



## English Teachers On Call **Schizophrenia**



<http://trialx.com/curetalk/2011/03/understanding-schizoaffective-disorder-vs-schizophrenia/>

**Schizophrenia** is characterized by **psychosis** (loss of contact with reality), **hallucinations** (false perceptions), **delusions** (false beliefs), disorganized speech and behavior, **flattened affect** (restricted range of emotions), **cognitive deficits** (impaired reasoning and problem solving), and occupational and social dysfunction. The cause is unknown, but evidence for a **genetic component** is strong. Symptoms usually begin in adolescence or early adulthood. One or more episodes of symptoms must last  $\geq 6$  mo before the diagnosis is made. Treatment consists of drug therapy, psychotherapy, and rehabilitation.

Worldwide, the **prevalence** of schizophrenia is about 1%. The rate is comparable among men and women and relatively constant **cross-culturally**. The rate is higher among lower socioeconomic classes in urban areas, perhaps because its disabling effects lead to unemployment and poverty. Similarly, a higher prevalence among single people may reflect the effect of illness or illness **precursors** on social functioning. The average age at onset is 18 yr in men and 25 yr in women. Onset is rare in childhood,

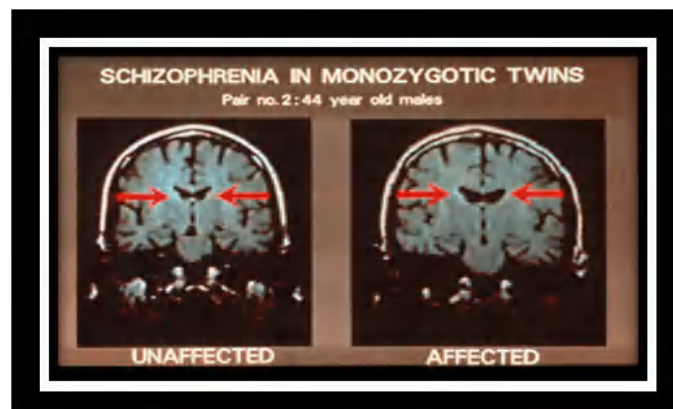
but early-adolescent onset or late-life onset (when it is sometimes called **paraphrenia**) may occur.

### Etiology

Although its specific cause is unknown, schizophrenia has a biologic basis, as evidenced by **alterations in brain** structure (eg, enlarged cerebral ventricles, decreased size of the **anterior hippocampus** and other brain regions) and by changes in neurotransmitters, especially altered activity of dopamine and glutamate. Some experts suggest that schizophrenia occurs in people with **neurodevelopmental vulnerabilities** and that the onset, remission, and recurrence of symptoms are the result of interactions between these enduring vulnerabilities and environmental **stressors**.

**Neurodevelopmental vulnerability:** Vulnerability may result from **genetic predisposition**; **intrauterine**, birth, or **postnatal complications**; or viral CNS infections. Maternal exposure to famine and influenza during the 2nd trimester of pregnancy, birth weight < 2500 g, Rh incompatibility during a 2nd pregnancy, and **hypoxia** increase risk.

Although most people with schizophrenia do not have a family history, genetic factors have been implicated. People who have a 1st-degree relative with schizophrenia have about a 10% risk of developing the disorder, compared with a 1% risk among the general population. **Monozygotic twins** have a **concordance** of about 50%. Sensitive neurologic and neuropsychiatric tests suggest that **aberrant** smooth-pursuit eye tracking, impaired cognition and attention, and deficient **sensory gating** occur more commonly among patients with schizophrenia than among the general population. These markers (**endophenotypes**) also occur among 1st-degree relatives of people with schizophrenia and may represent the inherited component of vulnerability.



<http://www.drjack.co.uk/wp-content/uploads/2011/03/schizotwinbrains21.gif>

**Environmental stressors:** Stressors can trigger the emergence or recurrence of symptoms in vulnerable people. Stressors may be primarily biochemical (eg, substance abuse, especially marijuana) or social (eg, becoming unemployed or **impoverished**, leaving home for college, breaking off a romantic relationship, joining the Armed Forces); however, these stressors are not causative. There is no evidence that schizophrenia is caused by poor parenting.

