideas and the overall sense of goal directedness; the words make sentences, but the sentences do not make sense
<b>Flight of ideas</b>	A succession of multiple associations so that thoughts seem to move abruptly from idea to idea; often (but not invariably) expressed through rapid, pressured speech
<b>Neologism</b>	The invention of new words or phrases or the use of conventional words in idiosyncratic ways
<b>Perseveration</b>	Repetition of out-of-context words, phrases, or ideas
<b>Tangentiality</b>	In response to a question, the patient gives a reply that is appropriate to the general topic without actually answering the question  Example: Doctor: "Have you had any trouble sleeping lately?" Patient: "I usually sleep in my bed, but now I'm sleeping on the sofa."
<b>Thought blocking</b>	A sudden disruption of thought or a break in the flow of ideas

<sup>a</sup> Modified with permission from Sadock BJ, et al.<sup>3</sup> © 2015 Lippincott, Williams & Wilkins.



status (or psychosocial functioning), disorder status (positive and negative symptoms), and subjective experience (personal well-being factors). Cognition, specifically social cognition, is a major determinant of functional status. Functional status has been shown to have a greater relationship to functional outcomes for patients with schizophrenia than disorder status (the presence of psychotic symptoms). Cognition, social cognition, and motivation are the main determinants of success in daily and community functioning. In this context, cognition refers to the ability to accurately perceive, attend to, and remember information. Social cognition includes the ability to identify and interpret social cues. Motivation involves the patient's desire to engage the community and relates to the negative symptoms of schizophrenia.<sup>7,8</sup>

### EVALUATION OF THE PATIENT WITH PSYCHOSIS

The therapeutic relationship is a key component to a successful evaluation of the patient with psychosis. The therapeutic relationship has been called by different names in the research literature (eg, therapeutic alliance or working alliance). Research on the therapeutic alliance in psychotherapy and psychiatric care has shown that it is linked with improved patient outcomes.<sup>9</sup> In patients who are already very distrustful and disorganized in their thinking, it is vital to establish a good working relationship for an evaluation to be successful. It is not uncommon for a patient with psychosis to become agitated and discontinue/disengage from the interview. In a review of the impact of the therapeutic relationship in psychotic disorders, it was found that a successful therapeutic relationship was judged to be “respectful, where shared decision making is the norm and where trust is mutual.”<sup>9</sup> It is widely known that medication noncompliance is a major barrier to treatment success in schizophrenia. Establishing a positive therapeutic relationship with patients in which they are involved in the decision-making process regarding medication and how/why it is to be taken can dramatically improve compliance.<sup>10</sup>

As in all areas of medicine, obtaining a thorough history of present illness is essential in establishing an accurate diagnosis. Onset, duration, precipitating/perpetuating factors, and stressors contributing to symptoms are important to help differentiate a primary psychotic disorder from psychosis that is secondary to a medical or neurologic disease as well as to develop the list of differential diagnoses for a primary psychotic disorder. As the rest of the psychiatric history is performed, the patient's physical appearance, mannerisms, and abnormal movements should be noted. In the review of symptoms for psychosis, all the areas discussed previously in this article should be addressed.

For the nonpsychiatric clinician, one of the most important goals in the interview of patients who present with acute-onset psychosis or are experiencing a change in the symptoms of their psychosis is to establish whether the symptoms are related to a primary psychotic disorder or secondary to an underlying medical or neurologic disease. Establishing a primary psychotic disorder diagnosis is a diagnosis of exclusion. It is diagnosed once all underlying medical or neurologic possibilities are ruled out. In the authors' personal experience, it is not uncommon for the psychosis related to a medical or neurologic disease to look very similar to a primary psychotic disorder. Psychoses resembling a primary psychotic disorder such as schizophrenia occur 6 to 12 times more frequently in patients with epilepsy than in the general population.<sup>11</sup> To make matters even more complex, a recently updated Cochrane Review details the

multiple studies that have documented that numerous anticonvulsants can precipitate psychosis.<sup>12</sup> A review on psychosis in multiple sclerosis (MS) confirmed that MS can present as acute-onset psychosis in a patient with no previous psychiatric history. The study was not able to confirm that psychotic symptoms that develop in a patient with already diagnosed MS represent an MS flare but did find that these patients responded poorly to antipsychotics and improved significantly with the administration of corticosteroids.<sup>13</sup>

