Psychosis in adults: Epidemiology, clinical manifestations, and diagnostic evaluation

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INTRODUCTION

Psychosis is a condition of the mind broadly defined as a loss of contact with reality. Psychotic symptoms can increase patients' risk for harming themselves or others or being unable to meet their basic needs.

Psychosis may be seen in many psychiatric disorders. It is commonly seen in schizophrenia and other conditions in the schizophrenia spectrum, and mood disorders including bipolar disorder and major depression with psychotic features. However, psychosis may also be a manifestation of substance use or underlying medical disease.

This topic will characterize different aspects of psychosis including epidemiology, pathogenesis, clinical manifestations, comorbid conditions, and initial diagnostic evaluation of psychosis in adults. Initial management of psychosis, maintenance treatment of psychosis and schizophrenia, management of side effects of antipsychotic medications, and management of mood disorders with psychosis are discussed elsewhere.

- (See "Schizophrenia in adults: Epidemiology and pathogenesis".)
- (See "Schizophrenia in adults: Clinical features, assessment, and diagnosis".)
- (See "Schizophrenia in adults: Maintenance therapy and side effect management".)
- (See "First-generation antipsychotic medications: Pharmacology, administration, and comparative side effects".)

- (See "Second-generation antipsychotic medications: Pharmacology, administration, and side effects".)
- (See "Schizophrenia in adults: Pharmacotherapy with long-acting injectable antipsychotic medication".)
- (See "Schizophrenia in adults: Psychosocial management".)
- (See "Co-occurring schizophrenia and substance use disorder: Psychosocial interventions".)
- (See "Evaluation and management of treatment-resistant schizophrenia".)
- (See "Brief psychotic disorder".)
- (See "Anxiety in schizophrenia".)
- (See "Depression in schizophrenia".)

EPIDEMIOLOGY

The incidence of psychosis worldwide has been estimated at approximately 50 in 100,000 people, while the incidence of schizophrenia (the most frequent eventual diagnosis among cases of first episode psychosis) is approximately 15 in 100,000 per year [1].

The 12-month prevalence rate for psychosis has been reported to be 4 per 1000 people, while the lifetime prevalence is reported to be 7.5 per 1000 people [2]. It is estimated that 13 to 23 percent of people experience psychotic symptoms at some point in their lifetime and 1 to 4 percent will meet criteria for a psychotic disorder [3,4].

The distribution by age of new cases of psychosis has not been well studied. Among all causes of psychosis, the distribution of the age of onset has not been well studied.

CAUSES OF PSYCHOSIS

Psychosis is a feature of many psychiatric disorders but may also be a manifestation of substance use or underlying medical disease.

Common or notable causes of psychosis include the following:

- **Primary psychotic disorders** – These include schizophrenia, schizoaffective disorder, schizophreniform disorder, brief psychotic disorder, and delusional disorders. (See 'Primary psychiatric causes and their differentiation' below.)

- **Psychosis due to another medical condition** – These include medical and neurologic disorders, infectious or inflammatory processes, endocrinologic, or other systemic illness. In some cases, psychotic symptoms are present with delirium.

  Examples of medical conditions that can present with psychosis include (see 'Medical and substance/medication-related causes' below):

  - Hepatic and renal disorders, such as hepatic or uremic encephalopathy.
  - Infectious disease, such as syphilis, herpes simplex encephalitis, or prion disease.
  - Inflammatory or demyelinating disorders, such as autoimmune encephalitis, systemic lupus encephalitis, or multiple sclerosis.
  - Neurodegenerative and neurologic disorders, such as dementia with Lewy bodies, Huntington disease, or Alzheimer disease.
  - Metabolic disorders, such as acute intermittent porphyria or Wilson disease.

- **Substance or medication induced psychotic disorders** – Many prescription medications, as well as illicit substances, can induce transient psychotic symptoms. Substances that can cause psychosis are included on the table (table 1). (See 'Medical and substance/medication-related causes' below.)

Evaluation for the cause of psychosis is discussed elsewhere. (See 'Determining the etiology' below.)