Protective factors that may **mitigate** the effect of stress on symptom formation or **exacerbation** include good social support, coping skills, and antipsychotics.

### Symptoms and Signs

Schizophrenia is a chronic illness that may progress through several phases, although duration and patterns of phases can vary. Patients with schizophrenia tend to develop psychotic symptoms an average of 12 to 24 mo before presenting for medical care.



<http://www.drjack.co.uk/the-future-of-schizophrenia-by-dr-jack-lewis/>

**Phases:** In the premorbid phase, patients may show no symptoms or may have impaired social competence, mild cognitive disorganization or **perceptual distortion**, a diminished capacity to experience pleasure (**anhedonia**), and other general coping deficiencies. Such traits may be mild and recognized only in **retrospect** or may be more noticeable, with impairment of social, academic, and vocational functioning.

In the **prodromal phase**, subclinical symptoms may emerge; they include withdrawal or isolation, irritability, suspiciousness, unusual thoughts, perceptual distortions, and disorganization. Onset of overt schizophrenia (delusions and hallucinations) may be sudden (over days or weeks) or slow and **insidious** (over years).

In the middle phase, symptomatic periods may be **episodic** (with identifiable exacerbations and **remissions**) or continuous; functional deficits tend to worsen.

In the late illness phase, the illness pattern may be established, and disability may stabilize or even diminish.

**Symptom categories:** Generally, symptoms are categorized as

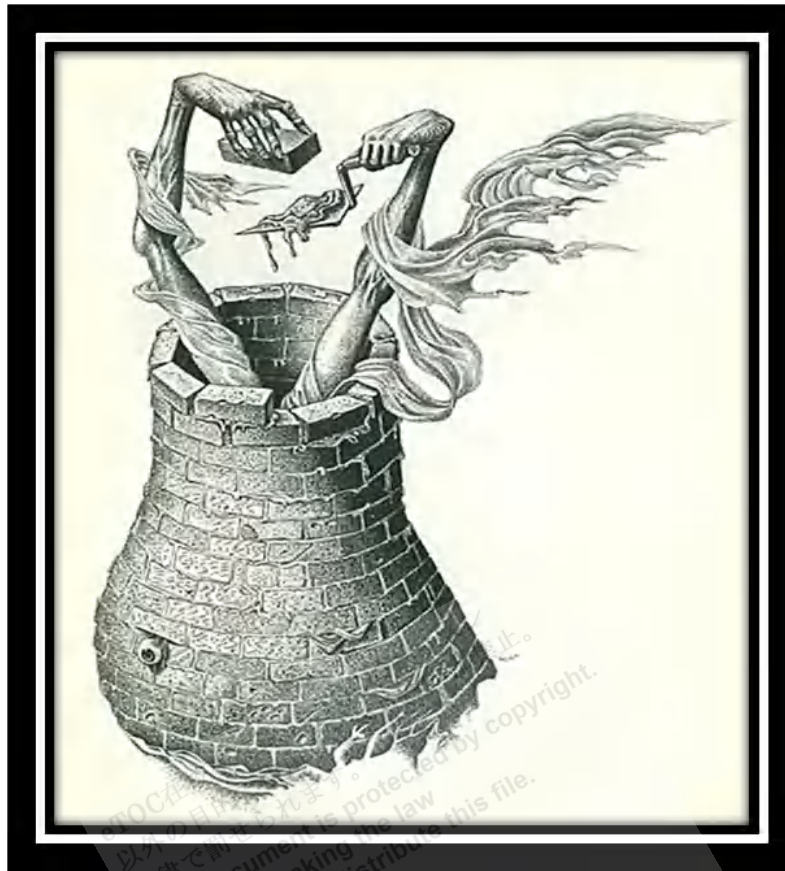
- Positive: An excess or distortion of normal functions
- Negative: **Diminution** or loss of normal functions
- Disorganized: Thought disorders and bizarre behavior
- Cognitive: Deficits in information processing and problem solving

Patients may have symptoms from one or all categories.