It is essential to rule out delirium when evaluating a psychotic patient. Wong and colleagues<sup>14</sup> found that health care workers fail to recognize more than half of delirium cases; thus, a careful cognitive assessment is key in identifying delirium and differentiating it from primary psychosis. Two types of delirium exist: hypoactive and hyperactive. Hypoactive delirium is characterized by lethargy and reduced psychomotor functioning, while hyperactive delirium is characterized by agitation, increased vigilance, and hallucinations. It is the hypoactive form that goes unrecognized most commonly.<sup>15</sup> In a patient with dementia, it is particularly difficult to recognize delirium. The prevalence of delirium superimposed on dementia ranges from 18% to 89% in hospitalized and community-dwelling elderly patients.

Another important but subtle distinction in the cognitive evaluation of the patient with psychosis is that the patient's ability to remain oriented to his or her surroundings is not impaired in primary psychosis. A patient can be floridly psychotic and still remain oriented to person, place, and time. An example seen by one of the authors was a patient who, when interviewed during morning rounds, described his plan to take a spaceship to Mars and even had drawings of the spaceship. A few hours later he was observed on the telephone, coherently negotiating his rent payment with his landlord. In a study of recent-onset and chronic schizophrenia, the cognitive domains affected by psychosis were efficiency of problem solving, fine motor dexterity, and episodic memory.<sup>16</sup>

Psychosis is commonly a symptom of dementia, and sometimes the psychosis is actually the presenting symptom. It is reported that psychosis has a lifetime risk of 23% and ranks as one of the most common conditions in late life.<sup>17</sup> Approximately 60% of elderly patients who present with new-onset psychosis are exhibiting symptoms of a secondary psychosis.<sup>17</sup> An evaluation of the "six D's" of late-life psychosis includes delirium, disease, drugs, dementia, depression, and delusions (denoting the schizophrenia spectrum disorders).<sup>17</sup> In elderly patients with chronic schizophrenia, it can be extremely difficult to differentiate whether a change in their psychotic symptoms is related to their primary psychotic disorder or due to a developing dementia. In these patients, the Montreal Cognitive Assessment (MoCA) can be particularly helpful, as it has been shown to be a useful screening tool to detect medically or neurologically based cognitive deficits in patients with severe mental illness, such as schizophrenia, and psychiatrically hospitalized patients.<sup>18,19</sup> A score of 23 or below was determined to screen positive for medically or neurologically based cognitive deficits.<sup>18</sup> As an interesting side-note, it has been postulated that "delusions' in dementia are not a psychotic symptom, but rather a byproduct of memory loss, thus deserving a different label."<sup>20</sup>

Laboratory and radiologic evaluations of the patient with acute psychosis should always be performed in accordance with the list of possible diagnoses

## KEY POINTS

- Negative symptoms include diminished emotional expression, avolition (a lack of motivation), alogia (poverty of speech), anhedonia (lack of the ability to experience pleasure), and asociality. It is now recognized that negative symptoms gravely impair an individual's ability to function productively in society.
- Functional status (psychosocial functioning) has been shown to have a greater relationship to functional outcomes in schizophrenic patients than disorder status (the presence of psychotic symptoms). In particular, social cognition is a major determinant of functional status.
- A positive therapeutic alliance is vital to a successful relationship with a psychotic patient. Research shows that a positive therapeutic relationship in which the patient is involved in the decision making and mutual respect exists between patient and clinician can dramatically impact treatment compliance and patient outcomes.
- For the nonpsychiatric clinician, one of the most important goals in the interview of patients who present with acute-onset psychosis or are experiencing a change in the symptoms of their psychosis is to establish whether the symptoms are related to a primary psychotic disorder or secondary to an underlying medical or neurologic disease. Establishing a primary psychotic disorder diagnosis is a diagnosis of exclusion.