CLINICAL MANIFESTATIONS

Psychosis refers to thinking that has lost touch with reality. Typical manifestations of psychosis include delusions, hallucinations, and disordered thinking [5]. In primary psychotic disorders, the first episode of psychosis is typically preceded by premorbid signs and symptoms and a prodromal period.

Defining features

Delusions — Delusions are defined as strongly held false beliefs that are not typical of the patient's cultural or religious background. Delusions can be categorized based on plausibility as bizarre (family members have been replaced by body-doubles) or nonbizarre (spouse is having an affair). Frequently encountered types of delusions include:

- Persecutory delusions or paranoid delusions (eg, believing one is being followed and harassed by gangs)
- Grandiose delusions (eg, believing one is a billionaire CEO who owns casinos around the world)
- Erotomanic delusions (eg, believing a famous movie star is in love with them)
- Somatic delusions (eg, believing one's sinuses have been infested by worms)
- Delusions of reference (eg, believing dialogue on a television program is directed specifically towards the patient)
- Delusions of control (eg, believing one's thoughts or actions are being controlled by other persons or objects)

Hallucinations — Hallucinations can be defined as wakeful sensory experiences of content that is not actually present. They are differentiated from illusions, which are distortions or misinterpretations of real sensory stimuli. Hallucinations can occur in any of the five sensory modalities. Auditory hallucinations (eg, hearing voices) are the most common, followed by visual, tactile, olfactory, and gustatory hallucinations. Auditory hallucinations can present as speech (including spoken commands or a running commentary on the patient's actions) or other sounds. Visual hallucinations can range from recognizable objects to more unformed lights or shadows. Olfactory hallucinations are frequently of unpleasant odors.

Thought disorganization — Commonly observed forms of thought disorganization include:

- Alogia/poverty of content – Very little information conveyed by speech.
- Thought blocking – Suddenly losing train of thought, exhibited by abrupt interruption in speech.
- Loosening of association – Speech content notable for ideas presented in sequence that are not closely related.
- Tangentiality – Answers to interview questions diverging increasingly from topic being asked about (called circumstantiality if content eventually returns to original topic).
- Clanging or clang association – Using words in a sentence that are linked by rhyming or phonetic similarity (eg, "I fell down the well sell bell.")
- Word salad – Real words are linked together incoherently, yielding nonsensical content.

- Perseveration – Repeating words or ideas persistently, often even after interview topic has changed.

Evidence for thought disorganization is derived from the patients' pattern of speech during the interview. While disorganized speech is a frequently observed symptom in psychosis, it is nonspecific and can also be present in delirium or other neurologic or cognitive disorders.

Associated clinical manifestations

Premorbid and prodromal periods in primary psychotic disorders

- **Premorbid features** – Individuals who develop psychosis may experience premorbid signs and symptoms including mood changes, neurocognitive impairments, functional decline, and social isolation. Minor physical anomalies suggestive of neurodevelopment abnormalities are also commonly noted prior to the onset of psychotic illness and include facial dysmorphia, such as a wide skull base or abnormal size of facial features [6-8].

- **Prodromal symptoms** – The prodromal period may last from a few weeks to a few years and is characterized by subsyndromal psychosis, negative symptoms, and a deterioration in functioning. The prodromal syndrome is usually diagnosed retrospectively. Prospectively, consistent symptoms represent a high, but not inevitable, risk for developing psychosis. Other terms used to describe the prodromal syndrome are attenuated psychosis syndrome and clinical high risk for psychosis.

  The presence of prodromal symptoms cannot predict a specific psychiatric disorder, although data on the eventual diagnosis among patients with prodromal symptoms are limited. In a sample of 89 clinical high-risk subjects from the North American Prodrome Longitudinal Study consortium, 56 percent were eventually diagnosed with schizophrenia spectrum psychosis, 10 percent with affective psychosis, and 34 percent with other psychosis, principally psychosis not otherwise specified [9].

Agitation/aggression — Agitation is a state of acute anxiety and heightened emotional arousal with increased motor activity. Although not specific to psychosis, untreated psychosis is associated with an increased risk for agitation and aggressive behaviors. These can sometimes lead to intentional or unintentional bodily harm to self or others. (See "Assessment and emergency management of the acutely agitated or violent adult" and "Psychosis in adults: Initial management", section on 'Psychiatric symptoms' and "Psychosis in adults: Initial management", section on 'Additional patient-specific considerations'.)

