CHAPTER 9

Antipsychotic Drugs

OBJECTIVES

After studying this chapter, you will be able to

1. Discuss common manifestations of psychotic disorders, including schizophrenia.
2. Discuss characteristics of phenothiazines and related antipsychotics.
3. Compare characteristics of "atypical" antipsychotic drugs with those of "typical" phenothiazines and related antipsychotic drugs.
4. Describe the main elements of acute and long-term treatment of psychotic disorders.
5. State interventions to decrease adverse effects of antipsychotic drugs.
6. State interventions to promote compliance with outpatient use of antipsychotic drugs.

APPLYING YOUR KNOWLEDGE

Caroline Jones is brought to the mental health clinic by a friend. The friend says that Caroline has been seeing things that are not there and has become more withdrawn. Caroline has not taken care of her personal hygiene for some time. She is diagnosed with acute psychosis and is treated with psychotherapy and the medications haloperidol and risperidone.

INTRODUCTION

Psychosis

Antipsychotic drugs are used mainly for the treatment of *psychosis,* a severe mental disorder characterized by disordered thought processes (disorganized and often bizarre thinking); blunted or inappropriate emotional responses; bizarre behavior ranging from hypoactivity to hyperactivity with agitation, aggressiveness, hostility, and combativeness; social withdrawal in which a person pays less-than-normal attention to the environment and other people; deterioration from previous levels of occupational and social functioning (poor self-care and interpersonal skills); hallucinations; and paranoid delusions. *Hallucinations* are sensory perceptions of people or objects that are not present in the external environment. More specifically, people see, hear, or feel stimuli that are not visible to external observers, and they cannot distinguish between these false perceptions and reality. Hallucinations occur in delirium, dementias, schizophrenia, and other psychotic states. In schizophrenia or bipolar affective disorder, they are usually auditory; in delirium, they are usually visual or tactile; and in dementia, they are usually visual. *Delusions* are false beliefs that persist in the absence of reason or evidence. Deluded people often believe that other people control their thoughts, feelings, and behaviors or seek to harm them (*paranoia*). Delusions indicate severe mental illness. Although they are commonly associated with schizophrenia, delusions also occur with delirium, dementias, and other psychotic disorders.

Psychosis may be acute or chronic. Acute episodes, also called *confusion* or *delirium,* have a sudden onset over hours to days and may be precipitated by physical disorders (eg, brain damage related to cerebrovascular disease or head injury; metabolic disorders; infections); drug intoxication with adrenergics, antidepressants, some anticonvulsants, amphetamines, cocaine, and others; and drug withdrawal after chronic use (eg, alcohol; benzodiazepine antianxiety or sedative-hypnotic agents). In addition, acute psychotic episodes may be superimposed on chronic dementias and psychoses, such as schizophrenia. This chapter focuses primarily on schizophrenia as a chronic psychosis.

Schizophrenia

Although *schizophrenia* is often referred to as a single disease, it includes a variety of related disorders. Risk factors include a genetic predisposition and environmental stresses.

Symptoms may begin gradually or suddenly, usually during adolescence or early adulthood. According to the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision* overt psychotic symptoms must be present for 6 months before schizophrenia can be diagnosed.

Behavioral manifestations of schizophrenia are categorized as positive and negative symptoms. *Positive symptoms* are characterized by central nervous system (CNS) stimulation and include agitation, behavioral disturbances, delusions, disorganized speech, hallucinations, insomnia, and paranoia. *Negative symptoms* are characterized by lack of pleasure (anhedonia), lack of motivation, blunted affect, poor grooming and hygiene, poor social skills, poverty of speech, and social withdrawal. However, all of these symptoms may occur in other disorders.

The etiology of schizophrenia is unclear. However, there is evidence that it results from abnormal neurotransmission systems in the brain, especially in the dopaminergic, serotonergic, and glutamatergic systems. There is also evidence of extensive interactions among neurotransmission systems. For example, the serotonergic and glutamatergic systems can alter dopaminergic activity, and drugs that may cause psychosis affect several systems (eg, adrenergics increase norepinephrine; antidepressants increase norepinephrine, serotonin, or both). Thus, schizophrenia probably results from imbalances and abnormal integration among several neurotransmission systems. In addition, illnesses or drugs that alter neurotransmission in one system are likely to alter neurotransmission in other systems. The dopaminergic, serotoninergic, and glutamatergic systems have been studied most.

The dopaminergic system has been more extensively studied than other systems, because schizophrenia has long been attributed to increased dopamine activity in the brain. Stimulation of dopamine can initiate psychotic symptoms or exacerbate an existing psychotic disorder. The importance of dopamine is further supported by two findings: (1) antipsychotic drugs exert their therapeutic effects by decreasing dopamine activity (ie, blocking dopamine receptors), and (2) drugs that increase dopamine levels in the brain (eg, bromocriptine, cocaine, levodopa) can cause signs and symptoms of psychosis.

In addition to the increased amount of dopamine, dopamine receptors are also involved. Two groups of dopamine receptors have been differentiated, mainly by the effects of the dopamine–receptor complex on intracellular functions. The first group stimulates cellular functions, whereas the second group decreases cellular functions and alters the movement of calcium and potassium ions across neuronal cell membranes. The second group (D_2 receptors) is considered important in the pathophysiology of schizophrenia. Thus, at the cellular level, dopamine activity is determined by its interaction with various receptors and the simultaneous actions of other neurotransmitters at the same target neurons. In general, overactivity of dopamine in some parts of the brain is thought to account for the positive symptoms of schizophrenia, and underactivity in another part of the brain is thought to account for the negative symptoms.

The serotonergic system, which is widespread in the brain, is mainly inhibitory in nature. In schizophrenia, serotonin apparently decreases dopamine activity in the part of the brain associated with negative symptoms, causing or aggravating these symptoms.

The glutamatergic neurotransmission system involves glutamate, the major excitatory neurotransmitter in the CNS. Glutamate receptors are widespread and possibly located on every neuron in the brain. They are also diverse, and their functions may vary according to subtypes and their locations in particular parts of the brain. When glutamate binds to its receptors, the resulting neuronal depolarization activates signaling molecules (eg, calcium, nitric oxide) within and between brain cells. Thus, glutamatergic transmission may affect every CNS neuron and is considered essential for all mental, sensory, motor, and affective functions. Dysfunction of glutamatergic neurotransmission has been implicated in the development of psychosis.

In addition, the glutamatergic system interacts with the dopaminergic and gamma-aminobutyric acid systems, and possibly other neurotransmission systems. In people with schizophrenia, evidence indicates the presence of abnormalities in the number, density, composition, and function of glutamate receptors. In addition, glutamate receptors are genetically encoded and can interact with environmental factors (eg, stress; alcohol and other drugs) during brain development. Thus, glutamatergic dysfunction may account for the roles of genetic and environmental risk factors in the development of schizophrenia as well as the cognitive impairments and negative symptoms associated with the disorder.

GENERAL CHARACTERISTICS OF ANTIPSYCHOTIC DRUGS

Antipsychotic drugs are derived from several chemical groups. These drugs may be broadly categorized as "typical," *conventional,* or *first-generation* agents (phenothiazines and older nonphenothiazines, such as haloperidol [Haldol], with similar pharmacologic actions, clinical uses, and adverse effects), or as "atypical" or *second-generation* agents, which can also be called *newer nonphenothiazines.*

Mechanism of Action

Most antipsychotic drugs bind to D_2 dopamine receptors and block the action of dopamine (Fig. 9-1). However, drug binding to the receptors does not account for antipsychotic effects because binding occurs within a few hours after a drug dose, and antipsychotic effects may not occur until the drugs have been given for a few weeks. Manifestations of hyperarousal (eg, anxiety, agitation, hyperactivity, insomnia, aggressive or combative behavior) are relieved more quickly than halluci-

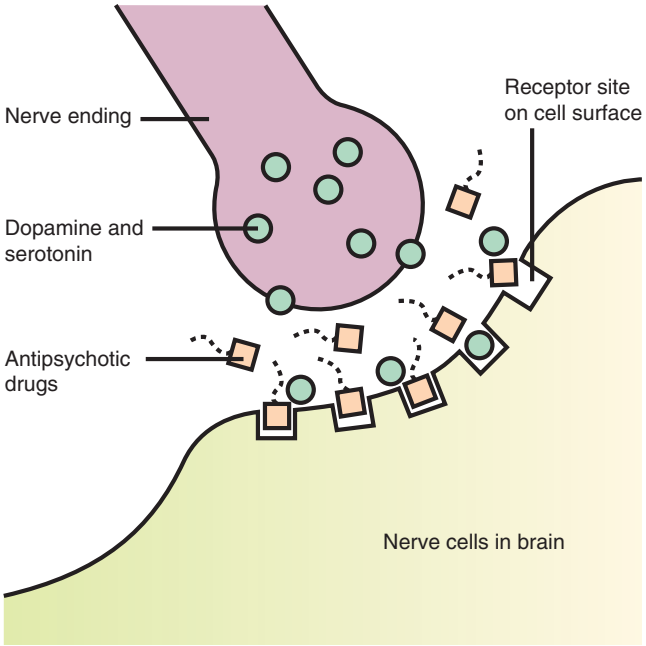

FIGURE 9-1 Antipsychotic drugs prevent dopamine and serotonin from occupying receptor sites on neuronal cell membranes and exerting their effects on cellular functions. This action leads to changes in receptors and cell functions that account for therapeutic effects (ie, relief of psychotic symptoms). Other neurotransmitters and receptors may also be involved.

nations, delusions, and thought disorders. One view of the delayed effects is that the blockade of dopamine receptors leads to changes in the receptors and postreceptor effects on cell metabolism and function. With chronic drug administration (ie, chronic blockade of dopamine receptors), there is an increased number of dopamine receptors on postsynaptic and possibly presynaptic nerve cell membranes (up-regulation). Clozapine (Clozaril) and other atypical agents interact with dopamine, serotonin, and glutamate receptors. Overall, the drugs re-regulate the abnormal neurotransmission systems associated with psychosis.