being considered. Diagnostic testing may include complete blood cell count, comprehensive metabolic panel, thyroid-stimulating hormone (TSH), vitamin B<sub>12</sub> level, folate, rapid plasma reagin (RPR), erythrocyte sedimentation rate, autoimmune antibody screens, human immunodeficiency virus (HIV) testing, and toxicology screen. Either a brain MRI or CT scan should be performed; EEG and additional testing may be ordered if the history indicates.<sup>17</sup>

### Assessment/Diagnosis of the Patient With Psychosis

Once it has been established that a patient's cognitive status is not compromised by delirium or dementia, the patient should be evaluated for a primary psychotic disorder. A detailed psychiatric examination should be performed, including a psychiatric review of systems, psychiatric history, family psychiatric history, and social history. The mental status examination takes careful note of the patient's physical appearance, behavior, mood, speech patterns, thought content, thought processes, cognition, insight, and judgment.<sup>21</sup> In a thorough psychiatric assessment, it is important to question a patient with a list of potential differential diagnoses in mind (TABLE 9-1). However, it is also important to rule out affective disorders with a psychotic component; personality disorders that have a psychotic component, such as borderline personality disorder; and autism spectrum disorders. The Brief Psychiatric Rating Scale is considered a clinically useful tool in evaluating patients with psychosis and gauging their response to treatment.<sup>22</sup> The following sections review each of the *DSM-5* diagnoses listed under "Schizophrenia Spectrum and Other Related Disorders."

**SCHIZOTYPAL PERSONALITY DISORDER.** *Schizotypal personality disorder* is a *DSM-5* personality disorder characterized by magical thinking, illusions, and ideas of reference. Patients with schizotypal personality disorder exhibit odd behavior, and their speech patterns may have particular significance to only them. In contrast to patients with psychotic disorders, these patients do not have persistent delusions or hallucinations. Patients with schizotypal personality disorder are very socially isolated. Schizotypal personality disorder is diagnosed in about 3% of the population.<sup>3</sup>

**DELUSIONAL DISORDER.** *Delusional disorder* is characterized by the presence of one or more delusions. The criteria state that the patient must hold the delusion(s) for at least 1 month and that the delusions cannot be explained by another mental disorder. Classically, the delusions are usually not bizarre in nature (ie, they could happen in real life, such as being loved at a distance by someone famous, being infected with a disease, or being followed). However, *DSM-5* now allows a subtype with bizarre (implausible) delusions. Whatever delusions are held, the patient's functioning is not significantly impacted, and his or her behavior is not usually considered odd or bizarre. The incidence of delusional disorder is 0.2% to 0.3%, making it rare.<sup>3</sup>

**BRIEF PSYCHOTIC DISORDER.** *Brief psychotic disorder* involves the development of acute psychotic symptoms that last at least 1 day but less than a month and resolve spontaneously. The episode may be secondary to a trauma (stressor), develop postpartum, or develop without an obvious precipitant. Patients return to their previous level of functioning. The incidence of brief psychotic disorder is unknown.<sup>3</sup>



**SCHIZOPHRENIFORM DISORDER.** In simple terms, *schizophreniform disorder* is similar to schizophrenia, except its duration from onset is less than 6 months. In contrast to brief psychotic disorder, the symptoms must last at least 1 month. In one-third of cases, the illness resolves completely in less than 6 months, with patients returning to their previous level of functioning. The remaining two-thirds of patients usually progress to another psychotic disorder, most often schizophrenia or schizoaffective disorder.<sup>3</sup>

