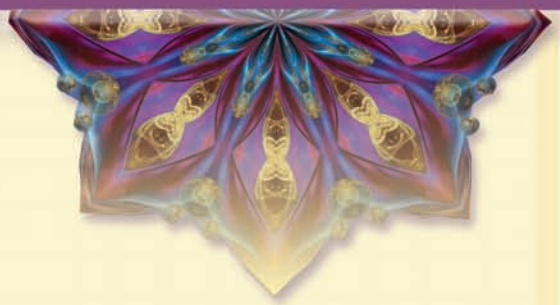
2 Neurobiologic Theories and Psychopharmacology



Key Terms

- akathisia
- anticholinergic side effects
- antidepressant drugs
- antipsychotic drugs
- anxiolytic drugs
- black box warning
- computed tomography (CT)
- depot injection
- dopamine
- dystonia
- efficacy
- epinephrine
- extrapyramidal symptoms (EPS)
- half-life
- kindling process
- limbic system
- magnetic resonance imaging (MRI)
- mood-stabilizing drugs
- neuroleptic malignant syndrome (NMS)
- neurotransmitter
- norepinephrine
- off-label use
- positron emission tomography (PET)
- potency
- pseudoparkinsonism
- psychoimmunology
- psychopharmacology
- psychotropic drugs
- rebound
- serotonin
- serotonin syndrome
- single photon emission computed tomography (SPECT)
- stimulant drugs
- tardive dyskinesia (TD)
- withdrawal

Learning Objectives

After reading this chapter, you should be able to

1. Discuss the structures, processes, and functions of the brain.
2. Describe the current neurobiologic research and theories that are the basis for current psychopharmacologic treatment of mental disorders.
3. Discuss the nurse's role in educating clients and families about current neurobiologic theories and medication management.
4. Identify pertinent teaching for clients and families about brain imaging techniques.
5. Discuss the categories of drugs used to treat mental illness and their mechanisms of action, side effects, and special nursing considerations.
6. Identify client responses that indicate treatment effectiveness.
7. Discuss common barriers to maintaining the medication regimen.
8. Develop a teaching plan for clients and families for implementation of the prescribed therapeutic regimen.

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Although much remains unknown about what causes mental illness, science in the past 20 years has made great strides in helping us understand how the brain works and in presenting possible causes of why some brains work differently from others. Such advances in neurobiologic research are continually expanding the knowledge base in the field of psychiatry and are greatly influencing clinical practice. The psychiatric–mental health nurse must have a basic understanding of how the brain functions and of the current theories regarding mental illness. This chapter includes an overview of the major anatomic structures of the nervous system and how they work—the neurotransmission process. It presents the major current neurobiologic theories regarding what causes mental illness, including genetics and heredity, stress and the immune system, and infectious agents.

The use of medications to treat mental illness (**psychopharmacology**) is related to these neurobiologic theories. These medications directly affect the central nervous system (CNS) and, subsequently, behavior, perceptions, thinking, and emotions. This chapter discusses five categories of drugs used to treat mental illness, including their mechanisms of action, their side effects, and the roles of the nurse in administration and client teaching. Although pharmacologic interventions are the most effective treatment for many psychiatric disorders, adjunctive therapies, such as cognitive and behavioral therapies, family therapy, and psychotherapy, greatly enhance the success of treatment and the client's outcome. Chapter 3 discusses these psychosocial modalities.

THE NERVOUS SYSTEM AND HOW IT WORKS

Central Nervous System

The CNS is composed of the brain, the spinal cord, and associated nerves that control voluntary acts. Structurally, the brain consists of the cerebrum, cerebellum, brain stem, and limbic system. Figures 2.1 and 2.2 show the locations of brain structures.

Cerebrum

The cerebrum is divided into two hemispheres; all lobes and structures are found in both halves except for the pineal body, or gland, which is located between the hemispheres. The pineal body is an endocrine gland that influences the activities of the pituitary gland, islets of Langerhans, parathyroids, adrenals, and gonads. The corpus callosum is a pathway connecting the two hemispheres and coordinating their functions. The left hemisphere controls the right side of the body and is the center for logical reasoning and analytic functions such as reading, writing, and mathematical tasks. The right hemisphere controls the left side of the body and is the center for creative thinking, intuition, and artistic abilities.

The cerebral hemispheres are divided into four lobes: frontal, parietal, temporal, and occipital. Some functions of the lobes are distinct; others are integrated. The frontal lobes control the organization of thought, body movement, memories, emotions, and moral behavior. The integration of all this information regulates arousal, focuses attention, and enables problem-solving and decision making. Abnormalities in the frontal lobes are associated with schizophrenia, attention deficit hyperactivity disorder (ADHD), and dementia. The parietal lobes interpret sensations of taste and touch and assist in spatial orientation. The temporal lobes are centers for the senses of smell and hearing and for memory and emotional expression. The occipital lobes assist in coordinating language generation and visual interpretation, such as depth perception.

Cerebellum

The cerebellum is located below the cerebrum and is the center for coordination of movements and postural adjustments.

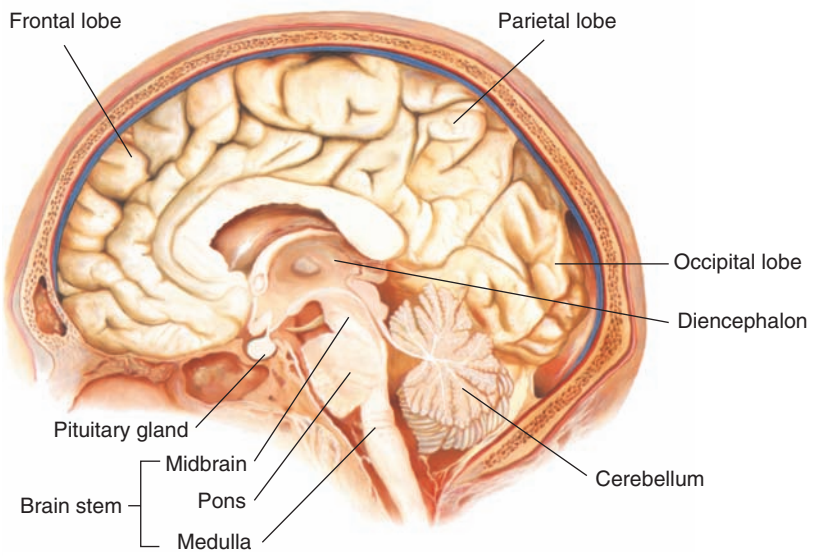


Figure 2.1. Anatomy of the brain.

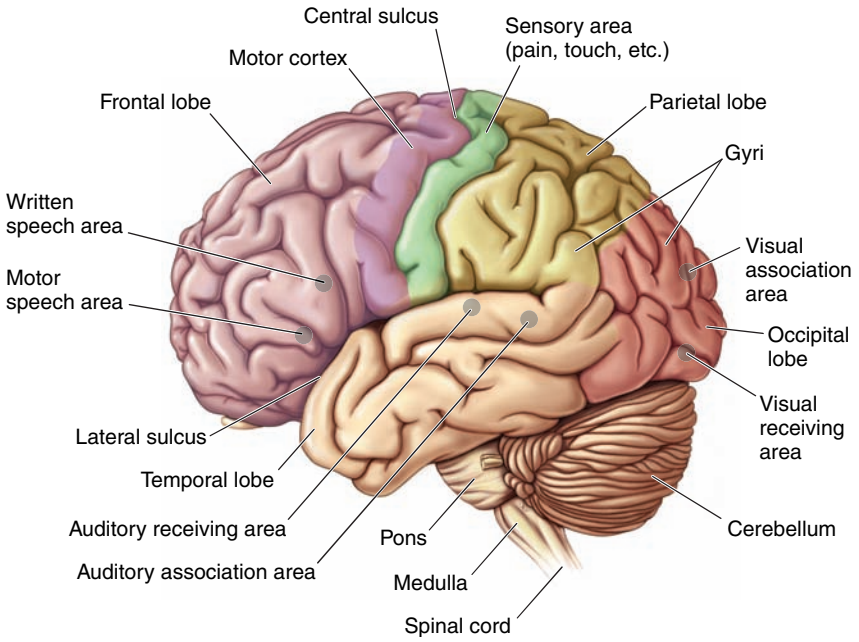


Figure 2.2. The brain and its structures.

It receives and integrates information from all areas of the body, such as the muscles, joints, organs, and other components of the CNS. Research has shown that inhibited transmission of dopamine, a neurotransmitter, in this area is associated with the lack of smooth coordinated movements in diseases such as Parkinson's disease and dementia.

Brain Stem

The brain stem includes the midbrain, pons, and medulla oblongata and the nuclei for cranial nerves III through XII. The medulla, located at the top of the spinal cord, contains vital centers for respiration and cardiovascular functions. Above the medulla and in front of the cerebrum, the pons bridges the gap both structurally and functionally, serving as a primary motor pathway. The midbrain connects the pons and cerebellum with the cerebrum. It measures only 0.8 inches (2 cm) long and includes most of the reticular activating system and the extrapyramidal system. The reticular activating system influences motor activity, sleep, consciousness, and awareness. The extrapyramidal system relays information about movement and coordination from the brain to the spinal nerves. The locus ceruleus, a small group of norepinephrine-producing neurons in the brain stem, is associated with stress, anxiety, and impulsive behavior.