Indications for Use

The major clinical indication for use of antipsychotic drugs is schizophrenia. The drugs also are used to treat psychotic symptoms associated with brain impairment induced by head injury, tumor, stroke, alcohol withdrawal, overdoses of CNS stimulant drugs, and other disorders. They may be useful in the manic phase of bipolar affective disorder to control manic behavior until lithium, the drug of choice, becomes effective.

The phenothiazines are also used for clinical indications not associated with psychiatric illness. These include treatment of nausea, vomiting, and intractable hiccups. The drugs relieve nausea and vomiting by blocking dopamine receptors in the chemoreceptor trigger zone, a group of neurons in the medulla oblongata that causes nausea and vomiting when activated by physical or psychological stimuli. The mechanism by which the drugs relieve hiccups is unclear.

Promethazine (Phenergan) is not used for antipsychotic effects, but is often used for antiemetic, sedative, and antihistaminic effects.

Contraindications to Use

Because of their wide-ranging adverse effects, antipsychotic drugs may cause or aggravate a number of conditions. They are contraindicated in clients with liver damage, coronary artery disease, cerebrovascular disease, parkinsonism, bone marrow depression, severe hypotension or hypertension, coma, or severely depressed states. They should be used cautiously in people with seizure disorders, diabetes mellitus, glaucoma, prostatic hypertrophy, peptic ulcer disease, and chronic respiratory disorders.

INDIVIDUAL DRUGS

Phenothiazines

These drugs are historically important because **chlorpromazine** (Thorazine), the first drug to effectively treat psychotic disorders, belongs to this group. These drugs have been used since the 1950s, but their usage and clinical importance have waned in recent years.

The phenothiazines are well absorbed after oral and parenteral administration. They are distributed to most body tissues and reach high concentrations in the brain. They are metabolized in the liver by the cytochrome P450 enzyme system; several produce pharmacologically active metabolites. Metabolites are excreted in urine. These drugs do not cause psychological dependence, but they may cause physical dependence manifested by withdrawal symptoms (eg, lethargy, difficulty sleeping) if they are abruptly discontinued. Pharmacokinetics of various antipsychotics are presented in Table 9-1.

Phenothiazines have many effects, including CNS depression, autonomic nervous system depression (antiadrenergic and anticholinergic effects), antiemetic effects, lowering of body temperature, hypersensitivity reactions, and others. Phenothiazines differ mainly in potency and adverse effects: Some are as effective in doses of a few milligrams as others are in doses of several hundred milligrams. All phenothiazines produce the same kinds of adverse effects, but individual drugs differ in the incidence and severity of particular adverse effects. Information about administration, dosage, and other characteristics of individual phenothiazine drugs are listed in Table 9-2.

Nonphenothiazines

Nonphenothiazines include first-generation "typical" antipsychotics, which share many similarities to phenothiazines,

TABLE 9-1 Pharmacokinetics of Antipsychotic Drugs

GENERIC NAME	ROUTE	ACTION			HALF-LIFE (HOURS)
		Onset	Peak	Duration	
Aripiprazole	PO	Varies	3–5 h	24 h	75–146
Chlorpromazine	PO	30–60 min	2–4 h	4–6 h (10–12 h for extended release)	3–40
	IM	Unknown	2–3 h	4–18 h	3–40
Clozapine	PO	Unknown	1–6 h	4–12 h	9–17
Fluphenazine decanoate	IM	24–72 h	24 h	1–3 wks	7–10 days
Fluphenazine enanthate	IM	24–72 h	48 h	>4 wks	4 days
Fluphenazine hydrochloride	PO	60 min	3–5 h	6–8 h	5–15
Haloperidol	PO	2 h	2–6 h	8–12 h	21–24
	IM	20–30 min	30–45 min	4–8 h	
Haloperidol decanoate	IM	3–9 days	Unknown	1 month	3 wk
Loxapine	PO	30 min	1.5–3 h	12 h	3–4
Molindone	PO	Varies	30–90 min	24–36 h	1.5–6
Olanzapine	PO	Varies	4–5 h	weeks	20–27
Perphenazine	PO	Varies	Unknown	Unknown	Unknown
	IM/IV	5–10 min	1–2 h	6 h	
Quetiapine	PO	Varies	2–4 h	8–10 h	6
Risperidone	PO	1–2 h	3–17 h	weeks	20–30
Thiothixene	PO	Slow	1–3 h	12 h	3–4
Trifluoperazine	PO	Varies	2–4 h	<12 h	3–40
	IM	Rapid	1–2 h	<12 h	3–40
Ziprasidone	PO	Varies	1 h	6–8 h	3

IM, intramuscular; IV, intravenous; PO, oral.

and second-generation "atypical" antipsychotics, which vary in relation to typical drugs and to each other. Details about administration, dosage, and other characteristics of selected nonphenothiazines are listed in Table 9-3.

First-Generation "Typical" Antipsychotics

Haloperidol (Haldol) is a butyrophenone used in psychiatric disorders. A related drug, droperidol, is used in anaesthesia and as an antiemetic. Haloperidol is a frequently used, potent, long-acting drug. It is well absorbed after oral or intramuscular (IM) administration, is metabolized in the liver, and is excreted in urine and bile. It may cause adverse effects similar to those of the phenothiazines. Usually, it produces a relatively low incidence of hypotension and sedation and a high incidence of extrapyramidal effects.

Haloperidol may be used as the initial drug for treating psychotic disorders or as a substitute in clients who are hypersensitive or refractory to the phenothiazines. It also is used to treat some conditions in which other antipsychotic drugs are not used, including mental retardation with hyperkinesia (abnormally increased motor activity), Tourette's syndrome (a rare disorder characterized by involuntary movements and vocalizations), and Huntington's disease (a rare genetic disorder that involves progressive psychiatric symptoms and involuntary movements). For clients who are unable or unwilling to take the oral drug as prescribed, a slowly absorbed, long-acting formulation (haloperidol decanoate) may be given IM, once monthly.

Loxapine (Loxitane) is similar to phenothiazines and related drugs. It is recommended for use in only the treatment of schizophrenia.

Molindone (Moban) differs chemically from other agents but has similar pharmacologic actions.

Pimozide (Orap) is approved only for the treatment of Tourette's syndrome in clients who fail to respond to haloperidol. Potentially serious adverse effects include tardive dyskinesia, major motor seizures, and sudden death.

Thiothixene (Navane) is used only for antipsychotic effects, although it produces other effects similar to those of the phenothiazines.

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Table 9-2 Drugs at a Glance: Phenothiazine Antipsychotic Drugs

GENERIC/TRADE NAME	ROUTES OF ADMINISTRATION AND DOSAGE RANGES	MAJOR SIDE EFFECTS (INCIDENCE)		
		Sedation	Extrapyramidal Reactions	Hypotension
P Chlorpromazine (Thorazine)	*Adults:* PO 200–600 mg daily in divided doses. Dose may be increased by 100 mg daily q2–3 days until symptoms are controlled, adverse effects occur, or a maximum daily dose of 2 g is reached. IM 25–100 mg initially for acute psychotic symptoms, repeated in 1–4 hours PRN until control is achieved. *Elderly or debilitated adults:* PO one third to one half usual adult dose, increased by 25 mg daily q2–3 days if necessary. IM 10 mg q6–8h until acute symptoms are controlled. *Children:* PO, IM 0.5 mg/kg q4–8h. Maximum IM dose, 40 mg daily in children under 5 y of age and 75 mg for older children.	High	Moderate	Moderate to high
Fluphenazine decanoate and enanthate (Prolixin Decanoate; Prolixin Enanthate)	*Adults under 50 y:* IM; Sub-Q 12.5 mg initially followed by 25 mg every 2 weeks. Dosage requirements rarely exceed 100 mg q2–6 wk. *Adults over 50 y, debilitated clients, or clients with a history of extrapyramidal reactions:* 2.5 mg initially followed by 2.5–5 mg q10–14 days *Children:* No dosage established	Low to moderate	High	Low
Fluphenazine hydrochloride (Prolixin, Permitil)	*Adults:* PO 2.5–10 mg initially, gradually reduced to maintenance dose of 1–5 mg (doses above 3 mg are rarely necessary). Acute psychosis: 1.25 mg initially, increased gradually to 2.5–10 mg daily in 3–4 divided doses. *Elderly or debilitated adults:* PO 1–2.5 mg daily; IM one third to one half the usual adult dose *Children:* PO 0.75–10 mg daily in children 5 to 12 y. IM no dosage established.	Low to moderate	High	Low
Perphenazine (Trilafon)	*Adults:* PO 16–64 mg daily in divided doses. Acute psychoses: IM 5–10 mg initially, then 5 mg q6h if necessary. Maximum daily dose, 15 mg for ambulatory clients and 30 mg for hospitalized clients. *Elderly or debilitated adults:* PO, IM one third to one half usual adult dose *Children:* PO dosages not established, but the following amounts have been given in divided doses: ages 1–6 y, 4–6 mg daily; 6–12 y, 6 mg daily; over 12 y, 6–12 mg daily	Low to moderate	High	Low
Prochlorperazine (Compazine)	*Adults:* PO 10 mg 3–4 times daily, increased gradually (usual daily dose, 100–150 mg). IM 10–20 mg; may be repeated in 2–4 h. Switch to oral form as soon as possible. *Children over 2 y:* PO, rectal 2.5 mg 2–3 times daily; IM 0.06 mg/lb	Moderate	High	Low

(continued)

Table 9-2 Drugs at a Glance: Phenothiazine Antipsychotic Drugs (continued)

GENERIC/TRADE NAME	ROUTES OF ADMINISTRATION AND DOSAGE RANGES	MAJOR SIDE EFFECTS (INCIDENCE)		
		Sedation	Extrapyramidal Reactions	Hypotension
Trifluoperazine (Stelazine)	*Adults:* Outpatients PO 2–4 mg daily in divided doses. Hospitalized clients, PO 4–10 mg daily in divided doses. Acute psychoses: IM 1–2 mg q4–5h, maximum of 10 mg daily. *Elderly or debilitated adults:* PO, IM one third to one half usual adult dose. If given IM, give at less frequent intervals than above. *Children 6 y and over:* PO, IM 1–2 mg daily, maximum daily dose 15 mg *Children under 6 y:* no dosage established	Moderate	High	Low

IM, intramuscular; IV, intravenous; PO, oral.