**Positive symptoms** can be further categorized as delusions and hallucinations.

Delusions are **erroneous beliefs**. In persecutory delusions, patients believe they are being **tormented**, followed, tricked, or spied on. In delusions of reference, patients believe that passages from books, newspapers, song lyrics, or other environmental cues are directed at them. In delusions of thought withdrawal or thought insertion, patients believe that others can read their mind, that their thoughts are being transmitted to others, or that thoughts and impulses are being imposed on them by outside forces. Hallucinations may be auditory, visual, olfactory, gustatory, or **tactile**, but auditory hallucinations are by far the most common. Patients may hear voices commenting on their behavior, conversing with one another, or making critical and abusive comments. Delusions and hallucinations may be extremely **vexing** to patients.

**Negative (deficit) symptoms** include **blunted affect**, poverty of speech, anhedonia, and **asociality**. With blunted affect, the patient's face appears immobile, with poor eye contact and lack of expressiveness. Poverty of speech refers to decreased speech and **terse** replies to questions, creating the impression of inner emptiness. Anhedonia may be reflected by a lack of interest in activities and increased purposeless activity. Asociality is shown by a lack of interest in relationships. Negative symptoms often lead to poor motivation and a diminished sense of purpose and goals.



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**Disorganized symptoms**, which can be considered a type of positive symptom, involve thought disorders and bizarre behaviors. Thinking is disorganized, with **rambling**, non-goal-directed speech that shifts from one topic to another. Speech can range from mildly disorganized to incoherent and **incomprehensible**. Bizarre behavior may include **childlike silliness**, agitation, and inappropriate appearance, hygiene, or conduct. **Catatonia** is an extreme behavior that can include maintaining a **rigid** posture and resisting efforts to be moved or engaging in purposeless and unstimulated motor activity.

**Cognitive deficits** include impairment in attention, processing speed, working memory, abstract thinking, problem solving, and understanding of social interactions. The patient's thinking may be inflexible, and the ability to problem solve, understand the viewpoints of other people, and learn from experience may be diminished. Symptoms of schizophrenia typically impair the ability to function and often markedly interfere with work, social relations, and self-care. Unemployment, isolation, deteriorated relationships, and diminished quality of life are common outcomes. Severity of cognitive impairment is a major determinant of overall disability.

**Subtypes:** Five subtypes of schizophrenia have been described:

- Paranoid: Characterized by delusions or auditory hallucinations, with preservation of cognition and affect
- Disorganized: Characterized by disorganized speech, disorganized behavior, and flat or inappropriate affect
- Catatonic: Characterized by physical symptoms, including either **immobility** or excessive motor activity and the assumption of bizarre postures
- Residual: A clear history of schizophrenia with more prominent symptoms, followed by a prolonged period of mild negative symptoms
- Undifferentiated: A mixture of symptoms from the other subtypes

Alternatively, some experts classify schizophrenia into deficit and non-deficit subtypes based on the presence and severity of negative symptoms, such as blunted affect, lack of motivation, and diminished sense of purpose. Patients with the deficit subtype have prominent negative symptoms unaccounted for by other factors (eg, depression, anxiety, an understimulating environment, drug adverse effects). Those with the nondeficit subtype may have delusions, hallucinations, and thought disorders but are relatively free of negative symptoms.

**Suicide:** About 10% of patients with schizophrenia commit suicide. Suicide is the major cause of **premature death** among people with schizophrenia and explains, in part, why on average the disorder reduces life span by 10 yr. Patients who have paranoid subtypes with late onset and good premorbid functioning—the very patients with the best prognosis for recovery—are also at the greatest risk of suicide. Because these patients retain the capacity for **grief** and **anguish**, they may be more prone to act in despair based on a realistic recognition of the effect of their disorder.

**Violence:** Schizophrenia is a relatively modest risk factor for violent behavior. Threats of violence and minor aggressive outbursts are far more common than seriously dangerous behavior. Patients more likely to engage in significant violence include those with substance abuse, persecutory delusions, or command hallucinations and those who do not take their prescribed drugs. A very few severely depressed, isolated, paranoid patients attack or murder someone whom they perceive as the single source of their difficulties (eg, an authority, a celebrity, their spouse).