Limbic System

The **limbic system** is an area of the brain located above the brain stem that includes the thalamus, hypothalamus, hippocampus, and amygdala (although some sources differ regarding the structures this system includes). The thalamus regulates activity, sensation, and emotion. The hypothalamus is involved in temperature regulation, appetite control, endocrine function, sexual drive, and impulsive behavior associated with feelings of anger, rage, or excitement. The hippocampus and amygdala are involved in emotional arousal and memory. Disturbances in the limbic system have been implicated in a variety of mental illnesses, such as the memory loss that accompanies dementia and the poorly controlled emotions and impulses seen with psychotic or manic behavior.

Neurotransmitters

Approximately 100 billion brain cells form groups of neurons, or nerve cells, that are arranged in networks. These neurons communicate information with one another by sending electrochemical messages from neuron to neuron, a process called *neurotransmission*. These electrochemical messages pass from the dendrites (projections from the cell body), through the soma or cell body, down the axon (long extended structures), and across the synapses (gaps between cells) to the dendrites of the next neuron. In the nervous system, the electrochemical messages cross the synapses between neural cells by way of special chemical messengers called neurotransmitters.

Neurotransmitters are the chemical substances manufactured in the neuron that aid in the transmission of information throughout the body. They either excite or stimulate an action in the cells (excitatory) or inhibit or stop an action (inhibitory). These neurotransmitters fit into specific receptor cells embedded in the membrane of the dendrite, just like a certain key shape fits into a lock. After neurotransmitters are released into the synapse and relay the message to the receptor cells, they are either transported back from the synapse to the axon to be stored for later use (reuptake) or

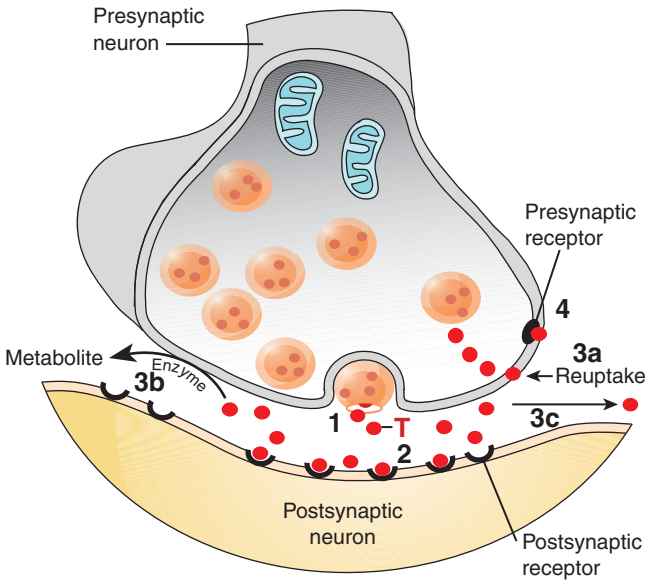


Figure 2.3. Schematic illustration of (1) neurotransmitter (T) release; (2) binding of transmitter to postsynaptic receptor; termination of transmitter action by (3a) reuptake of transmitter into the presynaptic terminal, (3b) enzymatic degradation, or (3c) diffusion away from the synapse; and (4) binding of transmitter to presynaptic receptors for feedback regulation of transmitter release.

metabolized and inactivated by enzymes, primarily monoamine oxidase (MAO) (Figure 2.3).

These neurotransmitters are necessary in just the right proportions to relay messages across the synapses. Studies are beginning to show differences in the amount of some neurotransmitters available in the brains of people with certain mental disorders compared with people who have no signs of mental illness (Figure 2.4).

Major neurotransmitters have been found to play a role in psychiatric illnesses as well as in the actions and side effects of psychotropic drugs. Table 2.1 lists the major neurotransmitters and their actions and effects. Dopamine and serotonin have received the most attention in terms of the study and treatment of psychiatric disorders (Tecott & Smart, 2005). The following sections discuss the major neurotransmitters associated with mental disorders.

Dopamine

Dopamine, a neurotransmitter located primarily in the brain stem, has been found to be involved in the control of complex movements, motivation, cognition, and regulation of emotional responses. It is generally excitatory and is synthesized from tyrosine, a dietary amino acid. Dopamine is implicated in schizophrenia and other psychoses as well as in movement disorders such as Parkinson's disease. Antipsychotic medications work by blocking dopamine receptors and reducing dopamine activity.

Norepinephrine and Epinephrine

Norepinephrine, the most prevalent neurotransmitter in the nervous system, is located primarily in the brain stem and plays a role in changes in attention, learning and memory, sleep and wakefulness, and mood regulation. Norepinephrine and its derivative, **epinephrine**, are also known as noradrenaline and adrenaline, respectively. Excess norepinephrine has been implicated in several anxiety disorders; deficits may contribute to memory loss, social withdrawal, and depression. Some antidepressants block the reuptake of norepinephrine, whereas others inhibit MAO from metabolizing it. Epinephrine has limited distribution in the brain but controls the fight-or-flight response in the peripheral nervous system.

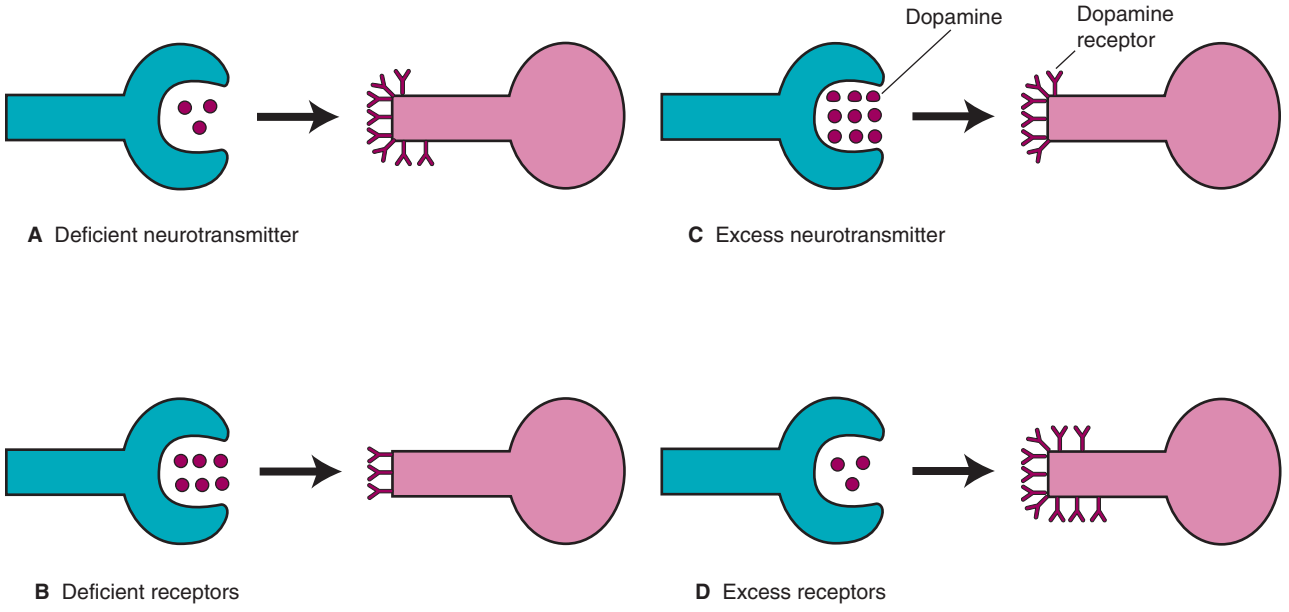


Figure 2.4. Abnormal neurotransmission causing some mental disorders because of excess transmission or excess responsiveness of receptors.

Table 2.1 MAJOR NEUROTRANSMITTERS

Type	Mechanism of Action	Physiologic Effects
Dopamine	Excitatory	Controls complex movements, motivation, cognition; regulates emotional response
Norepinephrine (noradrenaline)	Excitatory	Causes changes in attention, learning and memory, sleep and wakefulness, mood
Epinephrine (adrenaline)	Excitatory	Controls fight-or-flight response
Serotonin	Inhibitory	Controls food intake, sleep and wakefulness, temperature regulation, pain control, sexual behaviors, regulation of emotions
Histamine	Neuromodulator	Controls alertness, gastric secretions, cardiac stimulation, peripheral allergic responses
Acetylcholine	Excitatory or inhibitory	Controls sleep and wakefulness cycle; signals muscles to become alert
Neuropeptides	Neuromodulators	Enhance, prolong, inhibit, or limit the effects of principal neurotransmitters
Glutamate	Excitatory	Results in neurotoxicity if levels are too high
Gamma-aminobutyric acid (GABA)	Inhibitory	Modulates other neurotransmitters

Serotonin

Serotonin, a neurotransmitter found only in the brain, is derived from tryptophan, a dietary amino acid. The function of serotonin is mostly inhibitory, and it is involved in the control of food intake, sleep and wakefulness, temperature regulation, pain control, sexual behavior, and regulation of emotions. Serotonin plays an important role in anxiety and mood disorders and schizophrenia. It has been found to contribute to the delusions, hallucinations, and withdrawn behavior seen in schizophrenia. Some antidepressants block serotonin reuptake, thus leaving it available longer in the synapse, which results in improved mood.

Histamine

The role of histamine in mental illness is under investigation. It is involved in peripheral allergic responses, control of gastric secretions, cardiac stimulation, and alertness. Some psychotropic drugs block histamine, resulting in weight gain, sedation, and hypotension.