Table 9-3 Drugs at a Glance: Nonphenothiazine Antipsychotic Drugs

GENERIC/TRADE NAME	ROUTES AND DOSAGE RANGES	
	Adults	Children
First-Generation, "Typical" Drugs		
Haloperidol (Haldol)	Acute psychosis, PO 1–15 mg/d initially in divided doses, gradually increased to 100 mg/d, if necessary; usual maintenance dose, 2–8 mg daily; IM 2–10 mg q1–8h until symptoms are controlled (usually within 72 h) Chronic schizophrenia, PO 6–15 mg/d; maximum 100 mg/d; dosage is reduced for maintenance, usually 15–20 mg/d Haloperidol decanoate IM, initial dose up to 100 mg, depending on the previous dose of oral drug, then titrated according to response. Usually given every 4 weeks. Tourette's syndrome, PO 6–15 mg/d; maximum 100 mg/d; usual maintenance dose, 9 mg/d Mental retardation with hyperkinesia, PO 80–120 mg/d, gradually reduced to a maintenance dose of approximately 60 mg/d; IM 20 mg/d in divided doses, gradually increased to 60 mg/d if necessary. Oral administration should be substituted after symptoms are controlled. *Elderly or debilitated adults:* Same as for children <12 y	*12 y and older:* Acute psychosis, chronic refractory schizophrenia, Tourette's syndrome, mental retardation with hyperkinesia: same as for adults *<12 y:* Acute psychosis, PO 0.5–1.5 mg/d initially, gradually increased in increments of 0.5 mg; usual maintenance dose, 2–4 mg/d. IM dosage not established. Chronic refractory schizophrenia, dosage not established Tourette's syndrome, PO 1.5–6 mg/d initially in divided doses; usual maintenance dose, 1.5 mg/d Mental retardation with hyperkinesia, PO 1.5 mg/d initially, in divided doses, gradually increased to a maximum of 15 mg/d, if necessary. When symptoms are controlled, dosage is gradually reduced to the minimum effective level. IM dosage not established.

(continued)

Table 9-3 Drugs at a Glance: Nonphenothiazine Antipsychotic Drugs (continued)

GENERIC/TRADE NAME	ROUTES AND DOSAGE RANGES: Adults	ROUTES AND DOSAGE RANGES: Children
Loxapine (Loxitane)	PO 10 mg twice a day initially, may be increased to 50 mg/d in severe psychoses; usual maintenance dose 20–60 mg/d; maximum dose, 250 mg/d IM 12.5–50 mg q4–6h or longer, depending on response. Change to oral drug when symptoms controlled. Elderly or debilitated adults: One third to one half the usual adult dosage	*16 y and older:* Same as adults *<16 y:* Not recommended
Molindone (Moban)	PO 50–75 mg/d, increased gradually if necessary up to 225 mg/d, then reduced for maintenance; usual maintenance dose, 15–40 mg/d Elderly or debilitated adults: One third to one half the usual adult dosage	*<12 y:* Dosage not established
Pimozide (Orap)	PO 1–2 mg/d in divided doses initially, increased if necessary; usual maintenance dose, approximately 10 mg/d; maximum dose, 20 mg/d	
Thiothixene (Navane)	PO 6–10 mg/d in divided doses; maximum 60 mg/d Acute psychosis, IM 8–16 mg/d in divided doses; maximum 30 mg/d *Elderly or debilitated adults:* PO, IM one third to one half the usual adult dosage	*12 y and older:* Same as adults *<12 y:* Dosage not established
Second-Generation, "Atypical" Drugs		
Aripiprazole (Abilify)	PO 10–15 mg once daily; maximum dose 30 mg/d	Dosage not established
P **Clozapine** (Clozaril)	PO 25 mg once or twice daily initially, increased by 25–50 mg/d, if tolerated, to 300–450 mg/d by end of 2nd wk	Dosage not established
Olanzapine (Zyprexa)	PO 5–10 mg/d initially; given once daily at bedtime; increased over several weeks to 20 mg/d, if necessary	Dosage not established
Quetiapine (Seroquel)	PO 25 mg bid initially; increased by 25–50 mg two or three times daily on second and third days, as tolerated, to 300–400 mg, in two or three divided doses on the fourth day Additional increments or decrements can be made at 2-day intervals; maximum dose 800 mg/d Elderly or debilitated adults: Use lower initial doses and increase more gradually, to a lower target dose than for other adults. Hepatic impairment: PO, same as for elderly or debilitated adults	Dosage not established

(continued)

Table 9-3 Drugs at a Glance: Nonphenothiazine Antipsychotic Drugs (continued)

GENERIC/TRADE NAME	ROUTES AND DOSAGE RANGES	
	Adults	Children
Risperidone (Risperdal)	PO, initially 1 mg twice daily (2 mg/d); increase to 2 mg twice daily on the second day (4 mg/d); increase to 3 mg twice daily on the third day (6 mg/d), if necessary. Usual maintenance dose, 4 to 8 mg/d. After initial titration, dosage increases or decreases should be made at a rate of 1 mg/wk. *Elderly or debilitated adults:* PO, initially 0.5 mg twice daily (1 mg/d); increase in 0.5-mg increments to 1.5 mg twice daily (3 mg/d) *Renal or hepatic impairment:* PO, same as for elderly or debilitated adults	*<12 y:* Dosage not established
(Risperdal Consta)	IM 25 mg every 2 wk; maximum dose not to exceed 50 mg/2 wk. Oral Risperdal should be continued for first 3 weeks of therapy to ensure adequate blood levels are maintained.	*< 18 y:* Dosage not established
Ziprasidone (Geodon)	PO 20 mg twice daily with food, initially; gradually increased up to 80 mg twice daily, if necessary	

IM, intramuscular; IV, intravenous; PO, oral.

Second-Generation "Atypical" Antipsychotics

In recent years, the "atypical" or newer nonphenothiazines have become the drugs of first choice. They have virtually replaced phenothiazines and related drugs except in clients doing well on older drugs and in the treatment of acute psychotic episodes. The atypical drugs have both similarities and differences when compared with other antipsychotic drugs and with each other. The main similarity is their effectiveness in treating the positive symptoms of psychosis; the main differences are greater effectiveness in relieving negative symptoms of schizophrenia and fewer resulting movement disorders (ie, extrapyramidal symptoms such as acute dystonia, parkinsonism, akathisia, and tardive dyskinesia). Although adverse effects are generally milder and more tolerable than with older drugs, clozapine may cause life-threatening agranulocytosis, and some of these drugs have been associated with weight gain, hyperglycemia, diabetes, and neuroleptic malignant syndrome.

P **Clozapine** (Clozaril), the prototype of the atypical agents, is chemically different from the older antipsychotic drugs. It blocks both dopamine and serotonin receptors in the brain. Clozapine is indicated for clients with schizophrenia, including those who have exhibited recurrent suicidal behavior.

Advantages of clozapine include improvement of negative symptoms, without causing the extrapyramidal effects associated with older antipsychotic drugs. However, despite these advantages, it is a second-line drug, recommended only for clients who have not responded to treatment with at least two other antipsychotic drugs or who have disabling tardive dyskinesia. The reason for the second-line status of clozapine is its association with agranulocytosis, a life-threatening decrease in white blood cells (WBCs), which usually occurs during the first 3 months of therapy. Weekly WBC counts are required during the first 6 months of therapy; if acceptable WBC counts are maintained, then WBC counts can be monitored every other week. In addition, clozapine is reportedly more likely to cause constipation, dizziness, drowsiness, hypotension, seizures, and weight gain than other atypical drugs.

Olanzapine (Zyprexa) has therapeutic effects similar to those of clozapine, but adverse effects may differ. Compared with clozapine, olanzapine is more likely to cause extrapyramidal effects and less likely to cause agranulocytosis. Compared with the typical antipsychotics, olanzapine reportedly causes less sedation, extrapyramidal symptoms, anticholinergic effects, and orthostatic hypotension. However, it has been associated with weight gain, hyperglycemia, and initiation or aggravation of diabetes mellitus.

The drug is well absorbed after oral administration; its absorption is not affected by food. A steady-state concentration is reached after approximately 1 week of once-daily administration. Olanzapine is metabolized in the liver and excreted in urine and feces.

Quetiapine (Seroquel), like the other atypical agents, blocks both dopamine and serotonin receptors and relieves both positive and negative symptoms of psychosis. After oral administration, quetiapine is well absorbed and may be taken without regard to meals. It is extensively metabolized in the liver by the cytochrome P450 enzyme system. Clinically significant drug interactions may occur with drugs that induce or inhibit the liver enzymes, and dosage of quetiapine may need to be increased in clients taking enzyme inducers (eg, carbamazepine, phenytoin, rifampin) or decreased in clients taking enzyme inhibitors (eg, cimetidine, erythromycin). Common adverse effects include drowsiness, headache, orthostatic hypotension, and weight gain.