Catatonia — Catatonia is a syndrome manifested by inability to move normally. It can present as either extreme negativism (eg, passive resistance to movement), mutism, or catatonic excitement (eg, excessive, purposeless motor activity). The presence of catatonia should alert the clinician to the possibility of an underlying medical disorder and should be thoroughly investigated. Treatment of catatonia is reviewed in more detail elsewhere. (See "Catatonia: Treatment and prognosis" and "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis".)

Negative symptoms — Negative symptoms, also called deficit symptoms, include decreased expressiveness, apathy, flat affect, anergia. These symptoms may be secondary to other manifestations of the illness (ie, depression) or due to treatment of psychosis (extrapyramidal symptoms).

Neurocognitive deficits — Neurocognitive impairment may be prominent prior to the onset of psychotic illness and when present in the prodromal state are predictive of a later development of psychotic illness [10-12]. Neurocognitive dysfunction is commonly noted in domains of memory, attention, processing speed, and executive functioning. (See "The mental status examination in adults", section on 'Mental status examination' and "The mental status examination in adults", section on 'Executive functioning'.)

Functional impairment — Functional impairment is linked to neurocognitive impairment and is often present before the onset of psychosis. Functional impairment in the prodrome is a predictor of later developmental of a full psychotic episode. Early psychosis treatment programs use recovery-based services to target the significant functional impairment that occurs early in the course of the illness.

COMORBID DISORDERS

Psychotic illness is associated with several comorbid diagnoses that may be present at all stages of the psychotic illness.

Substance use disorders — Patients with psychosis and underlying psychotic disorders overall have higher rates of co-occurring substance use disorders (SUDs) compared with the general population.

In one study of 404 patients with first episode psychosis at 34 community mental health centers across the United States, 52 percent of patients met criteria for any lifetime or drug use disorder [13]. Additionally, the study reported the following rates of other SUDs in first episode psychosis:

- Cannabis use disorder – 35 percent (versus 11 percent in general population)
- Stimulant use disorder – 5 percent (versus 2 percent in general population)
- Opioid use disorders – 5 percent (versus 3 percent in general population)

In contrast, the rate of lifetime alcohol use disorder in first episode psychosis was found to be similar to that in the young adult general population (35 versus 37 percent) [14].

Studies have found associations between substance use, generally cannabis use, and increased risk of developing psychotic symptoms [15]. Some experts believe that early cannabis use is a causal factor in developing schizophrenia. In a sample of 291 individuals meeting the criteria for attenuated psychotic syndrome, a history of any SUD was one of five predictors of conversion to psychosis [16]. (See "Cannabis use and disorder: Epidemiology, pharmacology, comorbidities, and adverse effects", section on 'Psychiatric effects'.)

Mood disorders and suicidal ideation — Depressive symptoms including dysphoria, anhedonia, amotivation, and sleep disturbance are common during the prodromal phase and first episode of psychosis. Additionally, the risk of suicide is high early in the course of psychosis and at the onset of schizophrenia [17].

The presence of depression during the prodromal phase is a significant predictor of future depression and is associated with acts of self-harm and a less favorable outcome [18]. In one study, it was reported to occur in 80 percent of patients at one or more phases of the first episode of psychosis. The combination of depression and suicidal thinking was present in 63 percent [19].

Factors associated with increased suicidal behavior are previous suicide attempt, history of sexual abuse, substance use (eg, cannabis use), lower baseline functioning, greater psychotic symptoms, and family history of severe mental disorder [20]. (See "Schizophrenia in adults: Clinical features, assessment, and diagnosis", section on 'Suicide'.)

Anxiety disorders — Anxiety disorders are prevalent in the premorbid and prodromal phases of psychosis as well as during the first episode of psychosis. In a large sample of 500 patients with a first episode of psychosis, 17 percent of their sample met criteria for an anxiety disorder [21]. In a sample of 744 prodromal phase patients, the prevalence of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) anxiety disorders was 47 percent, with an additional 9 percent meeting criteria for obsessive-compulsive disorder or posttraumatic stress disorder [22].