Acetylcholine

Acetylcholine is a neurotransmitter found in the brain, spinal cord, and peripheral nervous system, particularly at the neuromuscular junction of skeletal muscle. It can be excitatory or inhibitory. It is synthesized from dietary choline found in red meat and vegetables and has been found to affect the sleep–wake cycle and to signal muscles to become active. Studies have shown that people with Alzheimer's disease have decreased acetylcholine-secreting neurons, and people with myasthenia gravis (a muscular disorder in which impulses fail to pass the myoneural junction, which causes muscle weakness) have reduced acetylcholine receptors.

Glutamate

Glutamate is an excitatory amino acid that at high levels can have major neurotoxic effects. It has been implicated in the brain damage caused by stroke, hypoglycemia, sustained hypoxia or ischemia, and some degenerative diseases such as Huntington's or Alzheimer's.

Gamma-Aminobutyric Acid

Gamma-aminobutyric acid (γ-aminobutyric acid, or GABA), an amino acid, is the major inhibitory neurotransmitter in the brain and has been found to modulate other neurotransmitter systems rather than to provide a direct stimulus (Plata-Salaman, Shank, & Smith-Swintosky, 2005). Drugs that increase GABA function, such as benzodiazepines, are used to treat anxiety and to induce sleep.

BRAIN IMAGING TECHNIQUES

At one time, the brain could be studied only through surgery or autopsy. During the past 25 years, however, several brain imaging techniques have been developed that now allow visualization of the brain's structure and function. These techniques are useful for diagnosing some disorders of the brain and have helped to correlate certain areas of the brain with specific functions. Brain imaging techniques are also useful in research to find the causes of mental

Table 2.2 BRAIN IMAGING TECHNOLOGY

Procedure	Imaging Method	Results	Duration
Computed tomography (CT)	Serial x-rays of brain	Structural image	20–40 minutes
Magnetic resonance imaging (MRI)	Radio waves from brain detected from magnet	Structural image	45 minutes
Positron emission tomography (PET)	Radioactive tracer injected into bloodstream and monitored as client performs activities	Functional	2–3 hours
Single photon emission computed tomography (SPECT)	Same as PET	Functional	1–2 hours

disorders. Table 2.2 describes and compares several of these diagnostic techniques.

Types of Brain Imaging Techniques

Computed tomography (CT), also called computed axial tomography (CAT), is a procedure in which a precise x-ray beam takes cross-sectional images (slices) layer by layer. A computer reconstructs the images on a monitor and also stores the images on magnetic tape or film. CT can visualize the brain's soft tissues, so it is used to diagnose primary tumors, metastases, and effusions and to determine the size of the ventricles of the brain. Some people with schizophrenia have been shown to have enlarged ventricles; this finding is associated with a poorer prognosis and marked negative symptoms (Figure 2.5; see Chapter 14). The person undergoing CT must lie motionless on a stretcher-like table for about 20 to 40 minutes as the stretcher passes through a tunnel-like "ring" while the serial x-rays are taken.

In **magnetic resonance imaging (MRI)**, a type of body scan, an energy field is created with a huge magnet and radio waves. The energy field is converted to a visual image or scan. MRI produces more tissue detail and contrast than CT and can show blood flow patterns and tissue changes such as edema. It also can be used to measure the size and thickness of brain structures; persons with schizophrenia can have as much as 7% reduction in cortical thickness. The person undergoing an MRI must lie in a small, closed chamber and remain motionless during the procedure, which takes about 45 minutes. Those who feel claustrophobic or have increased anxiety may require sedation before the procedure. Clients with pacemakers or metal implants, such as heart valves or orthopedic devices, cannot undergo MRI.

More advanced imaging techniques, such as **positron emission tomography (PET)** and **single photon emission computed tomography (SPECT)**, are used to examine the function of the brain. Radioactive substances are injected into the blood; the flow of those substances in the brain is monitored as the client performs cognitive activities as instructed by the operator. PET uses two photons simultaneously; SPECT uses a single photon. PET provides

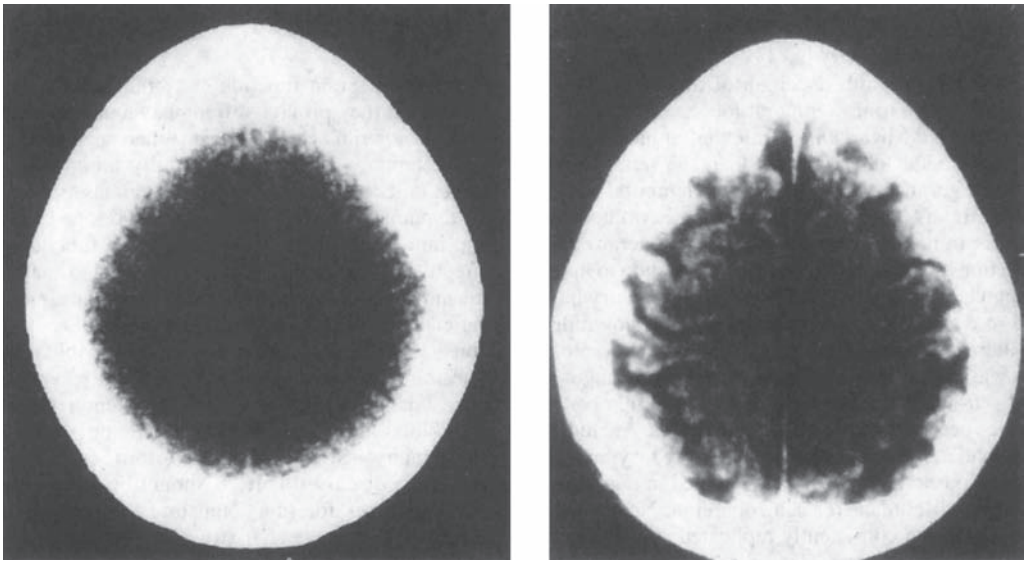


Figure 2.5. Example of computed tomography of the brain of a patient with schizophrenia (*right*) compared with a normal control (*left*).

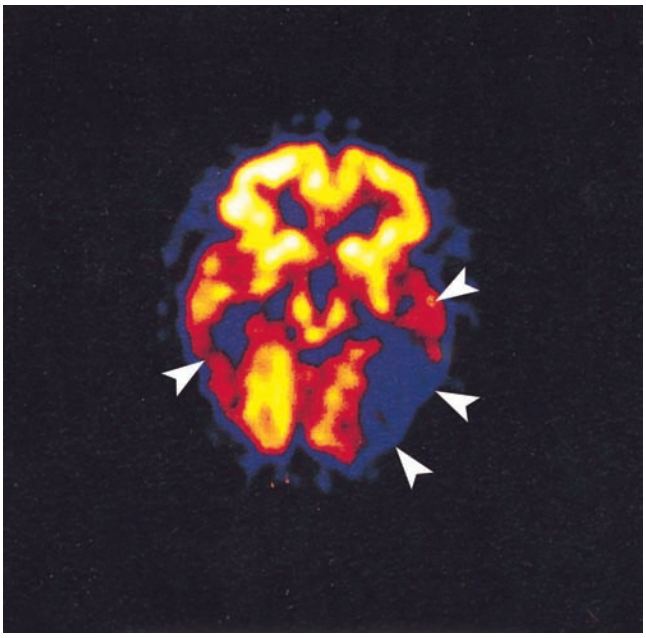


Figure 2.6. Example of axial (horizontal) positron emission tomography of a male patient with Alzheimer's disease, showing defects (*arrowheads*) in metabolism in the regions of the cerebral cortex of brain.

better resolution with sharper and clearer pictures and takes about 2 to 3 hours; SPECT takes 1 to 2 hours. PET and SPECT are used primarily for research, not for the diagnosis and treatment of clients with mental disorders (Fujita, Kugaya, & Innis, 2005; Vythilingam et al., 2005) (Figure 2.6). A recent breakthrough is the use of the chemical marker FDDNP with PET to identify the amyloid plaques and tangles of Alzheimer's disease in living clients; these conditions previously could be diagnosed only through autopsy. These scans have shown that clients with Alzheimer's disease have decreased glucose metabolism in the brain and decreased cerebral blood flow. Some persons with schizophrenia also demonstrate decreased cerebral blood flow.

Limitations of Brain Imaging Techniques

Although imaging techniques such as PET and SPECT have helped bring about tremendous advances in the study of brain diseases, they have some limitations:

- The use of radioactive substances in PET and SPECT limits the number of times a person can undergo these tests. There is the risk that the client will have an allergic reaction to the substances. Some clients may find receiving intravenous doses of radioactive material frightening or unacceptable.
- Imaging equipment is expensive to purchase and maintain, so availability can be limited. A PET camera costs about $2.5 million; a SPECT camera costs about $500,000.
- Some persons cannot tolerate these procedures because of fear or claustrophobia.
- Researchers are finding that many of the changes in disorders such as schizophrenia are at the molecular and chemical levels and cannot be detected with current imaging techniques (Fujita et al., 2005; Vythilingam et al., 2005).

NEUROBIOLOGIC CAUSES OF MENTAL ILLNESS

Genetics and Heredity

Unlike many physical illnesses that have been found to be hereditary, such as cystic fibrosis, Huntington's disease, and Duchenne's muscular dystrophy, the origins of mental disorders do not seem to be that simple. Current theories and studies indicate that several mental disorders may be linked to a specific gene or combination of genes but that the source is not solely genetic; nongenetic factors also play important roles.