Risperidone (Risperdal) also blocks both dopamine and serotonin receptors and relieves both positive and negative symptoms of psychosis. It is a frequently prescribed, first-choice agent that is usually well tolerated. In a study that compared risperidone and olanzapine, researchers concluded that both drugs were well tolerated and effective in treating schizophrenia, but risperidone relieved positive symptoms, anxiety, and depression to a greater degree and caused less weight gain than olanzapine.

Risperidone is well absorbed with oral administration. Peak blood levels occur in 1 to 2 hours, but therapeutic effects are delayed for 1 to 2 weeks. Risperidone is metabolized mainly in the liver by the cytochrome P450 2D6 enzymes and produces an active metabolite. Effects are attributed approximately equally to risperidone and the metabolite. Most (70%) of the drug is excreted in urine and some (14%) in feces. Adverse effects include agitation, anxiety, headache, insomnia, dizziness, and hypotension. Risperidone may also cause parkinsonism and other movement disorders, especially at higher doses, but is less likely to do so than the typical antipsychotic drugs.

Ziprasidone (Geodon) is another atypical agent used to treat schizophrenia. It is effective in suppressing many of the negative symptoms such as blunted affect, lack of motivation, and social withdrawal. It is contraindicated in people who are allergic to the drug; who are pregnant or lactating; who have a prolonged QT/QTc interval on electrocardiogram (ECG); or who have a history of severe heart disease. It must be used cautiously in people with impaired renal or hepatic function and cardiovascular disease. Because it may prolong the QT/QTc interval and cause torsades de pointes, a potentially fatal type of ventricular tachycardia, ziprasidone is probably not a drug of first choice.

Ziprasidone is metabolized in the liver and excreted in urine. Adverse effects include cardiac dysrhythmias, drowsiness, headache, and nausea; weight gain is less likely than with other antipsychotic drugs.

Aripiprazole (Abilify), the newest atypical drug, is approved for the treatment of schizophrenia and is the first in a new category of drugs called *partial dopamine agonists.* A *partial agonist* is a drug that has the ability to block a receptor if it is overstimulated and to stimulate a receptor if it is understimulated. The beneficial effect of aripiprazole in patients with schizophrenia is proposed to involve a combination of partial agonist activity at D_2 and serotonin 5-HT_{1A} receptors and antagonist activity at serotonin 5-HT_{2A} receptors. Aripiprazole also affects $alpha_1$ adrenergic receptors and histamine (H_1) receptors. Antagonism of $alpha_1$ adrenergic receptors may account for the occurrence of adverse effects such as orthostatic hypotension. Aripiprazole may also cause neuroleptic malignant syndrome, tardive dyskinesia, weight gain, hyperglycemia, and diabetes mellitus.

Aripiprazole is well absorbed orally, with or without food. It is 99% protein bound. It is metabolized in the liver by the CYP3A4 and CYP2D6 enzyme systems and has an active metabolite. Generally, no dosage adjustment for aripiprazole is required on the basis of hepatic or renal impairment. About 8% of the Caucasian population lacks the capacity to metabolize CYP2D6 substrates and therefore requires significantly lower doses of aripiprazole to avoid drug toxicity.

APPLYING YOUR KNOWLEDGE 9-1

After 6 weeks of therapy, Ms. Jones has far fewer symptoms; however, she has been observed to have a gradual loss of muscle movement. What adverse reaction is likely to be occurring?

NURSING PROCESS

Assessment

Assess the client's mental health status, need for antipsychotic drugs, and response to drug therapy. There is a wide variation in response to drug therapy. Close observation of physical and behavioral reactions is necessary to evaluate effectiveness and to individualize dosage schedules. Accurate assessment is especially important when starting drug therapy and when increasing or decreasing dosage. Some assessment factors include the following:

- Interview the client and family members. Attempts to interview an acutely psychotic person yield little useful information because of the client's distorted perception of reality. The nurse may be able to assess the client's level of orientation and delusional and hallucinatory activity. If possible, try to determine from family members or others what the client was doing or experiencing when the acute episode began (ie, predisposing factors, such as increased environmental stress or alcohol or drug ingestion); whether this is a first or a repeated episode of psychotic behavior; whether the person has physical illnesses, takes any drugs, or uses alcohol; whether the client seems to be a hazard to self or others; and some description of pre-illness personality traits, level of social interaction, and ability to function in usual activities of daily living.

- Observe the client for the presence or absence of psychotic symptoms such as agitation, hyperactivity, combativeness, and bizarre behavior.
- Obtain baseline data to help monitor the client's response to drug therapy. Some authorities advocate initial and periodic laboratory tests of liver, kidney, and blood functions, as well as electrocardiograms. Such tests may assist in early detection and treatment of adverse drug effects. Baseline blood pressure readings also may be helpful.
- Continue assessing the client's response to drug therapy and his or her ability to function in activities of daily living, whether the client is hospitalized or receiving outpatient treatment.

Nursing Diagnoses

- Altered Thought Processes related to psychosis
- Self-Care Deficit related to the disease process or drug-induced sedation
- Impaired Physical Mobility related to sedation
- Altered Tissue Perfusion related to hypotension
- Risk for Injury related to excessive sedation and movement disorders (extrapyramidal effects)
- Risk for Violence: Self-Directed or Directed at Others
- Noncompliance related to underuse of prescribed drugs

Planning/Goals

The client will

- Become less agitated within a few hours of the start of drug therapy, and less psychotic within 1–3 weeks
- Be kept safe while sedated from drug therapy
- Be cared for by staff in areas of nutrition, hygiene, exercise, and social interactions when unable to provide self-care
- Improve in ability to participate in self-care activities
- Avoid preventable adverse drug effects, especially those that impair safety
- Be helped to take medications as prescribed and return for follow-up appointments with health care providers

Interventions

Use nondrug measures when appropriate to increase the effectiveness of drug therapy and to decrease adverse reactions.

- Drug therapy is ineffective if the client does not receive sufficient medication; many people are unable or unwilling to take medications as prescribed. Any nursing action aimed toward more accurate drug administration increases the effectiveness of drug therapy.

  Specific nursing actions must be individualized to the client and/or caregiver. Some general nursing actions that may be helpful include emphasizing the therapeutic benefits expected from drug therapy; answering questions or providing information about drug therapy and other aspects of the treatment plan; devising a schedule of administration times that is as convenient as possible for the client; and assisting the client or caregiver in preventing or managing adverse drug effects (see accompanying client teaching guidelines). Most adverse effects are less likely to occur or be severe with the newer atypical drugs than with phenothiazines and other older drugs.
- Supervise ambulation to prevent falls or other injuries if the client is drowsy or elderly or has postural hypotension.
- Several measures can help prevent or minimize hypotension, such as having the client lie down for approximately an hour after a large oral dose or an injection of antipsychotic medication; applying elastic stockings; and instructing the client to change positions gradually, elevate legs when sitting, avoid standing for prolonged periods, and avoid hot baths (hot baths cause vasodilation and increase the incidence of hypotension). In addition, the daily dose can be decreased or divided into smaller amounts.
- Dry mouth and oral infections can be decreased by frequently brushing the teeth; rinsing the mouth with water; chewing sugarless gum or candy; and ensuring an adequate fluid intake. Excessive water intake should be discouraged because it may lead to serum electrolyte deficiencies.
- The usual measures of increasing fluid intake, dietary fiber, and exercise can help prevent constipation.
- Support caregivers in efforts to maintain contact with inpatients and provide care for outpatients. One way is to provide caregivers with telephone numbers of health care providers and to make periodic telephone calls to caregivers.
- Provide client teaching regarding drug therapy (see accompanying display).

APPLYING YOUR KNOWLEDGE 9-2

Ms. Jones says she is dizzy when she gets up. What nursing measures can be implemented to prevent injury?

Evaluation

- Interview the client to determine the presence and extent of hallucinations and delusions.
- Observe the client for decreased signs and symptoms.
- Document abilities and limitations in self-care.
- Note whether any injuries have occurred during drug therapy.
- Interview the caregiver about the client's behavior and medication response (ie, during a home visit or telephone call).

CLIENT TEACHING GUIDELINES

Antipsychotic Drugs

Antipsychotic drugs are given to clients with schizophrenia, a chronic mental illness. Because of the nature of the disease, a responsible adult caregiver is needed to prompt a client about taking particular doses and to manage other aspects of the drug therapy regimen, as follows.