**SCHIZOPHRENIA.** *Schizophrenia* is one of the most common severe mental illnesses and is reported to have a lifetime incidence of 1%. Schizophrenia is typically diagnosed before age 25 and is diagnosed equally in men and women. When it is diagnosed after age 45, it is considered late onset. Schizophrenia is diagnosed by the presence of at least two of the following five symptoms: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, and negative symptoms. At least one of the symptoms must be delusions, hallucinations, or grossly disorganized behavior (**CASE 9-1**).<sup>3</sup>

**SCHIZOAFFECTIVE DISORDER.** *Schizoaffective disorder* is a combination of schizophrenia and a mood disorder. Both disorders could be diagnosed separately and are present in full in the same patient. Critically, the psychosis must be present for at least 2 weeks when the mood disorder is not present. Additionally, the mood disorder must be diagnostically present during a majority of the active and residual phases of the illness.<sup>3</sup> In other words, more than 50% of the time either depression or bipolar disorder must be evident. Major depression with psychosis is different than schizoaffective disorder because the psychosis is only present when the patient is severely depressed. The incidence of schizoaffective disorder is less than 1%.<sup>3</sup>

**SUBSTANCE/MEDICATION-INDUCED DISORDER.** *Substance/medication-induced disorder* is diagnosed when a patient experiences psychosis in direct relationship to ingestion of a substance or medication. If the substance or medication is taken intentionally to achieve chemical alteration, it is termed substance intoxication.

**PSYCHOTIC DISORDER DUE TO ANOTHER MEDICAL CONDITION.** *Psychotic disorder due to another medical condition* is the diagnosis given for patients who experience psychosis in the context of a medical condition (eg, lung neoplasm, MS, epilepsy). This diagnosis is not given if the psychosis occurs exclusively during the course of delirium.<sup>1</sup>

**CATATONIA.** *Catatonia* is diagnosed by the presence of three or more of the following symptoms: stupor (no psychomotor activity [movement that is impacted by thinking]), catalepsy (passive induction of a posture held against gravity), waxy flexibility (slight, even resistance to positioning by examiner), mutism (little or no verbal response), negativism (opposition or no response to instructions or external stimuli), posturing (spontaneous and active maintenance of posture against gravity), mannerism (odd, circumstantial caricature of normal actions), stereotypy (repetitive, abnormally frequent, non-goal-directed movements), agitation (not influenced by external stimuli), grimacing, echolalia (mimicking another's speech), and echopraxia (mimicking another's movements). The *DSM-5* diagnoses for catatonia are *catatonia*

## KEY POINTS

- An important but subtle distinction in the cognitive evaluation of the patient with psychosis is that the patient's ability to remain oriented to his or her surroundings is not impaired in primary psychosis. A patient can be floridly psychotic and still remain oriented to person, place, and time.
- Evaluating a patient's cognitive status is an essential component in differentiating primary psychosis from secondary psychosis.
- The mental status examination takes careful note of the patient's physical appearance, behavior, mood, speech patterns, thought content, thought processes, cognition, insight, and judgment.

**CASE 9-1**

A 24-year-old man presented for a follow-up visit after a recent psychiatric hospitalization. He had been seen in the clinic since age 18. The recent hospitalization was for command auditory hallucinations telling him to kill himself and persecutory delusions that his parents were poisoning him. He had finished high school in the top 20% of his class and was in his second year of college (at age 20) when he started experiencing symptoms of psychosis. He had been hospitalized 5 times in the past 4 years for delusions that his parents were poisoning him and auditory hallucinations telling him his neighbors were going to harm him. Initial workup for this patient included a urine drug screen, comprehensive metabolic profile, complete blood cell count, thyroid-stimulating hormone (TSH), and brain CT. During each of his five hospitalizations, he responded well to medication, and his symptoms improved, but when he was released from the hospital, he stopped his medication and symptoms recurred. He had to drop out of school after his second year because his psychosis interfered with his ability to focus on his schoolwork.