To date, one of the most promising discoveries is the identification in 2007 of variations in the gene *SORL1* that may be a factor in late-onset Alzheimer's disease. Research is continuing in an attempt to find genetic links to other diseases such as schizophrenia and mood disorders. This is the focus of the ongoing research in the Human Genome Project, funded by the National Institutes of Health (NIH) and the U.S. Department of Energy. This international research project, started in 1988, is the largest of its kind. It has identified all human DNA and continues with research to discover the human characteristics and diseases each gene is related to (encoding). In addition, the project also addresses the ethical, legal, and social implications of human genetics research. This program (known as ELSI) focuses on privacy and fairness in the use and interpretation of genetic information, clinical integration of new genetic technologies, issues surrounding genetics research, and professional and public education (NIH, 2007). The researchers publish their results in the journal *Science;* further information can be obtained at www.genome.gov.

Three types of studies are commonly conducted to investigate the genetic basis of mental illness:

1. *Twin studies* are used to compare the rates of certain mental illnesses or traits in monozygotic (identical) twins, who have an identical genetic makeup, and dizygotic (fraternal) twins, who have a different genetic makeup. Fraternal twins have the same genetic similarities and differences as nontwin siblings.
2. *Adoption studies* are used to determine a trait among biologic versus adoptive family members.
3. *Family studies* are used to compare whether a trait is more common among first-degree relatives (parents, siblings, and children) than among more distant relatives or the general population.

Although some genetic links have been found in certain mental disorders, studies have not shown that these illnesses

are solely genetically linked. Investigation continues about the influence of inherited traits versus the influence of the environment—the "nature versus nurture" debate. The influence of environmental or psychosocial factors is discussed in Chapter 3.

Stress and the Immune System (Psychoimmunology)

Researchers are following many avenues to discover possible causes of mental illness. **Psychoimmunology**, a relatively new field of study, examines the effect of psychosocial stressors on the body's immune system. A compromised immune system could contribute to the development of a variety of illnesses, particularly in populations already genetically at risk. So far, efforts to link a specific stressor with a specific disease have been unsuccessful.

Infection as a Possible Cause

Some researchers are focusing on infection as a cause of mental illness. Most studies involving viral theories have focused on schizophrenia, but so far none has provided specific or conclusive evidence. Theories that are being developed and tested include the existence of a virus that has an affinity for tissues of the CNS, the possibility that a virus may actually alter human genes, and maternal exposure to a virus during critical fetal development of the nervous system.

Swedo and Grant (2005) studied the relation of streptococcal bacteria and obsessive–compulsive disorder (OCD) and tics. They found enlarged basal ganglia, indicating a possible autoimmune response to streptococcal infection. When blood plasma (high in streptococcal antibodies) was replaced by transfusion with healthy donor plasma, the incidence of tics decreased by 50%, and other OCD symptoms were reduced by 60%. Studies such as this are promising in discovering a link between infection and mental illness.

THE NURSE'S ROLE IN RESEARCH AND EDUCATION

Amid all the reports of research in these areas of neurobiology, genetics, and heredity, the implications for clients and their families are still not clear or specific. Often, reports in the media regarding new research and studies are confusing, contradictory, or difficult for clients and their families to understand. The nurse must ensure that clients and families are well informed about progress in these areas and must also help them to distinguish between facts and hypotheses. The nurse can explain if or how new research may affect a client's treatment or prognosis. The nurse is a good resource for providing information and answering questions.

Keeping clients informed

PSYCHOPHARMACOLOGY

Medication management is a crucial issue that greatly influences the outcomes of treatment for many clients with mental disorders. The following sections discuss several categories of drugs used to treat mental disorders (**psychotropic drugs**): antipsychotics, antidepressants, mood stabilizers, anxiolytics, and stimulants. Nurses should understand how these drugs work; their side effects, contraindications, and interactions; and the nursing interventions required to help clients manage medication regimens.

Several terms used in discussions of drugs and drug therapy are important for nurses to know. **Efficacy** refers to the maximal therapeutic effect that a drug can achieve. **Potency** describes the amount of the drug needed to achieve that maximum effect; low-potency drugs require higher dosages to achieve efficacy, whereas high-potency drugs achieve efficacy at lower dosages. **Half-life** is the time it takes for half of the drug to be removed from the bloodstream. Drugs with a shorter half-life may need to be given three or four times a day, but drugs with a longer half-life may be given once a day. The time that a drug needs to leave the body completely after it has been discontinued is about five times its half-life.

The U.S. Food and Drug Administration (FDA) is responsible for supervising the testing and marketing of

medications for public safety. These activities include clinical drug trials for new drugs and monitoring the effectiveness and side effects of medications. The FDA approves each drug for use in a particular population and for specific diseases. At times, a drug will prove effective for a disease that differs from the one involved in original testing and FDA approval. This is called **off-label use.** An example is some anticonvulsant drugs (approved to prevent seizures) that are prescribed for their effects in stabilizing the moods of clients with bipolar disorder (off-label use). The FDA also monitors the occurrence and severity of drug side effects. When a drug is found to have serious or life-threatening side effects, even if such side effects are rare, the FDA may issue a **black box warning.** This means that package inserts must have a highlighted box, separate from the text, which contains a warning about the serious or life-threatening side effects. Several psychotropic medications discussed later in this chapter carry black box warnings.

Principles That Guide Pharmacologic Treatment

The following are several principles that guide the use of medications to treat psychiatric disorders:

- A medication is selected based on its effect on the client's target symptoms such as delusional thinking, panic attacks, or hallucinations. The medication's effectiveness is evaluated largely by its ability to diminish or eliminate the target symptoms.
- Many psychotropic drugs must be given in adequate dosages for some time before their full effect is realized. For example, tricyclic antidepressants can require 4 to 6 weeks before the client experiences optimal therapeutic benefit.
- The dosage of medication often is adjusted to the lowest effective dosage for the client. Sometimes a client may need higher dosages to stabilize his or her target symptoms, whereas lower dosages can be used to sustain those effects over time.
- As a rule, older adults require lower dosages of medications than do younger clients to experience therapeutic effects. It also may take longer for a drug to achieve its full therapeutic effect in older adults.
- Psychotropic medications often are decreased gradually (tapering) rather than abruptly. This is because of potential problems with **rebound** (temporary return of symptoms), recurrence of the original symptoms, or **withdrawal** (new symptoms resulting from discontinuation of the drug).
- Follow-up care is essential to ensure compliance with the medication regimen, to make needed adjustments in dosage, and to manage side effects.
- Compliance with the medication regimen often is enhanced when the regimen is as simple as possible in terms of both the number of medications prescribed and the number of daily doses.

Antipsychotic Drugs

Antipsychotic drugs, also known as *neuroleptics,* are used to treat the symptoms of psychosis, such as the delusions and hallucinations seen in schizophrenia, schizoaffective disorder, and the manic phase of bipolar disorder. Off-label uses of antipsychotics include treatment of anxiety and insomnia; aggressive behavior; and delusions, hallucinations, and other disruptive behaviors that sometimes accompany Alzheimer's disease. Antipsychotic drugs work by blocking receptors of the neurotransmitter dopamine. They have been in clinical use since the 1950s. They are the primary medical treatment for schizophrenia and also are used in psychotic episodes of acute mania, psychotic depression, and drug-induced psychosis. Clients with dementia who have psychotic symptoms sometimes respond to low dosages of conventional antipsychotics. Atypical antipsychotics can increase mortality rates in elderly clients with dementia-related psychosis. Short-term therapy with antipsychotics may be useful for transient psychotic symptoms such as those seen in some clients with borderline personality disorder.

Table 2.3 lists available dosage forms, usual daily oral dosages, and extreme dosage ranges for conventional and atypical antipsychotic drugs. The low end of the extreme range typically is used with older adults or children with psychoses, aggression, or extreme behavior management problems.

Mechanism of Action

The major action of all antipsychotics in the nervous system is to block receptors for the neurotransmitter dopamine; however, the therapeutic mechanism of action is only partially understood. Dopamine receptors are classified into subcategories (D1, D2, D3, D4, and D5), and D2, D3, and D4 have been associated with mental illness. The typical antipsychotic drugs are potent antagonists (blockers) of D2, D3, and D4. This makes them effective in treating target symptoms but also produces many extrapyramidal side effects (discussion to follow) because of the blocking of the D2 receptors. Newer, atypical antipsychotic drugs, such as clozapine (Clozaril), are relatively weak blockers of D2, which may account for the lower incidence of extrapyramidal side effects. In addition, atypical antipsychotics inhibit the reuptake of serotonin, as do some of the antidepressants, increasing their effectiveness in treating the depressive aspects of schizophrenia. Paliperidone (Invega) is the newest atypical antipsychotic, gaining approval for distribution in the United States in January 2007. It is chemically similar to risperidone (Risperdal); however, it is an extended-release preparation. This means the client can take one daily dose in most cases, which may be a factor in increased compliance.