Attention deficit hyperactivity disorder — Across multiple studies, a premorbid history of attention deficit hyperactivity disorder (ADHD) is present in approximately 17 to 50 percent of

patients presenting with a first episode of psychosis [23-25]. For example, in a prospective study involving 744 patients who were at clinically high risk for psychosis (eg, presence of subthreshold psychotic symptoms, brief intermittent psychosis, or genetic risk with decline in function) 18 percent of the subjects met criteria for ADHD versus 2 percent of the healthy control subjects [22].

Metabolic syndrome — Metabolic syndrome (MetS), including abdominal obesity, insulin resistance, and dyslipidemia, in patients with chronic psychotic illness has traditionally been attributable to antipsychotic medication and unhealthy lifestyles [26]. However, they have also been reported in the first psychotic episode of patients diagnosed with schizophrenia who had no prior exposure to antipsychotic medications [27-29]. In one meta-analysis, almost one in three patients with schizophrenia met criteria for an MetS [30]. Additionally, one in five patients with schizophrenia but unmedicated met criteria for MetS. This suggests that chronic psychotic disorders may be systemic diseases in which metabolic abnormalities are intertwined with psychopathologic features in a complex network that may even precede the onset of the illness. (See "Metabolic syndrome in patients with severe mental illness: Epidemiology, contributing factors, pathogenesis, and clinical implications".)

DIAGNOSTIC EVALUATION

Psychosis can be a manifestation of an underlying acute medical illness or chronic condition. We rule out medical causes and medication and substance-related causes before considering primary psychiatric causes of the psychosis.

Initial assessment — The goal of the initial assessment is to identify the cause of the psychosis and the effect of the psychosis on the patient's functioning. Additionally, assessment of safety risk and the level of care needed should be part of the initial assessment [31]. These are done primarily through the interview of the patient and other reliable sources such as family members or medical or mental health providers. Ruling out nonpsychiatric causes, in particular, often necessitates physical examination and laboratory screening.

Interview — The interview should be conducted in a private setting with minimal distraction. Disorganized thinking or other thought disorder (eg, paranoia) may prevent the patient from giving a coherent history. We suggest seeking corroborative sources of information whenever possible. Important components of the initial psychiatric interview for a patient presenting with psychosis include:

- History of present illness

- Rate of symptom onset (eg, acute or insidious onset)
- Timeline of symptoms (eg, how long have symptoms been present, are symptoms worsening or improving)
- Character of symptoms (eg, bizarre versus nonbizarre, are the symptoms culturally or religiously sanctioned)
- Response to symptoms (ie, is the patient acting on the delusion or hallucination)
- Stressors or precipitating symptoms
- Presence of mood symptoms
- Thoughts of or recent self-injurious behavior, self-harm, or harm to others

- Psychiatric history
  - Establish a timeline of past psychiatric symptoms and diagnosis
  - Past medication and psychotherapy trials
  - Prior emergency department visits and hospitalizations
  - Prior history of self-injurious behavior, self-harm, or harm to others
- Past medical history
  - Focus on history of neurologic disorders and neurocognitive disorders (eg, dementia, seizures or epilepsy, stroke, head injuries)
  - Review of current medications that may be exacerbating psychosis (table 1)
- Developmental history
- History of substance use
  - Current and past use or use disorder (eg, alcohol, cannabis, cocaine, opioids) (table 1)
  - Recent change in frequency or amount of substance use
- Family history of psychiatric illness
- Psychosocial history
  - Trauma exposure and history (eg, physical, sexual, or emotional)
  - Psychosocial stressors
  - Support system or other social network

Mental status examination — A complete mental status examination should be conducted (see "The mental status examination in adults"). For patients with psychosis we focus on the

following:

- General behavior and demeanor – Level of awareness of surroundings, cooperation with interviewer, eye contact
- Assessment of mood – Presence of depression or mania
- Affect – Intensity, appropriateness, lability and range of affect
- Thought process – Loosening of associations, flight of ideas, thought blocking
- Thought content – Paranoia, delusions, referential thinking (messages from television, radio, or others), internal preoccupations, thought control
- Perceptual disturbance – Hallucination (auditory, visual, tactile, olfactory, gustatory)
- Thoughts of self-harm or harm to others
- Cognitive screen – Attention, concentration, memory

Initial medical screening and laboratory testing — Medical comorbidities should be identified prior to starting antipsychotic therapy. This is done through general physical examination and laboratory screening.