### Diagnosis

- Combination of history, symptoms, and signs

No definitive test for schizophrenia exists. Diagnosis is based on a comprehensive assessment of history, symptoms, and signs. Information from **collateral sources**, such

as family members, friends, teachers, and coworkers, is often important. According to the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition Text Revision (DSM-IV-TR), the diagnosis requires both of the following:

- $\geq 2$  characteristic symptoms (delusions, hallucinations, disorganized speech, disorganized behavior, negative symptoms) for a significant portion of a 1-mo period
- **Prodromal** or **attenuated signs** of illness with social, occupational, or self-care impairments evident for a 6-mo period that includes 1 mo of active symptoms

Psychosis due to other medical disorders or substance abuse must be ruled out by history and examination that includes laboratory tests and neuroimaging. Although some patients with schizophrenia have structural brain abnormalities present on imaging, these abnormalities are insufficiently specific to have diagnostic value.

Other mental disorders with similar symptoms include several that are related to schizophrenia: brief psychotic disorder, schizophreniform disorder, schizoaffective disorder, and delusional disorder. In addition, mood disorders can cause psychosis in some people. Certain personality disorders (especially schizotypal) cause symptoms similar to those of schizophrenia, although they are usually milder and do not involve psychosis.

### Prognosis

During the first 5 yr after onset of symptoms, functioning may deteriorate and social and work skills may decline, with progressive neglect of self-care. Negative symptoms may increase in severity, and cognitive functioning may decline. Thereafter, the level of disability tends to **plateau**. Some evidence suggests that severity of illness may lessen in later life, particularly among women. Spontaneous movement disorders may develop in patients who have severe negative symptoms and cognitive dysfunction, even when antipsychotics are not used.

Prognosis varies depending on the subtype. Patients with paranoid schizophrenia tend to be less severely disabled and more responsive to available treatments. Patients with the deficit subtype are typically more disabled, have a poorer prognosis, and are more resistant to treatment.

Schizophrenia can occur with other mental disorders. When associated with significant obsessive-compulsive symptoms, prognosis is particularly poor; with symptoms of borderline personality disorder, prognosis is better. About 80% of people with

schizophrenia experience one or more episodes of major depression at some time in their life.

For the first year after diagnosis, prognosis is closely related to adherence to prescribed psychoactive drugs. Overall, one third of patients achieve significant and lasting improvement; one third improve somewhat but have **intermittent relapses** and **residual disability**; and one third are severely and permanently incapacitated. Only about 15% of all patients fully return to their pre-illness level of functioning.

Factors associated with a good prognosis include

- Good premorbid functioning (eg, good student, strong work history)
- Late and/or sudden onset of illness
- Family history of mood disorders other than schizophrenia
- Minimal cognitive impairment
- Few negative symptoms
- Paranoid or non-deficit subtype

Factors associated with a poor prognosis include

- Young age at onset
- Poor premorbid functioning
- Family history of schizophrenia
- Disorganized or deficit subtype with many negative symptoms

Men have poorer outcomes than women; women respond better to treatment with antipsychotics.

Substance abuse is a significant problem in up to 50% of patients with schizophrenia. **Anecdotal evidence** suggests that use of marijuana and other hallucinogens is highly disruptive for patients with schizophrenia and should be strongly discouraged. Comorbid substance abuse is a significant predictor of poor outcome and may lead to drug nonadherence, repeated relapse, frequent rehospitalization, declining function, and loss of social support, including homelessness.

### Treatment

- Antipsychotic drugs
- Rehabilitation, including community support services
- Psychotherapy



The time between onset of psychotic symptoms and first treatment **correlates** with the rapidity of initial treatment response, quality of treatment response, and severity of negative symptoms. When treated early, patients tend to respond more quickly and fully. Without ongoing use of antipsychotics after an initial episode, 70 to 80% of patients have a subsequent episode within 12 mo. Continuous use of antipsychotics can reduce the 1-yr relapse rate to about 30%.

General goals are to reduce severity of psychotic symptoms, prevent recurrences of symptomatic episodes and associated deterioration of functioning, and help patients function at the highest level possible. Antipsychotics, rehabilitation with community support services, and psychotherapy are the major components of treatment. Because schizophrenia is a long-term and recurrent illness, teaching patients illness self-management skills is a significant overall goal.