A new generation of antipsychotics, called dopamine system stabilizers, is being developed. These drugs are thought to stabilize dopamine output; that is, they preserve or enhance dopaminergic transmission when it is too low and reduce it when it is too high. This results in control of

Table 2.3 ANTIPSYCHOTIC DRUGS

Generic (Trade) Name	Forms	Daily Dosage*	Extreme Dosage Ranges*
Conventional Antipsychotics			
Phenothiazines			
Chlorpromazine (Thorazine)	T, L, INJ	200–1,600	25–2,000
Perphenazine (Trilafon)	T, L, INJ	16–32	4–64
Fluphenazine (Prolixin)	T, L, INJ	2.5–20	1–60
Thioridazine (Mellaril)	T, L	200–600	40–800
Mesoridazine (Serentil)	T, L, INJ	75–300	30–400
Trifluoperazine (Stelazine)	T, L, INJ	6–50	2–80
Thioxanthene			
Thiothixene (Navane)	C, L, INJ	6–30	6–60
Butyrophenones			
Haloperidol (Haldol)	T, L, INJ	2–20	1–100
Droperidol (Inapsine)	INJ	2.5	
Dibenzazepine			
Loxapine (Loxitane)	C, L, INJ	60–100	30–250
Dihydroindolone			
Molindone (Moban)	T, L	50–100	15–250
Atypical Antipsychotics			
Clozapine (Clozaril)	T	150–500	75–700
Fazclo (clozapine)	DT	150–500	75–700
Risperidone (Risperdal)	T, L, DT	2–8	1–16
Olanzapine (Zyprexa)	T	5–15	5–20
Quetiapine (Seroquel)	T	300–600	200–750
Ziprasidone (Geodon)	C, INJ	40–160	20–200
Paliperidone (Invega)	T	6	3–12
New Generation Antipsychotic			
Aripiprazole (Abilify)	T	15–30	10–40

*Values are in milligrams per day for oral doses only.

T, tablet; C, capsule; L, liquid for oral use; INJ, injection for IM (usually PRN) use; DT, orally disintegrating tablet.

symptoms without some of the side effects of other antipsychotic medications. Aripiprazole (Abilify), the first drug of this type, was approved for use in November 2002. In clinical trials, the most common side effects were headache, anxiety, and nausea.

Four antipsychotics are available in **depot injection**, a time-release form of medication for maintenance therapy. Two conventional antipsychotics use sesame oil as the vehicle for these injections, so the medication is absorbed slowly over time; thus, less frequent administration is needed to maintain the desired therapeutic effects. Prolixin (decanoate fluphenazine) has a duration of 7 to 28 days, and Haldol (decanoate haloperidol) has a duration of 4 weeks. After the client's condition is stabilized with oral doses of these medications, administration by depot injection is required every 2 to 4 weeks to maintain the therapeutic effect. Risperidone (Risperdal Consta) Paliperidone (Invega Sustenna), atypical antipsychotics, encapsulates active medication into polymer-based microspheres that degrade slowly in the body, gradually releasing the drug at a controlled rate. Risperdal Consta, 25 mg, is given every 2 weeks. Paliperidone (Invega Sustenna) 117mg is given every 4 weeks.

WARNING ⬢ Atypical Antipsychotics

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk for death. Causes of death were varied, but most of the deaths appeared to be either cardiovascular or infectious in nature.

Side Effects

Extrapyramidal Side Effects. Extrapyramidal symptoms (EPS), serious neurologic symptoms, are the major side effects of antipsychotic drugs. They include acute dystonia, pseudoparkinsonism, and akathisia. Although often collectively referred to as EPS, each of these reactions has distinct features. One client can experience all the reactions in the same course of therapy, which makes distinguishing among them difficult. Blockade of D2 receptors in the midbrain region of the brain stem is responsible for the development of EPS. Conventional antipsychotic drugs cause a greater incidence of EPS than do atypical

antipsychotic drugs, with ziprasidone (Geodon) rarely causing EPS (Daniel, Copeland, & Tamminga, 2006).

WARNING Geodon

Contraindicated in patients with a known history of QT prolongation, recent myocardial infarction, or uncompensated heart failure, it should not be used with other QT-prolonging drugs.

Therapies for acute dystonia, pseudoparkinsonism, and akathisia are similar and include lowering the dosage of the antipsychotic, changing to a different antipsychotic, or administering anticholinergic medication (discussion to follow). Whereas anticholinergic drugs also produce side effects, atypical antipsychotic medications are often prescribed because the incidence of EPS side effects associated with them is decreased.

Acute **dystonia** includes acute muscular rigidity and cramping, a stiff or thick tongue with difficulty swallowing, and, in severe cases, laryngospasm and respiratory difficulties. Dystonia is most likely to occur in the first week of treatment, in clients younger than 40 years, in males, and in those receiving high-potency drugs such as haloperidol and thiothixene. Spasms or stiffness in muscle groups can produce *torticollis* (twisted head and neck), *opisthotonus* (tightness in the entire body with the head back and an arched neck), or *oculogyric crisis* (eyes rolled back in a locked position). Acute dystonic reactions can be painful and frightening for the client. Immediate treatment with anticholinergic drugs, such as intramuscular benztropine mesylate (Cogentin) or intramuscular or intravenous diphenhydramine (Benadryl), usually brings rapid relief.

Table 2.4 lists the drugs, and their routes and dosages, used to treat EPS. The addition of a regularly scheduled oral anticholinergic such as benztropine may allow the client to continue taking the antipsychotic drug with no further dystonia. Recurrent dystonic reactions would necessitate a lower dosage or a change in the antipsychotic drug. Assessment of EPS using the Simpson–Angus rating scale is discussed further in Chapter 14.

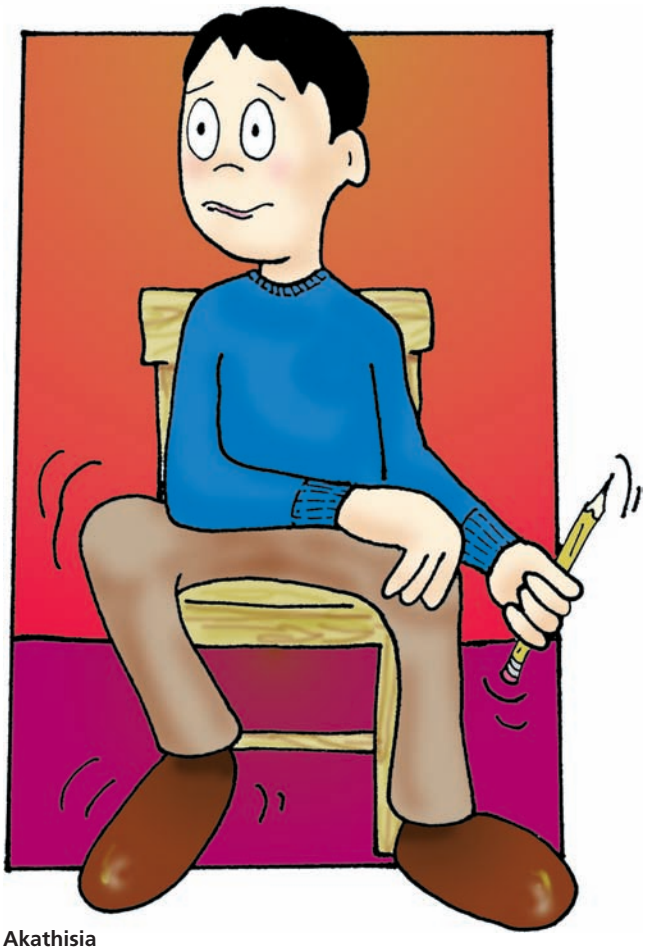
Drug-induced parkinsonism, or **pseudoparkinsonism**, is often referred to by the generic label of EPS. Symptoms resemble those of Parkinson's disease and include a stiff, stooped posture; mask-like facies; decreased arm swing; a shuffling, festinating gait (with small steps); cogwheel rigidity (ratchet-like movements of joints); drooling; tremor; bradycardia; and coarse pill-rolling movements of the thumb and fingers while at rest. Parkinsonism is treated by changing to an antipsychotic medication that has a lower incidence of EPS or by adding an oral anticholinergic agent or amantadine, which is a dopamine agonist that increases transmission of dopamine blocked by the antipsychotic drug.

Akathisia is reported by the client as an intense need to move about. The client appears restless or anxious and agitated, often with a rigid posture or gait and a lack of spontaneous gestures. This feeling of internal restlessness and the inability to sit still or rest often leads clients to discontinue their antipsychotic medication. Akathisia can be treated by a change in antipsychotic medication or by the addition of an oral agent such as a beta-blocker, anticholinergic, or benzodiazepine.

Neuroleptic Malignant Syndrome. **Neuroleptic malignant syndrome (NMS)** is a potentially fatal idiosyncratic reaction to an antipsychotic (or neuroleptic) drug. Although the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision* (American Psychiatric Association, 2000) notes that the death rate from this syndrome has been reported at 10% to 20%, those figures may have resulted from biased reporting; the reported rates are now decreasing. The major symptoms of NMS are rigidity; high fever; autonomic instability such as unstable blood pressure, diaphoresis, and pallor; delirium; and elevated levels of enzymes, particularly creatine phosphokinase. Clients with NMS usually are confused and often mute; they may fluctuate from agitation to stupor. All antipsychotics seem to have the potential to cause NMS, but high dosages of

Table 2.4 DRUGS USED TO TREAT EXTRAPYRAMIDAL SIDE EFFECTS

Generic (Trade) Name	Oral Dosages (mg)	IM/IV Doses (mg)	Drug Class
Amantadine (Symmetrel)	100 bid or tid	—	Dopaminergic agonist
Benztropine (Cogentin)	1–3 bid	1–2	Anticholinergic
Biperiden (Akineton)	2 tid–qid	2	Anticholinergic
Diazepam (Valium)	5 tid	5–10	Benzodiazepine
Diphenhydramine (Benadryl)	25–50 tid or qid	25–50	Antihistamine
Lorazepam (Ativan)	1–2 tid	—	Benzodiazepine
Procyclidine (Kemadrin)	2.5–5 tid	—	Anticholinergic
Propranolol (Inderal)	10–20 tid; up to 40 qid	—	Beta-blocker
Trihexyphenidyl (Artane)	2–5 tid	—	Anticholinergic



Akathisia

high-potency drugs increase the risk. NMS most often occurs in the first 2 weeks of therapy or after an increase in dosage, but it can occur at any time.