General Considerations

- ✔ Ask about the planned drug therapy regimen, including the desired results, when results can be expected, and the tentative length of drug therapy.
- ✔ Maintain an adequate supply of medication to ensure regular administration. Consistent blood levels are necessary to control symptoms and to prevent recurring episodes of acute illness and hospitalization.
- ✔ Do not allow the client to drive a car, operate machinery, or perform activities that require alertness when drowsy from medication. Drowsiness, slowed thinking, and impaired muscle coordination are especially likely during the first 2 weeks of drug therapy but tend to decrease with time.
- ✔ Report unusual side effects and all physical illnesses, because changes in drug therapy may be indicated.
- ✔ Try to prevent the client from taking unprescribed medications, including those available without prescription or those prescribed for another person, to prevent undesirable drug interactions. Alcohol and sleeping pills should be avoided because they may cause excessive drowsiness and decreased awareness of safety hazards in the environment.
- ✔ Keep all physicians informed about all the medications being taken by the client, to decrease risks of undesirable drug interactions.
- ✔ These drugs should be tapered in dosage and discontinued gradually; they should not be stopped abruptly.
- ✔ Notify your physician if you become pregnant or intend to become pregnant

Medication Administration

Assist or prompt the client to:

- ✔ Take medications in the correct doses and at the correct times, to maintain blood levels and beneficial effects.
- ✔ Avoid taking these medications with antacids. If an antacid is needed (eg, for heartburn), it should be taken 1 hour before or 2 hours after the antipsychotic drug. Antacids decrease absorption of these drugs from the intestine.
- ✔ Lie down for approximately an hour after receiving medication, if dizziness and faintness occur.
- ✔ Take the medication at bedtime, if able, so that drowsiness aids sleep and is minimized during waking hours.
- ✔ Practice good oral hygiene, including dental checkups, thorough and frequent toothbrushing, drinking fluids, and frequent mouth rinsing. Mouth dryness is a common side effect of the drugs. Although it is usually not serious, dry mouth can lead to mouth infections and dental cavities.
- ✔ Minimize exposure to sunlight, wear protective clothing, and use sunscreen lotions. Sensitivity to sunlight occurs with some of the drugs and may produce a sunburn type of skin reaction.
- ✔ Avoid exposure to excessive heat. Some of these medications may cause fever and heat prostration with high environmental temperatures. In hot weather or climates, keep the client indoors and use air conditioning or fans during the hours of highest heat levels.

PRINCIPLES OF THERAPY

Goals of Therapy

Overall, the goal of treatment is to relieve symptoms with minimal or tolerable adverse drug effects. In clients with acute psychosis, the goal during the first week of treatment is to decrease symptoms (eg, aggression, agitation, combativeness, hostility) and normalize patterns of sleeping and eating. The next goals may be increased ability for self-care and increased socialization. Therapeutic effects usually occur gradually, over 1 to 2 months. Long-term goals include increasing the client's ability to cope with the environment, promoting optimal functioning in self-care and activities of daily living, and preventing acute episodes and hospitalizations. With drug therapy, clients often can participate in psychotherapy, group therapy, or other treatment modalities; return to community settings; and return to their pre-illness level of functioning.

Drug Selection

The physician caring for a client with psychosis has a greater choice of drugs than ever before. Some general factors to consider include the client's age and physical condition, the severity and duration of illness, the frequency and severity of adverse effects produced by each drug, the client's use of and response to antipsychotic drugs in the past, the supervision available, and the physician's experience with a particular drug.

The atypical drugs (eg, risperidone) are the drugs of choice, especially for clients who are newly diagnosed with schizophrenia, because these drugs may be more effective in relieving some symptoms; they usually produce milder adverse effects; and clients seem to take them more consistently. The ability of the atypical antipsychotics to reduce adverse effects is seen as a significant advantage, because clients are more likely to take the drugs. Better compliance with drug therapy helps prevent acute episodes of psychosis and repeated hospi-

talizations, thereby reducing the overall cost of care, according to studies. A major drawback is the high cost of these drugs, which may preclude their use in some clients.

An additional drawback and concern is weight gain and abnormal glucose metabolism. Most of the drugs in the atypical group have been associated with weight gain, especially with the chronic use required for treatment of schizophrenia. Recent reports also associate clozapine, olanzapine, quetiapine, and aripiprazole with changes in blood glucose levels, including hyperglycemia and diabetes mellitus. In some extreme cases, ketoacidosis, hyperosmolar coma, and death have been reported. A causal relationship between use of these drugs and onset of diabetes has not been established. However, before starting one of the drugs, clients should be assessed for diabetes or risk factors related to the development of diabetes (eg, obesity; personal or family history of diabetes; symptoms of diabetes such as polyuria, polydipsia, or polyphagia). If symptoms or risk factors are identified, blood glucose levels should be checked before starting the drug and periodically during treatment.

When compared with atypical antipsychotic drugs, traditional or typical antipsychotic drugs are apparently equally effective, but some clients who do not respond well to one of them may respond to another. Because the typical drugs are similarly effective, some physicians base their choice on a drug's adverse effects. In addition, some physicians use a phenothiazine first and prescribe a nonphenothiazine as a second-line drug for clients with chronic schizophrenia whose symptoms have not been controlled by the phenothiazines and for clients with hypersensitivity reactions to the phenothiazines. Thioridazine (Mellaril), formerly a commonly used drug, is now indicated only when other drugs are ineffective because of its association with serious cardiac dysrhythmias.

Clients who are unable or unwilling to take daily doses of a maintenance antipsychotic drug may be given periodic injections of a long-acting form of fluphenazine, haloperidol, or risperidone. Extrapyramidal symptoms may be more problematic with depot injections of antipsychotic drugs.

Any person who has had an allergic or hypersensitivity reaction to an antipsychotic drug usually should not be given that drug (or any drug in the same chemical group) again. Cross-sensitivity occurs, and the likelihood of another allergic reaction is high.

There is no logical basis for giving more than one antipsychotic drug at a time. There is no therapeutic advantage, and the risk of serious adverse reactions is increased.

Dosage and Administration

Dosage and route of administration must be individualized according to the client's condition and response. Oral drugs undergo extensive first-pass metabolism in the liver so that a significant portion of a dose does not reach the systemic circulation and low serum drug levels are produced. In contrast, IM doses avoid first-pass metabolism and produce serum drug levels approximately double those of oral doses. Thus, usual IM doses are approximately half the oral doses.

Initial drug therapy for acute psychotic episodes may require IM administration and hospitalization; symptoms are usually controlled within 48 to 72 hours, after which oral drugs can be given. When treatment is initiated with oral drugs, divided daily doses are recommended. For maintenance therapy, once-daily dosing is usually preferred. A single bedtime dose is effective for most clients. This schedule increases compliance with prescribed drug therapy, allows better nighttime sleep, and decreases hypotension and daytime sedation. Effective maintenance therapy requires close supervision and contact with the client and family members.

Duration of Therapy

In schizophrenia, antipsychotic drugs are usually given for years because there is a high rate of relapse (acute psychotic episodes) when drug therapy is discontinued, most often by clients who become unwilling or unable to continue their medication regimen. Drug therapy usually is indicated for at least 1 year after an initial psychotic episode and for at least 5 years, perhaps for life, after multiple episodes. Several studies indicate that low-dose, continuous maintenance therapy is effective in long-term prevention of recurrent psychosis. With wider use of maintenance therapy and the newer, better-tolerated antipsychotic drugs, clients may experience fewer psychotic episodes and hospitalizations.

Drug Withdrawal: Recognition and Treatment

Antipsychotic drugs can cause symptoms of withdrawal when suddenly or rapidly discontinued. Specific symptoms are related to drug potency, extent of dopaminergic blockade, and anticholinergic effects. Low-potency drugs (eg, chlorpromazine), for example, have strong anticholinergic effects, and sudden withdrawal can cause cholinergic effects such as diarrhea, drooling, and insomnia. To prevent withdrawal symptoms, drugs should be tapered in dosage and gradually discontinued over several weeks.

Treatment of Extrapyramidal Symptoms

Extrapyramidal effects (ie, abnormal movements) are more likely to occur with usage of older antipsychotic drugs than with the newer atypical agents. If they do occur, an anticholinergic antiparkinson drug (see Chap. 12) can be given. Such neuromuscular symptoms appear in fewer than half of the clients taking traditional antipsychotic drugs and are better handled by reducing dosage, if this does not cause recurrence of psychotic symptoms. If antiparkinson drugs are given, they should be gradually discontinued in about 3 months. Extrapyramidal symptoms do not usually recur despite continued administration of the same antipsychotic drug at the same dosage.

APPLYING YOUR KNOWLEDGE 9-3

When making a home visit to Ms. Jones, the nurse observes that the client is confused, is experiencing muscle twitching, and has a fever. What is the most likely explanation for these symptoms?

Perioperative Use

A major concern about giving traditional antipsychotic drugs perioperatively is their potential for adverse interactions with other drugs. For example, the drugs potentiate the effects of general anesthetics and other CNS depressants that are often used before, during, and after surgery. As a result, risks of hypotension and excessive sedation are increased unless doses of other drugs are reduced. If hypotension occurs and requires vasopressor drugs, phenylephrine or norepinephrine should be used rather than epinephrine because antipsychotic drugs inhibit the vasoconstrictive (blood pressure–raising) effects of epinephrine. Guidelines for perioperative use of the newer, atypical drugs have not been developed. Cautious use is indicated because they may also cause hypotension, sedation, and other adverse effects.

Use in Special Populations

Use in Children

Antipsychotic drugs are used mainly for childhood schizophrenia, which is often characterized by more severe symptoms and a more chronic course than adult schizophrenia. Drug therapy is largely empiric, because few studies have been conducted in children and adolescents. Guidelines for the use of antipsychotic drugs have been published by the American Academy of Child and Adolescent Psychiatry. Major recommendations are listed in Box 9-1.