For all patients with new onset of psychosis or in cases where antipsychotic medications are to be started or restarted, we suggest the following screening:

- Vital signs, height, weight, body mass index, general physical examination
- Chemistry panel – To evaluate for disturbances in fluid or electrolytes
- Complete blood count with differential
- Lipid panel
- Electrocardiogram – To evaluate for arrhythmia or QTc interval lengthening
- Urine pregnancy test in persons of childbearing potential

For cases where a medically related cause of psychosis is of further consideration, we recommend the following panel of tests. These tests can rule out some of the more common medical etiologies that can be associated with delirium and psychosis. These include hepatic encephalopathy, hyperthyroidism, and vitamin deficiency. These are discussed elsewhere. (See "Hepatic encephalopathy in adults: Clinical manifestations and diagnosis" and "Diagnosis of

hyperthyroidism" and "Neurosyphilis" and "Acute and early HIV infection: Clinical manifestations and diagnosis" and "Clinical manifestations and diagnosis of systemic lupus erythematosus in adults" and "Clinical manifestations and diagnosis of vitamin B12 and folate deficiency".)

- Hepatic function panel
- Thyroid-stimulating hormone level
- Serum treponemal test, such as fluorescent treponemal antibody absorption, to screen for syphilis
- Vitamin B12 level
- Erythrocyte sedimentation rate and antinuclear antibodies
- Urinalysis to evaluate for urinary tract infection or other abnormalities, with reflex culture
- Urine drug screen to evaluate for recent substance use
- HIV test

Determining the etiology

Factors differentiating medical versus psychiatric causes — Several features of the presentation may help to differentiate medical (or substance)-related causes from primary psychiatric causes of the psychosis. These include:

- Rate of onset – Acute onset is suggestive of an underlying medical or substance-related cause. Insidious onset is suggestive of underlying psychiatric illness (ie, prodromal syndrome).
- Age at onset – Onset at age 40 years or older is suggestive of a medical or substance-related cause. Primary psychiatric illnesses usually present at a younger age.
- Type of hallucinations – Nonauditory hallucinations (eg, olfactory, tactile, gustatory) is more suggestive of medical or substance-related cause. Auditory hallucinations are suggestive of primary psychiatric illness.
- Family history – A family psychiatric history is suggestive of an underlying psychiatric illness.
- Emergence of psychosis in general medical or intensive care unit setting – This is suggestive of an underlying medical or substance-related cause to the psychosis.

- Premorbid or prodromal symptoms – Presence of premorbid or prodromal symptoms are suggestive of a psychiatric cause to the psychosis. (See 'Premorbid and prodromal periods in primary psychotic disorders' above.)

Medical and substance/medication-related causes

Psychosis as a manifestation of delirium — In individuals with an acute or exacerbated chronic medical condition, psychosis is a common manifestation of delirium. Careful attention to the key features of acute onset, fluctuating course, altered consciousness, and cognitive decline can help distinguish delirium from primary psychiatric illness. When in doubt, the most useful rule-of-thumb is to assume delirium and attempt to rule out common medical etiologies. This is true even for patient with known psychiatric illness (including dementia), since they, too, are susceptive to delirium when acutely ill.

Frequent causes of delirium include fluid or electrolyte abnormalities, hypoglycemia, hypoxia, hypercapnia, infections, medication or substance-related, or withdrawal. Substances and medications with the capacity to induce psychosis are described in a table (table 1). Evaluation of psychosis as a manifestation of delirium and common causes of delirium are discussed further in this topic and elsewhere. (See "Diagnosis of delirium and confusional states" and 'Initial medical screening and laboratory testing' above and 'Evaluation for medical causes' below.)

Psychosis as a manifestation of delirium may improve after antipsychotic treatment; however, the underlying cause of the delirium needs to be identified and addressed [32,33].