Dehydration, poor nutrition, and concurrent medical illness all increase the risk for NMS. Treatment includes immediate discontinuance of all antipsychotic medications and the institution of supportive medical care to treat dehydration and hyperthermia until the client's physical condition stabilizes. After NMS, the decision to treat the client with other antipsychotic drugs requires full discussion between the client and the physician to weigh the relative risks against the potential benefits of therapy.

Tardive Dyskinesia. **Tardive dyskinesia (TD)**, a syndro me of permanent involuntary movements, is most commonly caused by the long-term use of conventional antipsychotic drugs. About 20% to 30% of patients on long-term treatment develop symptoms of TD (Sadock & Sadock, 2008). The pathophysiology is still unclear, and no effective treatment has been approved for general use. However, Woods, Saksa, Baker, Cohen, and Tek (2008) report success in treating TD with levetiracetam in clinical trials. The symptoms of TD include involuntary movements of the tongue, facial and neck muscles, upper and lower extremities, and truncal musculature. Tongue thrusting and protruding, lip smacking, blinking, grimacing, and other excessive unnecessary facial movements are characteristic. After it has developed, TD is irreversible, although decreasing or discontinuing antipsychotic medications can arrest its progression. Unfortunately, antipsychotic medications can mask the beginning symptoms of TD; that is, increased dosages of the antipsychotic medication cause the initial symptoms to disappear temporarily. As the symptoms of TD worsen, however, they "break through" the effect of the antipsychotic drug.

Preventing TD is one goal when administering antipsychotics. This can be done by keeping maintenance dosages as low as possible, changing medications, and monitoring the client periodically for initial signs of TD using a standardized assessment tool such as the Abnormal Involuntary Movement Scale (see Chapter 14). Clients who have already developed signs of TD but still need to take an antipsychotic medication often are given one of the atypical antipsychotic drugs that have not yet been found to cause or, therefore, worsen TD.

Anticholinergic Side Effects. **Anticholinergic side effects** often occur with the use of antipsychotics and include orthostatic hypotension, dry mouth, constipation, urinary hesitance or retention, blurred near vision, dry eyes, photophobia, nasal congestion, and decreased memory. These side effects usually decrease within 3 to 4 weeks but do not entirely remit. The client taking anticholinergic agents for EPS may have increased problems with anticholinergic side effects. Using calorie-free beverages or hard candy may alleviate dry mouth; stool softeners, adequate fluid intake, and the inclusion of grains and fruit in the diet may prevent constipation.

Other Side Effects. Antipsychotic drugs also increase blood prolactin levels. Elevated prolactin may cause breast enlargement and tenderness in men and women; diminished libido, erectile and orgasmic dysfunction, and menstrual irregularities; and increased risk for breast cancer, and may contribute to weight gain.

Weight gain can accompany most antipsychotic medications, but it is most likely with the atypical antipsychotic drugs, with ziprasidone (Geodon) being the exception. Weight increases are most significant with clozapine (Clozaril) and olanzapine (Zyprexa). Since 2004, the FDA has made it mandatory for drug manufacturers that atypical antipsychotics carry a warning of the increased risk for hyperglycemia and diabetes. Though the exact mechanism of this weight gain is unknown, it is associated with increased appetite, binge eating, carbohydrate craving, food preference changes, and decreased satiety in some clients. In addition, clients with a genetic predisposition for weight gain are at greater risk (Muller & Kennedy, 2006). Prolactin elevation may stimulate feeding centers, histamine antagonism stimulates appetite, and there may be an as yet undetermined interplay of multiple neurotransmitter and receptor interactions with resultant changes in appetite, energy intake, and feeding

behavior. Obesity is common in clients with schizophrenia, further increasing the risk for type 2 diabetes mellitus and cardiovascular disease (Newcomer & Haupt, 2006). In addition, clients with schizophrenia are less likely to exercise or eat low-fat nutritionally balanced diets; this pattern decreases the likelihood that they can minimize potential weight gain or lose excess weight. It is recommended that clients taking antipsychotics be involved in an educational program to control weight and decrease body mass index.

Most antipsychotic drugs cause relatively minor cardiovascular adverse effects such as postural hypotension, palpitations, and tachycardia. Certain antipsychotic drugs, such as thioridazine (Mellaril), droperidol (Inapsine), and mesoridazine (Serentil), also can cause a lengthening of the QT interval. A QT interval longer than 500 ms is considered

WARNING ⬣ Droperidol, Thioridazine, Mesoridazine

May lengthen the QT interval, leading to potentially life-threatening cardiac dysrhythmias or cardiac arrest.

dangerous and is associated with life-threatening dysrhythmias and sudden death. Though rare, the lengthened QT interval can cause torsade de pointes, a rapid heart rhythm of 150 to 250 beats per minute, resulting in a "twisted" appearance on the electrocardiogram; hence the name torsade de pointes (Glassman, 2005). Thioridazine and mesoridazine are used to treat psychosis; droperidol is most often used as an adjunct to anesthesia or to produce sedation. Sertindole (Serlect) was never approved in the United States to treat psychosis, but was used in Europe and was subsequently withdrawn from the market because of the number of cardiac dysrhythmias and deaths that it caused.

Clozapine produces fewer traditional side effects than do most antipsychotic drugs, but it has the potentially fatal side effect of agranulocytosis. This develops suddenly and is characterized by fever, malaise, ulcerative sore throat, and leukopenia. This side effect may not be manifested immediately and can occur up to 24 weeks after the initiation of therapy. Initially, clients needed to have a weekly white blood cell count (WBC) above 3,500 per mm^3 to obtain the next week's supply of clozapine. Currently, all clients must have weekly WBCs drawn for the first 6 months. If the WBC is 3,500 per mm^3 and the absolute neutrophil count (ANC) is 2,000 per mm^3, the client may have these labs monitored every 2 weeks for 6 months, and then every 4 weeks. This decreased monitoring is dependent on continuous therapy with clozapine. Any interruption in therapy requires a return to more frequent monitoring for a specified period of time. After clozapine has been discontinued, weekly monitoring of the WBC and ANC is required for 4 weeks.

WARNING ⬣ Clozapine

May cause agranulocytosis, a potentially life-threatening event. Clients who are being treated with clozapine must have a baseline WBC count and differential before initiation of treatment and a WBC count every week throughout treatment and for 4 weeks after discontinuation of clozapine.

Client Teaching

The nurse informs clients taking antipsychotic medication about the types of side effects that may occur and encourages clients to report such problems to the physician instead of discontinuing the medication. The nurse teaches the client methods of managing or avoiding unpleasant side effects and maintaining the medication regimen. Drinking sugar-free fluids and eating sugar-free hard candy ease dry mouth. The client should avoid calorie-laden beverages and candy because they promote dental caries, contribute to weight gain, and do little to relieve dry mouth. Methods to prevent or relieve constipation include exercising and increasing water and bulk-forming foods in the diet. Stool softeners are permissible, but the client should avoid laxatives. The use of sunscreen is recommended because photosensitivity can cause the client to sunburn easily.

Clients should monitor the amount of sleepiness or drowsiness they feel. They should avoid driving and performing other potentially dangerous activities until their response times and reflexes seem normal.

If the client forgets a dose of antipsychotic medication, he or she can take the missed dose if it is only 3 or 4 hours late. If the dose is more than 4 hours overdue or the next dose is due, the client can omit the forgotten dose. The nurse encourages clients who have difficulty remembering to take their medication to use a chart and to record doses when taken or to use a pillbox that can be prefilled with accurate doses for the day or week.

Antidepressant Drugs

Antidepressant drugs are primarily used in the treatment of major depressive illness, anxiety disorders, the depressed phase of bipolar disorder, and psychotic depression. Off-label uses of antidepressants include the treatment of chronic pain, migraine headaches, peripheral and diabetic neuropathies, sleep apnea, dermatologic disorders, panic disorder, and eating disorders. Although the mechanism of action is not completely understood, antidepressants somehow interact with the two neurotransmitters, norepinephrine and serotonin, that regulate mood, arousal, attention, sensory processing, and appetite.

Antidepressants are divided into four groups:

1. Tricyclic and the related cyclic antidepressants
2. Selective serotonin reuptake inhibitors (SSRIs)
3. MAO inhibitors (MAOIs)

4. Other antidepressants such as venlafaxine desvenlafaxine (Pristiq) (Effexor), bupropion (Wellbutrin), duloxetine (Cymbalta), trazodone (Desyrel), and nefazodone (Serzone).

Table 2.5 lists the dosage forms, usual daily dosages, and extreme dosage ranges.

The cyclic compounds became available in the 1950s and for years were the first choice of drugs to treat depression even though they cause varying degrees of sedation, orthostatic hypotension (drop in blood pressure on rising), and anticholinergic side effects. In addition, cyclic antidepressants are potentially lethal if taken in an overdose.