He had a past history of treatment for attention deficit hyperactivity disorder in late adolescence and an otherwise negative medical history. His family history revealed a maternal aunt who had been in and out of the hospital most of her life with psychotic symptoms. His parents were both healthy, although his father, who was an engineer, had a history of treatment for minor anxiety. The patient's older brother was physically and mentally healthy and attended law school. The patient was on disability and unable to hold a part-time job when he was not on his medication.

At the follow-up visit, the patient was slightly disheveled and had not bathed in a week. He made a moderate amount of eye contact during the interview and did not appear to be responding to internal stimuli. He stated that he did not believe anyone was poisoning him at the time and that he was taking his medication as prescribed. During his most recent hospitalization, he was placed on a long-acting injectable antipsychotic because of his history of noncompliance.

**COMMENT**

The most likely *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)* diagnosis for this patient would be schizophrenia, with the specifier "multiple episodes, currently in acute episode." He has poor insight and medication nonadherence, leading to frequent relapses. This patient shows a typical course for the cognitive ramifications of schizophrenia. In the absence of a diagnosis of schizophrenia, this patient could be expected to finish college and hold a higher-level degree. However, due to his schizophrenia, this patient has had significant cognitive decline and is unable to finish college or hold a steady job.

associated with another mental disorder (*catatonia specifier*) or *catatonic disorder due to another medical condition*. *Unspecified catatonia* is used when the underlying disorder is not known.<sup>1</sup>

**OTHER SCHIZOPHRENIA SPECTRUM AND OTHER PSYCHOTIC DISORDERS.** The diagnosis *other schizophrenia spectrum and other psychotic disorders* is used when a patient meets a significant level of schizophrenia spectrum or other psychotic disorder symptoms, but a full diagnosis cannot be made. The diagnosis *other specified schizophrenia spectrum and other psychotic disorders* is used when the clinician specifies the symptoms present, and the *unspecified schizophrenia spectrum and other psychotic disorders* diagnosis is given when the clinician does not specify the symptoms present.<sup>1</sup>

## TREATMENT

The first steps in the treatment of acute psychosis should be evaluation for agitation and harm prevention. Patients who are at an increased risk of harm to themselves or others may need to be hospitalized. Long-term goals of treatment include sustaining remission, reducing relapses, and improving the patient's level of functioning and quality of life.<sup>23</sup>

Antipsychotic medications are the mainstay of the treatment for psychosis and should be started promptly after an accurate diagnosis has been established. Antipsychotic medications have been extensively studied for the treatment of schizophrenia<sup>24</sup> and also appear to be effective for other types of psychosis. Studies have found antipsychotics to be effective for bipolar mania with psychosis,<sup>25</sup> depression with psychotic features (combination therapy with antidepressants),<sup>26</sup> Parkinson disease psychosis,<sup>27</sup> and psychosis related to dementia.<sup>28</sup>

The choice of an antipsychotic is primarily based on adverse effects and cost considerations, as they do not differ significantly as far as efficacy is concerned (with the exception of clozapine).<sup>29</sup> Clozapine has consistently been shown to be more effective than other oral antipsychotics in patients for whom a number of other antipsychotics have failed (ie, treatment-resistant psychosis) and has also been shown to be effective in reducing suicidal behaviors in patients with schizophrenia and schizoaffective disorder.<sup>30</sup> Clozapine can cause granulocytopenia or agranulocytosis in approximately 1% of patients, requiring regular blood cell count monitoring. Clozapine has been associated with excess risk of myocarditis and venous thromboembolic events, including fatal pulmonary embolism. **TABLE 9-3** lists the major adverse effects of all the antipsychotics available in the United States.<sup>31</sup>