It is not clear which antipsychotics are safest and most effective in children and adolescents. Factors to consider include the following:

- Drug pharmacodynamics and pharmacokinetics are likely to be different in children compared with adults. Pharmacodynamic differences may stem from changes in neurotransmission systems in the brain as children grow. Pharmacokinetic differences may stem from changes in distribution or metabolism of drugs; absorption seems similar to that of adults. In relation to distribution, children usually have a lesser percentage of body fat than adults. Thus, antipsychotic drugs, which are highly lipid soluble, cannot be as readily stored in fat as they are in adults. This often leads to shorter half-lives and the need for more frequent administration. In relation to metabolism, children usually have a faster rate than adults and may therefore require relatively high doses for their size and weight. In relation to excretion, children's renal function is usually similar to that of adults and most of the drugs are largely inactivated by liver metabolism. Thus, with normal renal function, excretion probably has little effect on blood levels of active drug or a child's response to the drug.
- Although the newer drugs are being used, children's dosages have not been established and long-term effects are unknown. Traditional drugs are not usually recommended for children younger than 12 years of age. However, prochlorperazine (Compazine), trifluoperazine (Stelazine), and haloperidol (Haldol) may be used in children aged 2 to 12 years.
- Dosage regulation is difficult because children may require lower plasma levels for therapeutic effects, but

Box 9-1 Guidelines for the Use of Antipsychotic Drugs by the American Academy of Child and Adolescent Psychiatry

- Give a thorough psychiatric and physical examination before starting drug therapy.
- Choose a medication based on potency, adverse effects, and the client's medication response history, if available. A newer, atypical drug is probably the drug of first choice.
- Give the chosen drug at least 4–6 weeks before evaluating its effectiveness. If an inadequate response is then evident, a new antipsychotic drug should be tried.
- After an adequate response is obtained, continue drug therapy for at least several months. For newly diagnosed children who are symptom free for 6–12 months, it may be feasible to stop the drug for a trial period to reassess condition and drug dosage. In general, the lowest effective dose is recommended.
- Use psychosocial and psychotherapeutic interventions along with antipsychotic drugs.
- Have the physician or another health care provider maintain contact with the child and his or her parents or guardian and monitor responses to the medication. For example, weight charts and calculations of body mass index should be maintained with the atypical drugs because most are associated with weight gain and some are associated with the development of diabetes.
- Conduct more controlled studies of drug effects in children and adolescents.

From the American Academy of Child and Adolescent Psychiatry's *Practice Parameter for the Assessment and Treatment of Children and Adolescents with Schizophrenia.*

they also metabolize antipsychotic drugs more rapidly than adults. A conservative approach is to begin with a low dose and increase it gradually (no more than once or twice a week), if necessary. Divided doses may be useful initially, with later conversion to once daily at bedtime. Older adolescents may require doses comparable with those of adults.

- Adverse effects may be different in children. For example, extrapyramidal symptoms with conventional drugs are more likely to occur in children than in adults. If they do occur, dosage reduction is more effective in alleviating them than are the anticholinergic antiparkinson drugs commonly used in adults. In addition, hypotension is more likely to develop in children. Blood pressure should be closely monitored during initial dosage titration.

Use in Older Adults

Antipsychotic drugs should be used cautiously in older adults. Before they are started, a thorough assessment is necessary, because psychiatric symptoms are often caused by organic disease or other drugs. If this is the case, treating the disease or stopping the offending drug may eliminate the need for an antipsychotic drug. In addition, older adults are more likely to have problems for which the drugs are contraindicated (eg, severe cardiovascular disease, liver damage, Parkinson's disease) or must be used very cautiously (diabetes mellitus, glaucoma, prostatic hypertrophy, peptic ulcer disease, chronic respiratory disorders).

If antipsychotic drugs are used to control acute agitation in older adults, they should be used in the lowest effective dose for the shortest effective duration. If the drugs are used to treat dementia, they may relieve some symptoms (eg, agitation, hallucinations, hostility, suspiciousness, uncooperativeness), but they do not improve memory loss and may further impair cognitive functioning.

For older adults in long-term care facilities, there is concern that antipsychotic drugs may be overused to control agitated or disruptive behavior caused by nonpsychotic disorders and for which other treatments are preferable. For example, clients with dementia may become agitated because of environmental or medical problems. Alleviating such causes, when possible, is safer and more effective than administering antipsychotic drugs. Inappropriate use of antipsychotic drugs exposes clients to adverse drug effects and does not resolve underlying problems.

Because of the many implications for client safety and welfare, federal regulations have been established for the use of antipsychotics in facilities receiving Medicare and Medicaid funds. These regulations include appropriate (eg, psychotic disorders; delusions; schizophrenia; dementia and delirium that meet certain criteria) and inappropriate (eg, agitation not thought to indicate potential harm to the resident or others; anxiety; depression; uncooperativeness; wandering) indications. When antipsychotics are required in older adults, several issues should be considered (Box 9-2).

Box 9-2 Considerations Regarding Use of Antipsychotic Drugs in Older Adults

Drug Selection

With traditional antipsychotic drugs, haloperidol and fluphenazine may be better tolerated, but they cause a high incidence of extrapyramidal symptoms. With atypical drugs, clozapine is a second-line agent because it produces many adverse effects. Olanzapine, quetiapine, risperidone, ziprasidone, or aripiprazole may be useful, but little information is available about their use in older adults. Ziprasidone should not be used in older adults with cardiac dysrhythmias or severe cardiovascular disease.

Dosage

When the drugs are required, the recommended starting dosage is 25%–33% of the dosage recommended for younger adults. Dosage should also be increased more gradually, if necessary, and according to clinical response. The basic principle of "start low, go slow" is especially applicable. After symptoms are controlled, dosage should be reduced to the lowest effective level. Some specific drugs and dosage ranges include haloperidol 0.25–1.5 mg qd to qid; clozapine 6.25 mg qd, initially; risperidone 0.5 mg qd, initially; quetiapine, a lower initial dose, slower dose titration, and a lower target dose in older adults. No reduction of dosage is required based on age for aripiprazole.

As in other populations, antipsychotic drugs should be tapered in dosage and discontinued gradually rather than discontinued abruptly.

Adverse Effects

Older adults are at high risk of adverse effects because metabolism and excretion are usually slower or more likely to be impaired than in younger adults. With traditional antipsychotic drugs, anticholinergic effects (eg, confusion, memory impairment, hallucinations, urinary retention, constipation, heat stroke) may be especially problematic. In addition, cardiovascular effects (eg, hypotension, dysrhythmias) may be especially dangerous in older adults, who often have underlying cardiovascular diseases. Tardive dyskinesia, which may occur with long-term use of the typical antipsychotic drugs, may develop more rapidly and at lower drug dosages in older adults than in younger clients. There is also a risk of neuroleptic malignant syndrome, a rare but serious disorder characterized by confusion, dizziness, fever, and rigidity. Other adverse effects include oversedation, dizziness, confusion, and impaired mobility, which may contribute to falls and other injuries unless clients are carefully monitored and safeguarded. With atypical drugs, many of these adverse effects are less likely to occur, especially at the reduced dosages recommended for older adults.

Use in Various Ethnic Groups

Antipsychotic drug therapy for nonwhite populations in the United States is based primarily on dosage recommendations, pharmacokinetic data, adverse effects, and other characteristics of antipsychotic drugs derived from white recipients. However, some groups respond differently. Most of the differences are attributed to variations in hepatic drug-metabolizing enzymes. Those with strong enzyme activity are known as *extensive* or *fast metabolizers,* whereas those with slower rates of enzyme activity are *poor* or *slow metabolizers.* Fast metabolizers eliminate drugs rapidly and may need a larger-than-usual dose to achieve therapeutic effects, and poor metabolizers eliminate drugs slowly and therefore are at risk of drug accumulation and adverse effects. For example, in extensive metabolizers, risperidone has a half-life of 3 hours and its active metabolite has a half-life of 21 hours. In slow metabolizers, risperidone has a half-life of 20 hours and its active metabolite has a half-life of 30 hours. About 6% to 8% of white people are thought to be slow metabolizers. Although little research has been done, especially with the atypical drugs, and other factors may be involved, several studies document differences in antipsychotic drug effects in non-Caucasian populations:

African Americans tend to respond more rapidly; experience a higher incidence of adverse effects, including tardive dyskinesia; and metabolize antipsychotic drugs more slowly than whites.

In addition, compared with whites with psychotic disorders, African Americans may be given higher doses and more frequent injections of long-acting antipsychotic drugs, both of which may increase the incidence and severity of adverse effects.

Asians generally metabolize antipsychotic drugs slowly and therefore have higher plasma drug levels for a given dose than whites. Most studies have been done with haloperidol and in a limited number of Asian subgroups. Thus, it cannot be assumed that all antipsychotic drugs and all people of Asian heritage respond in the same way. To avoid drug toxicity, initial doses should be approximately half the usual doses given to whites and later doses should be titrated according to clinical response and serum drug levels.

Hispanics' responses to antipsychotic drugs are largely unknown. Some are extremely fast metabolizers who may have low plasma drug levels in relation to a given dose.

Use in Clients With Renal Impairment

Because most antipsychotic drugs are extensively metabolized in the liver and the metabolites are excreted through the kidneys, the drugs should be used cautiously in clients with impaired renal function. Renal function should be monitored periodically during long-term therapy. If renal function test results (eg, blood urea nitrogen) become abnormal, the drug may need to be lowered in dosage or discontinued. Because risperidone is metabolized to an active metabolite, recommended dosage reductions and titrations for clients with renal impairment are the same as those for older adults.

With highly sedating antipsychotic drugs, it may be difficult to assess the client for excessive sedation because drowsiness, lethargy, and mental status changes may also occur with renal impairment.

Use in Clients With Hepatic Impairment

Antipsychotic drugs undergo extensive hepatic metabolism and then elimination in urine. In the presence of liver disease (eg, cirrhosis, hepatitis), metabolism may be slowed and drug elimination half-lives prolonged, with resultant accumulation and increased risk of adverse effects. Thus, the drugs should be used cautiously in clients with hepatic impairment.

Jaundice has been associated with phenothiazines, usually after 2 to 4 weeks of therapy. It is considered a hypersensitivity reaction, and clients should not be re-exposed to a phenothiazine. If antipsychotic drug therapy is required in these clients, a drug from a different chemical group should be given. Overall, there is no conclusive evidence that preexisting liver impairment increases the risk of jaundice, and clients with alcoholic cirrhosis have been treated without complications. With risperidone, recommended dosage reductions and titrations for clients with hepatic impairment are the same as those for older adults. With quetiapine, higher plasma levels occur in clients with hepatic impairment and a slower rate of dose titration and a lower target dose are recommended.