During that same period, the MAOIs were discovered to have a positive effect on people with depression. Although the MAOIs have a low incidence of sedation and anticholinergic effects, they must be used with extreme caution for several reasons:

- A life-threatening side effect, hypertensive crisis, may occur if the client ingests foods containing tyramine (an amino acid) while taking MAOIs.
- Because of the risk for potentially fatal drug interactions, MAOIs cannot be given in combination with other MAOIs, tricyclic antidepressants, meperidine (Demerol), CNS depressants, many antihypertensives, or general anesthetics.
- MAOIs are potentially lethal in overdose and pose a potential risk in clients with depression who may be considering suicide.

The SSRIs, first available in 1987 with the release of fluoxetine (Prozac), have replaced the cyclic drugs as the first choice in treating depression because they are equal in efficacy and produce fewer troublesome side effects. The SSRIs and clomipramine are effective in the treatment of OCD as well. Prozac Weekly is the first and only medication that can be given once a week as maintenance therapy for depression after the client has been stabilized on fluoxetine. It contains 90 mg of fluoxetine with an enteric coating that delays release into the bloodstream.

Table 2.5 ANTIDEPRESSANT DRUGS

Generic (Trade) Name	Forms	Usual Daily Dosages*	Extreme Dosage Ranges*
Selective Serotonin Reuptake Inhibitors			
Fluoxetine (Prozac)	C, L	20–60	10–80
Fluvoxamine (Luvox)	T	150–200	50–300
Paroxetine (Paxil)	T	20–40	10–50
Sertraline (Zoloft)	T	100–150	50–200
Citalopram (Celexa)	T, L	20–40	20–60
Escitalopram (Lexapro)	T	10–20	5–30
Cyclic Compounds			
Imipramine (Tofranil)	T, C, INJ	150–200	50–300
Desipramine (Norpramin)	T, C	150–200	50–300
Amitriptyline (Elavil)	T, INJ	150–200	50–300
Nortriptyline (Pamelor)	C, L	75–100	25–150
Doxepin (Sinequan)	C, L	150–200	25–300
Trimipramine (Surmontil)	C	150–200	50–300
Protriptyline (Vivactil)	T	15–40	10–60
Maprotiline (Ludiomil)	T	100–150	50–200
Mirtazapine (Remeron)	T	15–45	15–60
Amoxapine (Asendin)	T	150–200	50–250
Clomipramine (Anafranil)	C, INJ	150–200	50–250
Other Compounds			
Bupropion (Wellbutrin)	T	200–300	100–450
Venlafaxine (Effexor)	T, C	75–225	75–375
Desvenlafaxine (Pristiq)	T	50–100	50 every other day-400
Trazodone (Desyrel)	T	200–300	100–600
Nefazodone (Serzone)	T	300–600	100–600
Duloxetine (Cymbalta)	C	60	30–90
Monoamine Oxidase Inhibitors			
Phenelzine (Nardil)	T	45–60	15–90
Tranylcypromine (Parnate)	T	30–50	10–90
Isocarboxazid (Marplan)	T	20–40	10–60

*Values are in milligrams per day for oral doses only.

C, capsule; T, tablet; L, liquid; INJ, injection for IM use.

Preferred Drugs for Clients at High Risk for Suicide

Suicide is always a primary consideration when treating clients with depression. SSRIs, venlafaxine, nefazodone, and bupropion are often better choices for those who are potentially suicidal or highly impulsive because they carry no risk of lethal overdose, in contrast to the cyclic compounds and the MAOIs. However, SSRIs are effective only for mild and moderate depression. Evaluation of the risk for suicide must continue even after treatment with antidepressants is initiated. The client may feel more energized but still have suicidal thoughts, which increases the likelihood of a suicide attempt. Also, because it often takes weeks before the medications have a full therapeutic effect, clients may become discouraged and tired of waiting to feel better, which can result in suicidal behavior. There is an FDA-required warning for SSRIs and increased suicidal risk in children and adolescents.

Mechanism of Action

The precise mechanism by which antidepressants produce their therapeutic effects is not known, but much is known about their action on the CNS. The major interaction is with the monoamine neurotransmitter systems in the brain, particularly norepinephrine and serotonin. Both of these neurotransmitters are released throughout the brain and help to regulate arousal, vigilance, attention, mood, sensory processing, and appetite. Norepinephrine, serotonin, and dopamine are removed from the synapses after release by reuptake into presynaptic neurons. After reuptake, these three neurotransmitters are reloaded for subsequent release or metabolized by the enzyme MAO. The SSRIs block the reuptake of serotonin, the cyclic antidepressants and venlafaxine block the reuptake of norepinephrine primarily and block serotonin to some degree, and the MAOIs interfere with enzyme metabolism. This is not the complete explanation, however; the blockade of serotonin and norepinephrine reuptake and the inhibition of MAO occur in a matter of hours, whereas antidepressants are rarely effective until taken for several weeks. The cyclic compounds may take 4 to 6 weeks to be effective, MAOIs need 2 to 4 weeks for effectiveness, and SSRIs may be effective in 2 to 3 weeks. Researchers believe that the actions of these drugs are an "initiating event" and that eventual therapeutic effectiveness results when neurons respond more slowly, making serotonin available at the synapses (Lehne, 2006).

Side Effects of Selective Serotonin Reuptake Inhibitors

SSRIs have fewer side effects compared with the cyclic compounds. Enhanced serotonin transmission can lead to several common side effects such as anxiety, agitation, akathisia (motor restlessness), nausea, insomnia, and sexual dysfunction, specifically diminished sexual drive or difficulty achieving an erection or orgasm. In addition, weight gain is both an initial and ongoing problem during antidepressant therapy, although SSRIs cause less weight gain than other antidepressants. Taking medications with food usually can minimize nausea. Akathisia usually is treated with a beta-blocker such as propranolol (Inderal) or a benzodiazepine. Insomnia may continue to be a problem even if the client takes the medication in the morning; a sedative-hypnotic or low-dosage trazodone may be needed.

Less common side effects include sedation (particularly with paroxetine [Paxil]), sweating, diarrhea, hand tremor, and headaches. Diarrhea and headaches usually can be managed with symptomatic treatment. Sweating and continued sedation most likely indicate the need for a change to another antidepressant.

Side Effects of Cyclic Antidepressants

Cyclic compounds have more side effects than do SSRIs and the newer miscellaneous compounds. The individual medications in this category vary in terms of the intensity of side effects, but generally side effects fall into the same categories. The cyclic antidepressants block cholinergic receptors, resulting in anticholinergic effects such as dry mouth, constipation, urinary hesitancy or retention, dry nasal passages, and blurred near vision. More severe anticholinergic effects such as agitation, delirium, and ileus may occur, particularly in older adults. Other common side effects include orthostatic hypotension, sedation, weight gain, and tachycardia. Clients may develop tolerance to anticholinergic effects, but these side effects are common reasons that clients discontinue drug therapy. Clients taking cyclic compounds frequently report sexual dysfunction similar to problems experienced with SSRIs. Both weight gain and sexual dysfunction are cited as common reasons for noncompliance (Stahl, 2006).

Side Effects of Monoamine Oxidase Inhibitors

The most common side effects of MAOIs include daytime sedation, insomnia, weight gain, dry mouth, orthostatic hypotension, and sexual dysfunction. The sedation and insomnia are difficult to treat and may necessitate a change in medication. Of particular concern with MAOIs is the potential for a life-threatening hypertensive crisis if the client ingests food that contains tyramine or takes sympathomimetic drugs. Because the enzyme MAO is necessary to break down the tyramine in certain foods, its inhibition results in increased serum tyramine levels, causing severe hypertension, hyperpyrexia, tachycardia, diaphoresis, tremulousness, and cardiac dysrhythmias. Drugs that may cause potentially fatal interactions with MAOIs include SSRIs, certain cyclic compounds, buspirone (BuSpar), dextromethorphan, and opiate derivatives such as meperidine. The client must be able to follow a tyramine-free diet; Box 2.1 lists the foods to avoid.

Box 2.1 FOODS (CONTAINING TYRAMINE) TO AVOID WHEN TAKING MAOIs

- Mature or aged cheeses or dishes made with cheese, such as lasagna or pizza. All cheese is considered aged except cottage cheese, cream cheese, ricotta cheese, and processed cheese slices.
- Aged meats such as pepperoni, salami, mortadella, summer sausage, beef logs, meat extracts, and similar products. Make sure meat and chicken are fresh and have been properly refrigerated.
- Italian broad beans (fava), bean curd (tofu), banana peel, overripe fruit, and avocado.
- All tap beers and microbrewery beer. Drink no more than two cans or bottles of beer (including nonalcoholic beer) or 4 ounces of wine per day.
- Sauerkraut, soy sauce or soybean condiments, or marmite (concentrated yeast).
- Yogurt, sour cream, peanuts, Brewer's yeast, and monosodium glutamate (MSG).

Adapted from University of North Carolina Clinical Research Center (2004).

Studies are currently underway to determine whether a selegiline transdermal patch would be effective in treating depression without the risks of dietary tyramine and orally ingested MAOIs.