Drugs are divided into conventional antipsychotics and 2nd-generation antipsychotics (SGAs) based on their specific neurotransmitter receptor **affinity** and activity. SGAs may offer some advantages both in terms of modestly greater efficacy (although recent evidence casts doubt on SGAs' advantage as a class) and reduced likelihood of an involuntary movement disorder and related adverse effects. However, risk of metabolic syndrome (excess abdominal fat, insulin resistance, dyslipidemia, and hypertension) is greater with SGAs than with conventional antipsychotics.

**Conventional antipsychotics:** These drugs (see Table 1: [Schizophrenia and Related Disorders: Conventional Antipsychotics](#)) act primarily by blocking the dopamine-2 receptor (dopamine-2 blockers). Conventional antipsychotics can be classified as high, intermediate, or low potency. High-potency antipsychotics have a higher affinity for dopamine receptors and less for  $\alpha$ -adrenergic and muscarinic receptors. Low-potency antipsychotics, which are rarely used, have less affinity for dopamine receptors and relatively more affinity for  $\alpha$ -adrenergic, muscarinic, and histaminic receptors. Different drugs are available in tablet, liquid, and short- and long-acting IM preparations. A specific drug is selected primarily based on adverse effect profile, required route of administration, and the patient's previous response to the drug.

Table 1

| Conventional Antipsychotics |                     |                  |          |
|-----------------------------|---------------------|------------------|----------|
| Drug                        | Daily Dose (Range)* | Usual Adult Dose | Comments |
|                             |                     |                  |          |

**Phenothiazines, aliphatic**

Chlorpromazine 30–800 mg 400 mg po at bedtime Prototypic low-potency drug  
Also available as a rectal suppository

t.‡

**Phenothiazines, piperidine**

Thioridazine 150–800 mg 400 mg po at bedtime Only drug with an absolute maximum (800 mg/day) because it causes pigmentary retinopathy at higher doses and has a significant anticholinergic effect  
Warning about QTc prolongation added to label

**Phenothiazines, piperazines**

Trifluoperazine 2–40 mg 10 mg po at bedtime

t.‡

Fluphenazine 0.5–40 mg 7.5 mg po at bedtime Also available as fluphenazine

t.‡

decanoate and fluphenazine enanthate, which are IM depot forms (dose equivalents are not available)

Perphenazine 12–64 mg 16 mg po at bedtime

t.‡

**Dibenzoxazepine**

Loxapine 20–250 mg 60 mg po at bedtime Has affinity for dopamine  
-2 and 5-hydroxytryptamine (serotonin)-2 receptors

**Dihydroindolone**

Molindone 15–225 mg 60 mg po at bedtime Possibly associated with weight reduction

**Thioxanthene**

Thiothixene 8–60 mg 10 mg po at bedtime Has high incidence of akathisia

t.‡

**Butyrophenone**

Haloperidol 1–15 mg 4 mg po at bedtime Prototypic high-potency drug  
Haloperidol

†,‡

decanoate available as an IM depot  
Akathisia common

**Diphenylbutylpiperidine**

Pimozide 1–10 mg 3 mg po at bedtime Approved only for Tourette's syndrome

\*Current recommended dosing for conventional antipsychotics is to initiate at low range of displayed values and titrate upwards gradually to a single dose; dosing at bedtime is recommended. No evidence that rapid dose escalation is more effective.

†These drugs are available in an IM form for acute treatment.

‡These drugs are available as an oral concentrate.

QTc = QT interval corrected for heart rate.

Two conventional antipsychotics (and one SGA) are available as long-acting depot preparations (see Table 2: [Schizophrenia and Related Disorders: Depot Antipsychotic Drugs](#)). These preparations are useful for eliminating drug nonadherence. They may also help patients who, because of disorganization, indifference, or denial of illness, cannot reliably take daily oral drugs.