Periodic liver function tests (eg, gamma-glutamyl transpeptidase, alkaline phosphatase, bilirubin) are probably indicated, especially with long-term therapy or the use of clozapine, haloperidol, thiothixene, or a phenothiazine.

Use in Clients With Critical Illness

Antipsychotic drugs are infrequently used in clients who are critically ill. Some clients become acutely agitated or delirious and need sedation to prevent their injuring themselves by thrashing about, removing tubes and intravenous (IV) catheters, and so forth. Some physicians prefer a benzodiazepine-type of sedative, whereas others may use haloperidol. Before giving either drug, causes of delirium (eg, drug intoxication or withdrawal) should be identified and eliminated if possible.

If haloperidol is used, it is usually given IV, by bolus injection. The initial dose is 0.5 to 10 milligrams, depending on the severity of the agitation. It should be injected at a rate no faster than 5 milligrams per minute; the dose can be repeated every 30 to 60 minutes, up to a total amount of 30 milligrams, if necessary. Haloperidol has relatively weak sedative effects and does not cause respiratory depression. However, it can cause hypotension in clients who are volume depleted or receiving antihypertensive drugs. It can also cause cardiac dysrhythmias, including life-threatening torsades de pointes, in clients who are receiving large doses (>50 mg/day) or who have

abnormal serum electrolyte levels (eg, calcium, potassium, magnesium). Clients should be on a cardiac monitor and the ECG should be checked for a prolonged QT interval.

For clients with chronic schizophrenia who are stabilized on an antipsychotic drug when they experience a critical illness, either continuing or stopping the drug may cause difficulties. Continuing the drug may worsen signs and symptoms of the critical illness (eg, hypotension). Stopping it may cause symptoms of withdrawal.

Little information is available about the newer drugs. If quetiapine is used, very low doses are recommended in older adults, clients with hepatic impairment, debilitated clients, and those predisposed to hypotension. A critically ill client could have all of these conditions.

Use in Home Care

Chronically mentally ill clients, such as those with schizophrenia, are among the most challenging in the caseload of the home care nurse. Major recurring problems include failure to take antipsychotic medications as prescribed and the concurrent use of alcohol and other drugs of abuse. Either problem is likely to lead to acute psychotic episodes and hospitalizations. The home care nurse must assist and support caregivers' efforts to maintain medications and manage adverse drug effects, other aspects of daily care, and follow-up psychiatric care. In addition, the home care nurse may need to coordinate the efforts of several health and social service agencies or providers.

NURSING ACTIONS

Antipsychotic Drugs

NURSING ACTIONS	RATIONALE/EXPLANATION
1. Administer accurately	
a. Check doses carefully, especially when starting or stopping an antipsychotic drug, or substituting one for another.	Doses are often changed. When a drug is started, initial doses are usually titrated upward over days or weeks, then reduced for maintenance; when the drug is stopped, doses are gradually reduced; when substituting, dosage of one may be increased while dosage of the other is decreased.
b. With older, typical drugs:	
(1) Give once daily, 1–2 hours before bedtime, when feasible.	Peak sedation occurs in about 2 hours and aids sleep. Also, adverse effects such as dry mouth and hypotension are less bothersome.
(2) When preparing solutions, try to avoid skin contact. If contact is made, wash the area immediately.	These solutions are irritating to the skin and many cause contact dermatitis.
(3) Mix liquid concentrates with at least 60 mL of fruit juice or water just before administration.	To mask the taste. If the client does not like juice or water, check the package insert for other diluents. Some of the drugs may be mixed with coffee, tea, milk, or carbonated beverages.
(4) For intramuscular injections, give only those preparations labeled for IM use; do not mix with any other drugs in a syringe; change the needle after filling the syringe; inject slowly and deeply into gluteal muscles; and have the client lie down for 30–60 minutes after the injection.	These drugs are physically incompatible with many other drugs, and a precipitate may occur; parenteral solutions are irritating to body tissues and changing needles helps protect the tissues of the injection tract from unnecessary contact with the drug; injecting into a large muscle mass decreases tissue irritation; lying down helps to prevent orthostatic hypotension.
(5) With parenteral fluphenazine, give the hydrochloride salt IM only; give the decanoate and enanthate salts IM or subcutaneously (Sub-Q).	To decrease tissue irritation
c. With newer, atypical drugs:	
(1) Give aripiprazole once daily, without regard to meals.	Manufacturer's recommendation
(2) Give olanzapine once daily, without regard to meals; with oral disintegrating tablets, peel back foil covering, transfer tablet to dry cup or fingers, and place the tablet into the mouth.	Manufacturer's recommendation. The disintegrating tablet does not require fluid.
(3) Give quetiapine in 2 or 3 daily doses.	
(4) Give risperidone twice daily; mix the oral solution with 3–4 oz of water, coffee, orange juice, or low-fat milk; do not mix with cola drinks or tea.	Manufacturer's recommendation

NURSING ACTIONS	RATIONALE/EXPLANATION
(5) Give Risperdal Consta deep IM into gluteal muscles.	Manufacturer's recommendation
(6) Give ziprasidone twice daily with food.	Manufacturer's recommendation
2. Observe for therapeutic effects	
a. When the drug is given for acute psychotic episodes, observe for decreased agitation, combativeness, and psychomotor activity.	The sedative effects of antipsychotic drugs are exerted within 48–72 hours. Sedation that occurs with treatment of acute psychotic episodes is a therapeutic effect. Sedation that occurs with treatment of nonacute psychotic disorders, or excessive sedation at any time, is an adverse reaction.
b. When the drug is given for acute or chronic psychosis, observe for decreased psychotic behavior, such as:	These therapeutic effects may not be evident for 3–6 weeks after drug therapy is begun.
(1) Decreased auditory and visual hallucinations	
(2) Decreased delusions	
(3) Continued decrease in or absence of agitation, hostility, hyperactivity, and other behavior associated with acute psychosis	
(4) Increased socialization	
(5) Increased ability in self-care activities	
(6) Increased ability to participate in other therapeutic modalities along with drug therapy.	
c. When the drug is given for antiemetic effects, observe for decreased or absent nausea or vomiting.	
3. Observe for adverse effects	
a. With phenothiazines and related drugs, observe for:	
(1) Excessive sedation—drowsiness, lethargy, fatigue, slurred speech, impaired mobility, and impaired mental processes	Excessive sedation is most likely to occur during the first few days of treatment of an acute psychotic episode, when large doses are usually given. Psychotic clients also seem sedated because the drug lets them catch up on psychosis-induced sleep deprivation. Sedation is more likely to occur in elderly or debilitated people. Tolerance to the drugs' sedative effects develops, and sedation tends to decrease with continued drug therapy.
(2) Extrapyramidal reactions	
Akathisia—compulsive, involuntary restlessness and body movements	Akathisia is the most common extrapyramidal reaction, and it may occur about 5–60 days after the start of antipsychotic drug therapy. The motor restlessness may be erroneously interpreted as psychotic agitation necessitating increased drug dosage. This condition can sometimes be controlled by substituting an antipsychotic drug that is less likely to cause extrapyramidal effects or by giving an anticholinergic antiparkinson drug.
Parkinsonism—loss of muscle movement (akinesia), muscular rigidity and tremors, shuffling gait, postural abnormalities, mask-like facial expression, hypersalivation, and drooling	These symptoms are the same as those occurring with idiopathic Parkinson's disease. They can be controlled with anticholinergic antiparkinson drugs, given along with the antipsychotic drug for about 3 months, then discontinued. This reaction may occur about 5–30 days after antipsychotic drug therapy is begun.
Dyskinesias (involuntary, rhythmic body movements) and *dystonias* (uncoordinated, bizarre movements of the neck, face, eyes, tongue, trunk, or extremities)	These are less common extrapyramidal reactions, but they may occur suddenly, approximately 1–5 days after drug therapy is started, and be very frightening to the client and health care personnel. The movements are caused by muscle spasms and result in exaggerated posture and facial distortions. These symptoms are sometimes misinterpreted as seizures, hysteria, or other disorders. Antiparkinson drugs are given parenterally during acute dystonic reactions, but continued administration is not usually required. These reactions occur most often in younger people.