Evaluation for medical causes — Psychosis can be associated with many underlying medical causes, including neurologic disorders, infectious or inflammatory processes, endocrinologic, hepatic, or other systemic illness. In some cases, these are revealed on initial screening; however, in other cases, imaging or further laboratory testing may be warranted based on the clinical presentation. As examples:

- In patients presenting with focal weakness or acute language dysfunction (ie, aphasia), a structural brain problem such as stroke, tumor, other mass, or active demyelination should be considered. In these cases, we obtain neuroimaging, such as magnetic resonance imaging (MRI) or computed tomography (CT). (See "Overview of the clinical features and diagnosis of brain tumors in adults" and "Evaluation and diagnosis of multiple sclerosis in adults".)

- In patients with a history of progressive cognitive decline (eg, short-term memory loss) or functional decline, or in patients with a progressive language deficit (eg, word finding

difficulty or aphasia), a neurodegenerative disorder should be considered. In these cases, we obtain neuroimaging (MRI or CT, if not already done) and neurocognitive testing. (See "Evaluation of cognitive impairment and dementia".)

- In patients presenting with a head injury, a seizure or movements consistent with a seizure, or in cases with acute, subacute, or unexplained change in level of arousal and awareness, a seizure or interictal phenomena should be considered. In these cases, we obtain an electroencephalogram (EEG) in addition to imaging studies. (See "Comorbidities and complications of epilepsy in adults", section on 'Psychotic disorders'.)

- In patients presenting with fever or rapidly progressive symptoms, a central nervous system inflammatory, paraneoplastic, or infectious process should be considered. In such patients, when clinically appropriate, lumbar puncture and cerebral spinal fluid analysis should be considered after imaging studies such as MRI or CT scan. Additionally, in these cases, further rheumatologic evaluation may be indicated depending on the clinical presentation. (See "Overview of paraneoplastic syndromes of the nervous system" and "Viral encephalitis in adults" and "Herpes simplex virus type 1 encephalitis".)

Testing for other, less common causes of psychosis should be considered in select cases. As examples:

- In patients presenting with neurologic symptoms, such as gait disturbance, dysarthria, and seizures, and liver disease, ceruloplasmin and copper studies should be obtained. (See "Wilson disease: Clinical manifestations, diagnosis, and natural history".)

- In patients presenting with neurovisceral symptoms (eg, abdominal pain, peripheral neuropathy, cognitive deficits), urine porphyrins should be obtained. (See "Porphyrias: An overview".)

- In patients with tremor, headache, gastrointestinal symptoms, and exposure to heavy metals, a heavy metal screen should be obtained. (See "Lead exposure, toxicity, and poisoning in adults".)

- In patients with a family history of prion disease (eg, fatal familial insomnia) or other clinical features suggestive of prion disease, we suggest appropriate evaluation (eg, lumbar puncture, EEG). (See "Diseases of the central nervous system caused by prions".)

Rule out substance-induced psychosis — Many prescription medications, as well as illicit substances, can induce transient psychotic symptoms [34,35]. The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)

defines "substance/medication-induced psychotic disorder" as having the presence of delusions and/or hallucinations during or soon after intoxication, withdrawal, or exposure to a substance, with the disturbance not being better explained by another type of psychotic disorder.

Many people with underlying psychotic disorders use substances or have substance use disorders. The distinction between a substance-induced psychosis and a person with a psychotic disorder whose symptoms are exacerbated by substances can generally be made over time. For example, a substance-induced psychosis will generally be limited to the time period during or soon after intoxication, withdrawal, or exposure to the substance, after which the person will return to their baseline. (See "Co-occurring schizophrenia and substance use disorder: Epidemiology, pathogenesis, clinical manifestations, course, assessment and diagnosis".)

A table lists major substances, medications, and toxins that can cause transient psychoses (table 1).

Primary psychiatric causes and their differentiation — Primary psychiatric causes of psychosis are typically considered once medical and substance-related causes have been ruled out. Often, longitudinal follow-up is needed to clarify the diagnosis.

In considering the specific psychiatric process causing psychosis, the quality of the psychotic symptoms (ie, bizarre, nonbizarre, circumscribed, pervasive), their course, and their timing are informative. Certain clinical features can be suggestive of but are not pathognomonic for a particular diagnosis. An initial step is to categorize the presentation by the presence or absence of mood symptoms and their temporal relationship to psychosis (algorithm 1).