Long-acting injectable antipsychotic medications provide an alternative pharmacologic strategy for the treatment of psychosis and can be administered by injection at 2- to 12-week intervals. Long-acting injectable antipsychotic medications are usually reserved for patients in whom noncompliance to oral antipsychotics leads to frequent relapses, but more recently they also have been studied in early phases of schizophrenia. A systematic review involving 10 studies concluded that the use of long-acting injectable antipsychotic medications in early phases of schizophrenia may be more effective than other forms of antipsychotic medications in controlling symptoms and relapses.<sup>32</sup>

Electroconvulsive therapy should be considered for individuals who have severe psychosis and for whom multiple antipsychotic trials (including

## KEY POINTS

- Antipsychotic medications are the mainstay of the treatment for psychosis and should be started promptly after an accurate diagnosis has been established.
- The choice of an antipsychotic medication is primarily based on adverse effects and cost considerations, as they do not differ significantly as far as efficacy is concerned (with the exception of clozapine, which has consistently been shown to be more effective than other oral antipsychotics).
- Clozapine is effective in reducing suicidal behaviors in patients with schizophrenia and is also effective for psychotic symptoms associated with Parkinson disease. Clozapine can cause granulocytopenia or agranulocytosis in approximately 1% of patients, requiring regular blood cell count monitoring.

**TABLE 9-3 Selected Adverse Effects of Antipsychotic Medications for Schizophrenia<sup>a,b</sup>**

Medication	Weight Gain/Diabetes Mellitus	Hypercholesterolemia	Extrapyramidal Symptoms/ Tardive Dyskinesia
<b>First-generation agents</b>			
Chlorpromazine	+++	+++	+
Fluphenazine	+	+	+++
Haloperidol	+	+	+++
Loxapine	++	ND	++
Perphenazine	++	ND	++
Pimozide	+	ND	+++
Thioridazine <sup>c</sup>	++	ND	+
Thiothixene	++	ND	+++
Trifluoperazine	++	ND	+++
<b>Second-generation agents</b>			
Aripiprazole	+	-	+
Asenapine	++	-	++
Brexpiprazole <sup>d</sup>	+	+	+
Cariprazine <sup>d</sup>	+	-/+	++
Clozapine <sup>e</sup>	++++	++++	-/+
Iloperidone	++	++	-/+
Lurasidone	-/+	-/+	++
Olanzapine	++++	++++	+
Paliperidone	+++	+	+++
Pimavanserin	+	-	-/+
Quetiapine	+++	+++	-/+
Risperidone	+++	+	+++
Ziprasidone	-/+	-/+	+

ND = no data.

<sup>a</sup> Reprinted with permission from Stroup TS, Marder S, UpToDate.<sup>31</sup> © 2018 UpToDate, Inc.

<sup>b</sup> Adverse effects may be dose dependent.

<sup>c</sup> Thioridazine is also associated with dose-dependent retinitis pigmentosa.

<sup>d</sup> Based upon limited experience.

<sup>e</sup> Clozapine also causes granulocytopenia or agranulocytosis in approximately 1% of patients, requiring regular blood cell count monitoring. Clozapine has been associated with excess risk of myocarditis and venous thromboembolic events, including fatal pulmonary embolism.

Prolactin Elevation	Sedation	Anticholinergic Side Effects	Orthostatic Hypotension	QTc Prolongation
++	+++	+++	+++	+
+++	+	-/+	-	ND
+++	++	-/+	-	+
++	++	+	+	+
++	++	+	-	ND
++	+	+	+	++
+++	+++	++++	++++	+++
++	+	+	+	+
++	+	+	+	ND
-	+	-	-	-/+
++	++	-	+	+
-/+	+	-/+	-/+	-/+
-/+	+	-/+	-/+	-/+
-/+	+++	+++	+++	+
-/+	+	+	+++	++
-/+	++	-	+	-/+
+	++	++	+	+
+++	+	-	++	+
-	+	+	++	+
-/+	++	++	++	+
+++	+	+	+	+
+	+	-	+	++