(continued)

NURSING ACTIONS	RATIONALE/EXPLANATION
Tardive dyskinesia—hyperkinetic movements of the face (sucking and smacking of lips, tongue protrusion, and facial grimaces) and choreiform movements of the trunk and limbs	This syndrome occurs after months or years of high-dose antipsychotic drug therapy. The drugs may mask the symptoms so that the syndrome is more likely to be diagnosed when dosage is decreased or the drug is discontinued for a few days. It occurs gradually and at any age but is more common in older people, women, and people with organic brain disorders. The condition is usually irreversible, and there is no effective treatment. Symptoms are not controlled and may be worsened by antiparkinson drugs. Low dosage and short-term use of antipsychotic drugs help prevent tardive dyskinesia; drug-free periods may aid early detection.
(3) Antiadrenergic effects—hypotension, tachycardia, dizziness, faintness, fatigue	Hypotension is potentially one of the most serious adverse reactions to the antipsychotic drugs. It is most likely to occur when the client assumes an upright position after sitting or lying down (orthostatic or postural hypotension) but it does occur in the recumbent position. It is caused by peripheral vasodilation. Orthostatic hypotension can be assessed by comparing blood pressure readings taken with the client in supine and standing positions. Tachycardia occurs as a compensatory mechanism in response to hypotension and as an anticholinergic effect in which the normal vagus nerve action of slowing the heart rate is blocked.
(4) Anticholinergic effects—dry mouth, dental caries, blurred vision, constipation, paralytic ileus, urinary retention	These atropine-like effects are common with therapeutic doses and are increased with large doses of phenothiazines.
(5) Respiratory depression—slow, shallow breathing and decreased ability to breathe deeply, cough, and remove secretions from the respiratory tract	This stems from general central nervous system (CNS) depression, which causes drowsiness and decreased movement. It may cause pneumonia or other respiratory problems, especially in people with hypercarbia and chronic lung disease.
(6) Endocrine effects—menstrual irregularities, possibly impotence and decreased libido in the male client, weight gain	These apparently result from drug-induced changes in pituitary and hypothalamic functions.
(7) Hypothermia or hyperthermia	Antipsychotic drugs may impair the temperature-regulating center in the hypothalamus. Hypothermia is more likely to occur. Hyperthermia occurs with high doses and warm environmental temperatures.
(8) Hypersensitivity reactions:	
Cholestatic hepatitis—may begin with fever and influenza-like symptoms followed in approximately 1 week by jaundice	Cholestatic hepatitis results from drug-induced edema of the bile ducts and obstruction of the bile flow. It occurs most often in women and after 2–4 weeks of receiving the drug. It is usually reversible if the drug is discontinued.
Blood dyscrasias—leukopenia, agranulocytosis (fever, sore throat, weakness)	Some degree of leukopenia occurs rather often and does not seem to be serious. Agranulocytosis, on the other hand, occurs rarely but is life threatening. Agranulocytosis is most likely to occur during the first 4–10 weeks of drug therapy, in women, and in older people.
Skin reactions—photosensitivity, dermatoses	Skin pigmentation and discoloration may occur with exposure to sunlight.
(9) Electrocardiogram (ECG) changes, cardiac dysrhythmias	ECG changes may portend dysrhythmias, especially in people with underlying heart disease. Ziprasidone may prolong the QT/QTc interval, an ECG change associated with torsades de pointes, a life-threatening dysrhythmia.
(10) Neuroleptic malignant syndrome—fever (may be confused with heat stroke), muscle rigidity, agitation, confusion, delirium, dyspnea, tachycardia, respiratory failure, acute renal failure	A rare but potentially fatal reaction that may occur hours to months after initial drug use. Symptoms usually develop rapidly over 24–72 hours. Treatment includes stopping the antipsychotic drug, giving supportive care related to fever and other symptoms, and drug therapy (dantrolene, a skeletal muscle relaxant, and amantadine or bromocriptine, dopamine-stimulating drugs).

NURSING ACTIONS	RATIONALE/EXPLANATION
b. With aripiprazole, observe for:	
(1) CNS effects—anxiety, headache, somnolence, blurred vision, akathisia, tardive dyskinesia, neuroleptic malignant syndrome	
(2) GI effects—nausea, vomiting, constipation, dysphagia	
(3) Cardiovascular effects—orthostatic hypotension	
(4) Other—weight gain, hyperglycemia	
c. With clozapine, observe for:	
(1) CNS effects—drowsiness, dizziness, headache, seizures	
(2) Gastrointestinal (GI) effects—nausea, vomiting, constipation	
(3) Cardiovascular effects—hypotension, tachycardia	
(4) Hematologic effects—agranulocytosis	This is the most life-threatening adverse effect of clozapine. Clients' white blood cell (WBC) counts must be checked before starting clozapine, every week during the first six months of therapy, then every 2 weeks as long as WBC counts are satisfactory. WBC levels should be monitored weekly for 4 weeks after the drug is discontinued.
d. With olanzapine, observe for:	
(1) CNS effects—drowsiness, dizziness, akathisia, tardive dyskinesia, neuroleptic malignant syndrome	
(2) GI effects—constipation	
(3) Cardiovascular effects—hypotension, tachycardia	
(4) Other—weight gain, hyperglycemia, diabetes, hyperlipidemia	
e. With quetiapine, observe for:	
(1) CNS effects—drowsiness, dizziness, headache, tardive dyskinesia, neuroleptic malignant syndrome	
(2) GI effects—anorexia, nausea, vomiting	
(3) Cardiovascular effects—orthostatic hypotension, tachycardia	
(4) Other—weight gain, hyperglycemia, diabetes	
f. With risperidone, observe for:	
(1) CNS effects—agitation, anxiety, drowsiness, dizziness, headache, insomnia, tardive dyskinesia, neuroleptic malignant syndrome	
(2) GI effects—nausea, vomiting, constipation	
(3) Cardiovascular effects—orthostatic hypotension, dysrhythmias	
(4) Other—photosensitivity	
g. With ziprasidone, observe for:	
(1) CNS effects—drowsiness, headache, extrapyramidal reactions	
(2) GI effects—nausea, constipation	
(3) Cardiovascular effects—dysrhythmias, hypotension, ECG changes	
(4) Other—fever	
4. Observe for drug interactions	
a. Drugs that *increase* effects of antipsychotic drugs:	
(1) Anticholinergics (eg, atropine)	Additive anticholinergic effects

(continued)

NURSING ACTIONS	RATIONALE/EXPLANATION
(2) Antidepressants, tricyclic	Potentiation of sedative and anticholinergic effects. Additive CNS depression, sedation, orthostatic hypotension, urinary retention, and glaucoma may occur unless dosages are decreased. Apparently these two drug groups inhibit the metabolism of each other, thus prolonging the actions of both groups if they are given concurrently.
(3) Antihistamines	Additive CNS depression and sedation
(4) CNS depressants—alcohol, opioid analgesics, antianxiety agents, sedative-hypnotics	Additive CNS depression. Also, severe hypotension, urinary retention, seizures, severe atropine-like reactions, and other adverse effects may occur, depending on which group of CNS depressant drugs is given.
(5) Propranolol	Additive hypotensive and ECG effects
(6) Thiazide diuretics, such as hydrochlorothiazide	Additive hypotension
(7) Lithium	Acute encephalopathy, including irreversible brain damage and dyskinesias, has been reported.
b. Drugs that *decrease* effects of antipsychotic drugs:	
(1) Antacids	Oral antacids, especially aluminum hydroxide and magnesium trisilicate, may inhibit gastrointestinal absorption of antipsychotic drugs.
(2) Carbamazepine, phenytoin, rifampin	By induction of drug-metabolizing enzymes in the liver
(3) Norepinephrine, phenylephrine	Antagonize the hypotensive effects of antipsychotic drugs
c. Drugs that alter effects of quetiapine and aripiprazole:	
(1) Cimetidine, erythromycin, itraconazole, and ketoconazole *increase* effects.	These drugs inhibit cytochrome CYP3A4 enzymes and slow the metabolism of quetiapine.
(2) Quinidine, fluoxetine, and paroxetine *increase* effect of aripiprazole only.	These drugs inhibit cytochrome CYP2D6 and slow the metabolism of aripiprazole.
(3) Carbamazepine, phenytoin, and rifampin *decrease* effects of both drugs.	These drugs induce cytochrome CYP3A4 enzymes and speed up the metabolism of both drugs.

APPLYING YOUR KNOWLEDGE: ANSWERS

9-1 Parkinsonism is a common side effect of antipsychotic medication. Notify the physician; antiparkinson drugs may be given along with the antipsychotic drugs.

9-2 The dizziness is most likely due to orthostatic hypotension as a side effect of the risperidone. Have Ms. Jones change position gradually, lie down for an hour after taking her medication, elevate her legs when in a sitting position, and avoid hot baths.

9-3 These symptoms are typical of neuroleptic malignant syndrome. This is a rare but potentially fatal reaction that requires rapid treatment.

Review and Application Exercises

Short Answer Exercises

1. How do antipsychotic drugs act to relieve psychotic symptoms?
2. What are some uses of antipsychotic drugs other than the treatment of schizophrenia?
3. What are major adverse effects of older antipsychotic drugs?
4. When instructing a client to rise slowly from a sitting or lying position, which adverse effect of an antipsychotic drug is the nurse trying to prevent?
5. In a client receiving an antipsychotic drug, what appearances or behaviors would lead the nurse to suspect an extrapyramidal reaction?
6. Are antipsychotic drugs likely to be overused and abused? Why or why not?
7. In an older client taking an antipsychotic drug, what special safety measures are needed? Why?
8. How do clozapine, olanzapine, quetiapine, risperidone, ziprasidone, and aripiprazole compare with older antipsychotic drugs in terms of therapeutic and adverse effects?
9. What can the home care nurse do to prevent acute psychotic episodes and hospitalization of chronically mentally ill clients?

NCLEX-Style Questions

10. For clients taking clozapine, the nurse should assess which of the following laboratory values weekly?
a. complete blood count
b. hemoglobin and hematocrit
c. blood urea nitrogen and creatinine
d. liver enzyme studies

11. Patients taking ziprasidone (Geodon) may have prolonged QT intervals, placing them at risk for which of the following?
a. atrial fibrillation
b. torsades de pointes
c. complete heart block
d. atrial tachycardia

12. The nurse should administer long-acting injections of antipsychotic drugs in which of the following ways?
a. intramuscularly into the deltoid muscle
b. subcutaneously into the abdomen
c. intramuscularly into the gluteal muscle
d. intravenously into a large vein

13. When administering atypical antipsychotics, the nurse should be alert to possible
a. renal failure
b. liver failure
c. diabetes mellitus
d. hypertension

14. An adverse effect of long-term use of phenothiazine antipsychotics is the development of which of the following?
a. glaucoma
b. tardive dyskinesia
c. hypertension
d. diabetes

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