In some cases, chronic mild perceptual distortions or eccentricities of behavior that may be perceived as psychosis may be part of an underlying and pervasive personality disorder (eg, schizotypal personality disorder). In these cases, presumptive diagnosis should be individualized, taking into account the potential benefits of treating the psychosis weighed against the morbidity and side effects associated with antipsychotic medication. The effects of the symptom on lifestyle and functioning and patient preference should be carefully considered in making this decision.

Occasionally, features consistent with psychosis may be culturally sanctioned or religious beliefs (eg, mind reading, evil eye, sixth sense, magical thinking). In such cases, individuals are unlikely to present or be brought to medical attention. There is also evidence that the diagnostic process can be influenced by racial bias. For example, clinicians are more likely to diagnosis Black patients with schizophrenia than White patients [36].

Psychotic symptoms predominate — When psychotic symptoms predominate (ie, when mood symptoms are absent, or, if present, temporally overlap with the psychosis for only a minority of the course of the illness), the length of time the psychotic symptoms have been present is the primary distinguishing feature (algorithm 1).

- In patients whose symptoms are present for at least one day but not longer than one month, the likely diagnosis is brief psychotic disorder. Brief psychotic disorder is characterized by the presence of psychotic symptoms (eg, delusions, hallucinations, disorganized speech, or grossly disorganized or catatonic behavior) with eventual return to premorbid functioning. These episodes are often associated with an intense stressor or traumatic event. (See "Brief psychotic disorder".)

- In patients in which symptoms are present for at least one month, the diagnosis may be delusional disorder, schizophreniform disorder, or schizophrenia (if symptoms are present for more than six months with functional decline).

  - In cases without disorganized speech or behavior, and in which hallucinations (if present) are not prominent, the likely diagnosis is delusional disorder. This disorder is characterized by the presence of one (or more) delusions that are present for one month or longer. Typically, the delusion is described as well circumscribed and there is a lack of marked impairment in functioning or obvious bizarre behaviors. (See "Delusional disorder" and "Delusional infestation: Epidemiology, clinical presentation, assessment and diagnosis" and "Treatment of delusional infestation".)

  - In cases with disorganized speech or behavior, prominent hallucinations or delusions, or in which the symptoms cause impaired social or occupational functioning, the likely diagnosis is schizophreniform disorder. This disorder can be considered to have similar symptomatic presentation as schizophrenia, except with an episode lasting greater than one month but less than six months. Functional decline does not need to be present. (See "Schizophrenia in adults: Clinical features, assessment, and diagnosis", section on 'Differential diagnosis'.)

  - In cases with a minimum of six months of symptoms including disorganized speech or behavior, prominent hallucinations or delusions, or in which the symptoms cause impaired social or occupational functioning, the likely diagnosis is schizophrenia. (See "Schizophrenia in adults: Clinical features, assessment, and diagnosis", section on 'Differential diagnosis'.)

Mood symptoms predominate — Mood disorders, particularly depression, are common in the first episode of psychosis. If clinically significant mood symptoms are present (depressive

or manic symptoms), or if the patient has never manifested symptoms of psychosis without the presence of mood symptoms, then major depressive disorder with psychotic features or bipolar disorder with psychotic features should be considered as possibilities (algorithm 1).

- In patients with predominant mood symptoms as described above, who have a history of mania, the likely diagnosis is bipolar disorder with psychotic features. (See "Bipolar disorder in adults: Clinical features", section on 'Psychosis'.)

- In patients with predominant mood symptoms as described above, who have no history of mania, the likely diagnosis is major depressive disorder with psychotic features. (See "Unipolar major depression with psychotic features: Epidemiology, clinical features, assessment, and diagnosis".)

Psychosis and mood symptoms are both prominent — If the individual has an overlap of mood symptoms with psychosis for the majority (but not all) of the psychotic illness, schizoaffective disorder is the likely diagnosis. According to the DSM-5, this disorder is defined by the individual having an uninterrupted period of illness during which there is a major mood episode which is concurrent with psychotic symptoms. Additionally, one must have "delusions or hallucinations for two or more weeks in the absence of major mood symptoms at some point during the lifetime of the illness." (See "Bipolar disorder in adults: Assessment and diagnosis", section on 'Schizoaffective disorder'.)