**Table 2**

**Depot Antipsychotic Drugs**

| Drug*                        | Dosage   | Peak Level† |
|------------------------------|--|-------------|
| Fluphenazine<br>decanoate    | 12.5–50 mg q 2–4 wk                              | 1 day       |
| Fluphenazine<br>enanthate    | 12.5–50 mg q 1–2 wk                              | 2 days      |
| Haloperidol<br>decanoate     | 25–150 mg q 28 days (3–5 wk range is acceptable) | 7 days      |
| Risperidone<br>microspheres‡ | 12.5–50 mg q 2 wk                                | 35 days     |

\*Drugs are given IM with Z-track technique.

<sup>†</sup>Time until peak level after a single dose is listed.

<sup>‡</sup>Because of 3-wk lag time between first injection and achievement of adequate blood levels, patients should continue taking oral antipsychotics for 3 wk after the first injection. Assessment of **tolerability** with oral risperidone is recommended before initiating therapy.

Conventional antipsychotics have several adverse effects, such as sedation, cognitive blunting, dystonia and muscle stiffness, tremors, elevated prolactin levels, and weight. **Akathisia** (motor restlessness) is particularly unpleasant and may lead to nonadherence. These drugs may also cause tardive **dyskinesia**, an involuntary movement disorder most often characterized by puckering of the lips and tongue, writhing of the arms or legs, or both. The incidence of tardive dyskinesia is about 5%/yr of drug exposure among patients taking conventional antipsychotics. In about 2%, **tardive dyskinesia** is severely **disfiguring**. In some patients, tardive dyskinesia persists indefinitely, even after the drug is stopped. Because of this risk, patients receiving long-term maintenance therapy should be evaluated at least every 6 mo. Rating instruments, such as the Abnormal Involuntary Movement Scale, may be used (see Table 3: [Schizophrenia and Related Disorders: Abnormal Involuntary Movement Scale](#)). **Neuroleptic malignant syndrome**, a rare but potentially fatal adverse effect, is characterized by rigidity, fever, autonomic instability, and elevated CK.

Table 3

#### Abnormal Involuntary Movement Scale

1. Observe patient's gait on the way into the room.
2. Have patient remove gum or dentures if ill-fitting.
3. Determine whether patient is aware of any movements.
4. Have patient sit on a firm, armless chair with hands on knees, legs slightly apart, and feet flat on the floor. Now and throughout the examination, look at the entire body for movements.
5. Have patient sit with hands unsupported, dangling over the knees.
6. Ask patient to open mouth twice. Look for tongue movements.
7. Ask patient to stick out the tongue twice.
8. Ask patient to tap thumb against each finger for 15 sec with each hand. Observe face and legs.
9. Have patient stand with arms extended forward.

Rate each item on a 0 to 4 scale for the greatest severity observed:

0 = none

1 = minimal, may be extreme normal

2 = mild

3 = moderate

4 = severe

Movements that occur only on activation are given 1 point less than those that occur spontaneously.

|                           |   |           |
|---------------------------|---|-----------|
| Facial and oral movements | Muscles of facial expression  | 0 1 2 3 4 |
|                           | Lips and perioral area  | 0 1 2 3 4 |
|                           | Jaw   | 0 1 2 3 4 |
|                           | Tongue  | 0 1 2 3 4 |
| Extremity movements       | Arms  | 0 1 2 3 4 |
|                           | Legs  | 0 1 2 3 4 |
| Trunk movements           | Neck, shoulders, and hips   | 0 1 2 3 4 |
| Global judgments          | Severity of abnormal movements  | 0 1 2 3 4 |
|                           | Incapacitation due to abnormal movements  | 0 1 2 3 4 |
|                           | Patient's awareness of abnormal movements<br>(0 = unaware; 4 = severe distress) | 0 1 2 3 4 |

Adapted from Guy W: *ECDEU [Early Clinical Drug Evaluation Unit] Assessment Manual for Psychopharmacology*. Rockville (MD), National Institute of Health, Psychopharmacology Research Branch, 1976. Copyright 1976 by US Department of Health, Education and Welfare.

About 30% of patients with schizophrenia do not respond to conventional antipsychotics. They may respond to clozapine, an SGA.