## KEY POINT

● Although antipsychotic medications remain the mainstay of treatment for psychosis, most patients require one or more additional strategies, such as providing education and information about the disease, social skills training, cognitive-behavioral therapy, assertive community treatment, or problem-solving family therapy.

clozapine) have failed or could not be tolerated. Electroconvulsive therapy is also a treatment option for psychosis with prominent catatonic features.<sup>23</sup>

It is recommended that certain assessments be completed before the initiation of antipsychotics and periodically throughout the course of the treatment. These assessments include vital signs; body weight and height; complete blood cell count; blood electrolytes; glucose level; tests of liver, renal, and thyroid function; screening for diabetes mellitus; hyperprolactinemia and hyperlipidemia; ECG; and screening for a movement disorder, including extrapyramidal symptoms and tardive dyskinesia.<sup>23</sup>

Although antipsychotic medications remain the mainstay of treatment for psychosis, most patients require one or more additional strategies, such as providing education and information about the disease, social skills training, cognitive-behavioral therapy, assertive community treatment, or problem-solving family therapy.<sup>23,33</sup>

### Special Considerations

According to the practice guideline published by the American Psychiatric Association, antipsychotic medication should only be used for dementia-related psychosis when symptoms are severe or dangerous or cause significant distress to the patient.<sup>34</sup> An increased mortality risk is associated with the use of antipsychotic medication in elderly patients with dementia.

Pimavanserin is a newer medication marketed for the treatment of psychotic symptoms associated with Parkinson disease. It differs from other antipsychotics as it has no measurable dopaminergic activity.<sup>35</sup> Clozapine and quetiapine should also be considered in this patient population.<sup>27</sup>

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### CONCLUSION

Psychosis as a primary mental health disorder is a diagnosis of exclusion. Many different manifestations of psychotic symptoms are directly related to an underlying medical or neurologic disorder. Delirium and dementia are the two most important disorders to rule out and can present in a very subtle fashion. It is hoped that this article will help practitioners be more prepared to assess the patient with psychosis.

In a psychotic patient, it is important to establish a good therapeutic alliance. Psychosis can be a major barrier to treatment that is managed very well by a good therapeutic alliance with the patient. Once underlying medical or neurologic disorders have been ruled out and an appropriate primary psychotic disorder diagnosis is made, antipsychotic medication can be prescribed. Antipsychotic medication may also be used as an adjuvant to the treatment of a primary medical or neurologic disorder. With antipsychotic treatment, it is important to regularly assess vital signs, body weight and height, appropriate laboratory tests, and ECG and to screen for movement disorders such as extrapyramidal symptoms and tardive dyskinesia.

Social cognition is a major determiner to the outcome for patients with schizophrenia. Treatments such as psychoeducation, social skills training, and various forms of therapy can be very beneficial to the recovery of patients with psychosis.

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## USEFUL WEBSITES

### HOSPITAL ELDER LIFE PROGRAM (HELP) FOR PREVENTION OF DELIRIUM

The Hospital Elder Life Program website provides information about delirium for patients, caregivers, and clinicians.  
[hospitalelderlifeprogram.org](http://hospitalelderlifeprogram.org)

### MONTREAL COGNITIVE ASSESSMENT (MOCA)

The Montreal Cognitive Assessment website is a clinician-only website with free registration for access to use the MoCA tools.  
[mocatest.org](http://mocatest.org)

### PSYCHIATRIC TIMES—BPRS BRIEF PSYCHIATRIC RATING SCALE

The BPRS Brief Psychiatric Rating Scale page on the Psychiatric Times website provides a link to download the assessment.  
[psychiatrictimes.com/clinical-scales-schizophrenia/clinical-scales-schizophrenia/bprs-brief-psychiatric-rating-scale](http://psychiatrictimes.com/clinical-scales-schizophrenia/clinical-scales-schizophrenia/bprs-brief-psychiatric-rating-scale)

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