An algorithm describes the differential diagnosis of psychotic symptoms (algorithm 1).

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Psychotic disorders".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading

level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Schizophrenia (The Basics)" and "Patient education: Schizoaffective disorder (The Basics)" and "Patient education: Tardive dyskinesia (The Basics)" and "Patient education: Bipolar disorder (The Basics)")

- Beyond the Basics topic (see "Patient education: Bipolar disorder (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Psychosis** – Psychosis is a condition of the mind broadly defined as a loss of contact with reality. Delusions, hallucinations, and disordered thinking are the hallmark symptoms, and are present in variable degrees in patients with psychosis. (See 'Introduction' above and 'Causes of psychosis' above.)

- **Clinical manifestations** – Individuals with psychosis may display agitation, catatonia, negative symptoms, and neurocognitive deficits, all of which may contribute to the functional impairment associated with psychosis. (See 'Associated clinical manifestations' above.)

- **Comorbidity** – Psychotic illness is associated with several comorbid diagnoses that may be present at all stages of the psychotic illness. These include mood disorders, substance use disorders, anxiety disorders, attention deficit hyperactivity disorder, and metabolic syndrome. (See 'Comorbid disorders' above.)

- **Suicidal ideation** – The risk of suicide is high early in the course of psychosis and at the onset of schizophrenia. (See 'Mood disorders and suicidal ideation' above.)

- **Diagnostic evaluation** – Psychotic symptoms can be seen in many psychiatric and medical illnesses. Longitudinal follow-up is often needed to clarify to diagnosis. As part of our diagnostic evaluation of a patient with recent onset of psychosis, we include the following:

  - Interview of patient and family members to assess the quality and timeline of symptoms, co-occurring disorders that may be contributing to the psychosis, safety

risk, and level of care needed. (See 'Interview' above.)

- Review of past medical history, psychiatric history, developmental history, family history, and psychosocial history including history of substance use. (See 'Initial assessment' above.)
- Mental status examination including assessment of general behavior, mood, affect, thought process, thought content, hallucinations, thoughts of self-harm, and cognitive screen. (See 'Mental status examination' above.)
- We complete a physical examination and laboratory testing including complete blood count, lipid panel, chemistry panel, and electrocardiogram in order to screen for underlying medical causes of psychosis. We also perform a pregnancy test on all females of childbearing age. (See 'Initial medical screening and laboratory testing' above.)

- **Determining the etiology** – Clinical features of the presentation including rate of onset, age at onset, and type of hallucinations may help to differentiate medical (or substance) related causes from primary psychiatric causes of psychosis. (See 'Medical and substance/medication-related causes' above.)

In individuals with an acute or exacerbated chronic medical condition, psychosis is a common manifestation of delirium.

Additional laboratory testing, imaging studies, and cerebrospinal fluid analysis should be done in certain cases. These include (see 'Evaluation for medical causes' above):

- If a medically related or substance-induced cause is suspected – Hepatic function panel, thyroid-stimulating hormone, B12 level, erythrocyte sedimentation rate, antinuclear antibodies, HIV testing, urinalysis, and urine drug screen.
- Neuroimaging studies in cases with onset at older age, focal neurologic signs, rapidly progressive course, new or more frequent seizures.
- Cerebrospinal fluid studies and rheumatologic studies in cases of rapidly progressive illness.

- **Differentiating primary psychiatric cause** – The time, course, and quality of symptoms are the primary distinguishing features in determining the specific psychiatric diagnosis (algorithm 1). (See 'Determining the etiology' above.)

- If there is limited overlap of mood symptoms with psychosis (either no overlap or overlap only for a minority of the illness duration), then brief psychotic disorder, schizophreniform disorder, schizophrenia, and delusional disorder are possible diagnoses. (See 'Psychotic symptoms predominate' above.)

- If clinically significant mood symptoms are present (depressive or manic symptoms), then major depressive disorder with psychotic features, bipolar disorder with psychotic features, or schizoaffective disorder should be considered as possibilities. (See 'Mood symptoms predominate' above.)

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