**Second-generation antipsychotics:** SGAs block dopamine receptors more selectively than conventional antipsychotics, decreasing the likelihood of **extrapyramidal (motor) adverse effects**. Although greater binding to serotonergic receptors was initially thought to contribute to the efficacy of SGAs, recent studies suggest this binding is unrelated to efficacy or adverse effect profile. SGAs also do the following:

- Tend to alleviate positive symptoms
- May lessen negative symptoms to a greater extent than do conventional antipsychotics (although such differences have been questioned)
- May cause less cognitive blunting
- Are less likely to have extrapyramidal (motor) adverse effects
- Have a lower risk of causing tardive dyskinesia
- Increase prolactin slightly or not at all (except risperidone, which increases prolactin as much as do conventional antipsychotics)

Clozapine, the first SGA, is the only SGA shown to be effective in up to 50% of patients resistant to conventional antipsychotics. Clozapine reduces negative symptoms, has

few or no motor adverse effects, and has minimal risk of causing tardive dyskinesia, but it has other adverse effects, including sedation, hypotension, tachycardia, weight gain, type 2 diabetes, and **increased salivation**. It also may cause **seizures** in a dose-dependent fashion. The most serious adverse effect is **agranulocytosis**, which can occur in about 1% of patients. Consequently, frequent monitoring of WBCs is required, and clozapine is generally reserved for patients who have responded inadequately to other drugs.

Newer SGAs (see Table 4: [Schizophrenia and Related Disorders: Second-Generation Antipsychotics\\*](#)) provide some of the benefits of clozapine without the risk of agranulocytosis and are generally preferable to conventional antipsychotics for treatment of an acute episode and for prevention of recurrence. However, in a recent, large, long-term, controlled clinical trial, symptom relief using any of 4 SGAs (olanzapine, risperidone, quetiapine, ziprasidone) was no greater than that with perphenazine, a conventional antipsychotic. A follow-up study, in which patients who left the study prematurely were randomized to one of the 3 other study SGAs or to clozapine, demonstrated a clear advantage of clozapine over the other SGAs. Hence, clozapine seems to be the only effective treatment for patients who have failed treatment with a conventional antipsychotic or an SGA. However, clozapine remains underused, probably because of lower tolerability and need for continuous blood monitoring.

Table 4

**Second-Generation Antipsychotics\***

| Drug                    | Dose Range            | Usual Adult Dose     | Comment <sup>†</sup>   |
|-------------------------|-----------------------|----------------------|--|
| <b>Dibenzodiazepine</b> |                       |                      |  |
| Clozapine               | 150–450 mg po bid     | 400 mg po at bedtime | First SGA<br>Only one with demonstrated efficacy in patients unresponsive to other antipsychotics<br>Frequent WBC counts required because agranulocytosis is a risk<br>Increased risk of seizures and metabolic syndrome |
| <b>Benzisoxazoles</b>   |                       |                      |  |
| Risperidone             | 4–10 mg po at bedtime | 4 mg po at bedtime   | May cause extrapyramidal symptoms at doses > 6 mg, dose-dependent prolactin elevation, or metabolic syndrome<br>Only SGA with a long-acting injectable form  |

|                                   |                        |                     |  |
|-----------------------------------|------------------------|---------------------|--|
| Paliperidone                      | 3–12 mg po at bedtime  | 6 mg po at bedtime  | Metabolite of risperidone<br><br>Similar to risperidone  |
| <b>Thienobenzodiazepine</b>       |                        |                     |  |
| Olanzapine                        | 10–20 mg po at bedtime | 15 mg po at bedtime | Most common adverse effects: Somnolence, metabolic syndrome, and dizziness   |
| <b>Dibenzothiazepine</b>          |                        |                     |  |
| Quetiapine                        | 150–375 mg po bid      | 200 mg po bid       | Low potency allowing wide dosing<br>May cause metabolic syndrome<br>No anticholinergic effect<br>Dose titration required because of blocking of $\alpha_2$ receptors<br>Requires bid dosing  |
| <b>Benzisothiazolylpiperazine</b> |                        |                     |  |
| Ziprasidone                       | 40–80 mg po bid        | 80 mg po bid        | Inhibition of serotonin and norepinephrine reuptake, possibly with antidepressant effects<br>Shortest half-life of new drugs<br>Requires bid dosing with food<br>IM form available for acute treatment<br>Low risk of metabolic syndrome |
| <b>Dihydrocarostyryl</b>          |                        |                     |  |
| Aripiprazole                      | 10–30 mg po at bedtime | 15 mg po at bedtime | Dopamine $-2$ partial agonist<br>Low risk of metabolic syndrome  |

SGA = Second-generation antipsychotic.

\*Monitoring for metabolic syndrome and type 2 diabetes is recommended for this class of antipsychotics.

†All SGAs have been associated with increased mortality in elderly patients with dementia.

SGA = second-generation antipsychotic.

Newer SGAs are very similar to each other in efficacy but differ in adverse effects, so drug choice is based on individual response and on other drug characteristics. For example, olanzapine, which has a relatively high rate of **sedation**, may be prescribed for patients with prominent agitation or insomnia; less sedating drugs might be preferred for patients with lethargy. A 4- to 8-wk trial is usually required to assess efficacy. After acute symptoms have stabilized, maintenance treatment is initiated; for it, the lowest

dose that prevents symptom recurrence is used. Risperidone is the only SGA available in a long-acting injectable formulation.

Weight gain, hyperlipidemia, and elevated risk of type 2 diabetes are the major adverse effects of SGAs. Thus, before treatment with SGAs is begun, all patients should be screened for risk factors, including personal or family history of diabetes, weight, waist circumference, BP, and fasting plasma glucose and lipid profile. Those found to have or be at significant risk of metabolic syndrome may be better treated with ziprasidone or aripiprazole than the other SGAs. Patient and family education regarding symptoms and signs of diabetes, including **polyuria**, **polydipsia**, weight loss, and diabetic **ketoacidosis** (nausea, vomiting, dehydration, rapid respiration, clouding of sensorium), should be provided. In addition, nutritional and physical activity counseling should be provided to all patients when they start taking an SGA. All patients taking an SGA require periodic monitoring of weight, body mass index, and fasting plasma glucose and referral for specialty evaluation if they develop hyperlipidemia or type 2 diabetes.

**Rehabilitation and community support services:** Psychosocial skill training and vocational rehabilitation programs help many patients work, shop, and care for themselves; manage a household; get along with others; and work with mental health care practitioners. Supported employment, in which patients are placed in a competitive work setting and provided with an on-site job coach to promote adaptation to work, may be particularly valuable. In time, the job coach acts only as a backup for problem solving or for communication with employers.

Support services enable many patients with schizophrenia to reside in the community. Although most can live independently, some require supervised apartments where a staff member is present to ensure drug adherence. Programs provide a graded level of supervision in different residential settings, ranging from 24-h support to periodic home visits. These programs help promote patient autonomy while providing sufficient care to minimize the likelihood of relapse and need for inpatient hospitalization. **Assertive community treatment programs** provide services in the patient's home or other residence and are based on high staff-to-patient ratios; treatment teams directly provide all or nearly all required treatment services.

Hospitalization or crisis care in a hospital alternative may be required during severe relapses, and involuntary hospitalization may be necessary if patients pose a danger to themselves or others. Despite the best rehabilitation and community support services, a small percentage of patients, particularly those with severe cognitive deficits and those



poorly responsive to drug therapy, require long-term institutional or other supportive care.

**Psychotherapy:** The goal of psychotherapy is to develop a **collaborative relationship** between the patients, family members, and physician so that patients can learn to understand and manage their illness, take drugs as prescribed, and handle stress more effectively. Although individual psychotherapy plus drug therapy is a common approach, few **empirical guidelines** are available. Psychotherapy that begins by addressing the patient's basic social service needs, provides support and education regarding the nature of the illness, promotes adaptive activities, and is based on empathy and a sound dynamic understanding of schizophrenia is likely to be most effective. Many patients need empathic psychologic support to adapt to what is often a lifelong illness that can substantially limit functioning.

For patients who live with their families, psychoeducational family interventions can reduce the rate of relapse. Support and advocacy groups, such as the National Alliance for the Mentally Ill, are often helpful to families.



**Reference:** <http://www.merckmanuals.com>