Side Effects of Other Antidepressants

Of the other or novel antidepressant medications, nefazodone, trazodone, and mirtazapine commonly cause sedation. Both nefazodone and trazodone commonly cause headaches. Nefazodone also can cause dry mouth and nausea. Bupropion and venlafaxine desvenlafaxine may cause loss of appetite, nausea, agitation, and insomnia. Venlafaxine also may cause dizziness, sweating, or sedation. Sexual dysfunction is much less common with the novel antidepressants, with one notable exception: Trazodone can cause priapism (a sustained and painful erection that necessitates immediate treatment and discontinuation of the drug). Priapism also may result in impotence.

WARNING ⬢ Nefazodone

May cause rare but potentially life-threatening liver damage, which could lead to liver failure.

WARNING ⬢ Bupropion

Can cause seizures at a rate four times that of other antidepressants. The risk for seizures increases when doses exceed 450 mg/day (400 mg SR); dose increases are sudden or in large increments; the client has a history of seizures, cranial trauma, excessive use of or withdrawal from alcohol, or addiction to opiates, cocaine, or stimulants; the client uses OTC stimulants or anorectics; or the client has diabetes being treated with oral hypoglycemics or insulin.

Drug Interactions

An uncommon but potentially serious drug interaction, called **serotonin syndrome** (or serotonergic syndrome), can result from taking an MAOI and an SSRI at the same time. It also can occur if the client takes one of these drugs too close to the end of therapy with the other. In other words, one drug must clear the person's system before initiation of therapy with the other. Symptoms include agitation, sweating, fever, tachycardia, hypotension, rigidity, hyperreflexia, and, in extreme reactions, even coma and death (Krishnan, 2006). These symptoms are similar to those seen with an SSRI overdose.

Client Teaching

Clients should take SSRIs first thing in the morning unless sedation is a problem; generally, paroxetine most often causes sedation. If the client forgets a dose of an SSRI, he or she can take it up to 8 hours after the missed dose. To minimize side effects, clients generally should take cyclic compounds at night in a single daily dose when possible. If the client forgets a dose of a cyclic compound, he or she should take it within 3 hours of the missed dose or omit the dose for that day. Clients should exercise caution when driving or performing activities requiring sharp, alert reflexes until sedative effects can be determined.

Clients taking MAOIs need to be aware that a life-threatening hyperadrenergic crisis can occur if they do not observe certain dietary restrictions. They should receive a written list of foods to avoid while taking MAOIs. The nurse should make clients aware of the risk for serious or even fatal drug interactions when taking MAOIs and instruct them not to take any additional medication, including over-the-counter preparations, without checking with the physician or pharmacist.

Mood-Stabilizing Drugs

Mood-stabilizing drugs are used to treat bipolar disorder by stabilizing the client's mood, preventing or minimizing the highs and lows that characterize bipolar illness, and treating acute episodes of mania. Lithium is the most established mood stabilizer; some anticonvulsant drugs, particularly carbamazepine (Tegretol) and valproic acid

(Depakote, Depakene), are effective mood stabilizers. Other anticonvulsants, such as gabapentin (Neurontin), topiramate (Topamax), oxcarbazepine (Trileptal), and lamotrigine (Lamictal), are also used for mood stabilization. Occasionally, clonazepam (Klonopin) also is used to treat acute mania. Clonazepam is included in the discussion of antianxiety agents.

WARNING ⬢ Lamotrigine

Can cause serious rashes requiring hospitalization, including Stevens–Johnson syndrome and, rarely, life-threatening toxic epidermal necrolysis. The risk for serious rashes is greater in children younger than 16 years.

Mechanism of Action

Although lithium has many neurobiologic effects, its mechanism of action in bipolar illness is poorly understood. Lithium normalizes the reuptake of certain neurotransmitters such as serotonin, norepinephrine, acetylcholine, and dopamine. It also reduces the release of norepinephrine through competition with calcium and produces its effects intracellularly rather than within neuronal synapses; it acts directly on G proteins and certain enzyme subsystems such as cyclic adenosine monophosphates and phosphatidylinositol. Lithium is considered a first-line agent in the treatment of bipolar disorder (Howland, 2007).

The mechanism of action for anticonvulsants is not clear because it relates to their off-label use as mood stabilizers. Valproic acid and topiramate are known to increase levels of the inhibitory neurotransmitter GABA. Both valproic acid and carbamazepine are thought to stabilize mood by inhibiting the **kindling process**. This can be described as the snowball-like effect seen when minor seizure activity seems to build up into more frequent and severe seizures. In seizure management, anticonvulsants raise the level of the threshold to prevent these minor seizures. It is suspected that this same kindling process also may occur in the development of full-blown mania with stimulation by more frequent, minor episodes. This may explain why anticonvulsants are effective in the treatment and prevention of mania as well (Plata-Salaman et al., 2005).

Dosage

Lithium is available in tablets, capsules, liquid, and a sustained-released form; no parenteral forms are available. The effective dosage of lithium is determined by monitoring serum lithium levels and assessing the client's clinical response to the drug. Daily dosages generally range from 900 to 3,600 mg; more importantly, the serum lithium level should be about 1.0 mEq/L. Serum lithium levels of less than 0.5 mEq/L are rarely therapeutic, and levels of more than 1.5 mEq/L are usually considered toxic. The lithium level should be monitored every 2 to 3 days while the therapeutic dosage is being determined; then, it should be monitored weekly. When the client's condition is stable, the level may need to be checked once a month or less frequently.

WARNING ⬢ Lithium

Toxicity is closely related to serum lithium levels and can occur at therapeutic doses. Facilities for serum lithium determinations are required to monitor therapy.

Carbamazepine is available in liquid, tablet, and chewable tablet forms. Dosages usually range from 800 to 1,200 mg/day; the extreme dosage range is 200 to 2,000 mg/day. Valproic acid is available in liquid, tablet, and capsule forms and as sprinkles with dosages ranging from 1,000 to 1,500 mg/day; the extreme dosage range is 750 to 3,000 mg/day. Serum drug levels, obtained 12 hours after the last dose of the medication, are monitored for therapeutic levels of both these anticonvulsants.

Side Effects

Common side effects of lithium therapy include mild nausea or diarrhea, anorexia, fine hand tremor, polydipsia, polyuria, a metallic taste in the mouth, and fatigue or lethargy. Weight gain and acne are side effects that occur later in lithium therapy; both are distressing for clients. Taking the medication with food may help with nausea, and the use of propranolol often improves the fine tremor. Lethargy and weight gain are difficult to manage or minimize and frequently lead to noncompliance.

Toxic effects of lithium are severe diarrhea, vomiting, drowsiness, muscle weakness, and lack of coordination. Untreated, these symptoms worsen and can lead to renal failure, coma, and death. When toxic signs occur, the drug should be discontinued immediately. If lithium levels exceed 3.0 mEq/L, dialysis may be indicated.

Side effects of carbamazepine and valproic acid include drowsiness, sedation, dry mouth, and blurred vision. In addition, carbamazepine may cause rashes and orthostatic hypotension, and valproic acid may cause weight gain, alopecia, and hand tremor. Topiramate causes dizziness,

WARNING ⬢ Valproic Acid and Its Derivatives

Can cause hepatic failure, resulting in fatality. Liver function tests should be performed before therapy and at frequent intervals thereafter, especially for the first 6 months. Can produce teratogenic effects such as neural tube defects (e.g., spina bifida). Can cause life-threatening pancreatitis in both children and adults. Can occur shortly after initiation or after years of therapy.

sedation, weight loss (rather than gain), and increased incidence of renal calculi (Stahl, 2006).

WARNING ⬢ Carbamazepine

Can cause aplastic anemia and agranulocytosis at a rate five to eight times greater than the general population. Pretreatment hematologic baseline data should be obtained and monitored periodically throughout therapy to discover lowered WBC or platelet counts.

Client Teaching

For clients taking lithium and the anticonvulsants, monitoring blood levels periodically is important. The time of the last dose must be accurate so that plasma levels can be checked 12 hours after the last dose has been taken. Taking these medications with meals minimizes nausea. The client should not attempt to drive until dizziness, lethargy, fatigue, or blurred vision has subsided.

Antianxiety Drugs (Anxiolytics)

Antianxiety drugs, or **anxiolytic drugs**, are used to treat anxiety and anxiety disorders, insomnia, OCD, depression, posttraumatic stress disorder, and alcohol withdrawal. Antianxiety drugs are among the most widely prescribed medications today. A wide variety of drugs from different classifications have been used in the treatment of anxiety and insomnia. Benzodiazepines have proved to be the most effective in relieving anxiety and are the drugs most frequently prescribed. Benzodiazepines also may be prescribed for their anticonvulsant and muscle relaxant effects. Buspirone is a nonbenzodiazepine often used for the relief of anxiety and therefore is included in this section. Other drugs such as propranolol, clonidine (Catapres), and hydroxyzine (Vistaril) that may be used to relieve anxiety are much less effective and are not included in this discussion.

Periodic blood levels

Mechanism of Action

Benzodiazepines mediate the actions of the amino acid GABA, the major inhibitory neurotransmitter in the brain. Because GABA receptor channels selectively admit the anion chloride into neurons, activation of GABA receptors hyperpolarizes neurons and thus is inhibitory. Benzodiazepines produce their effects by binding to a specific site on the GABA receptor. Buspirone is believed to exert its anxiolytic effect by acting as a partial agonist at serotonin receptors, which decreases serotonin turnover (Arniel & Mathew, 2007).

The benzodiazepines vary in terms of their half-lives, the means by which they are metabolized, and their effectiveness in treating anxiety and insomnia. Table 2.6 lists dosages, half-lives, and speed of onset after a single dose. Drugs with a longer half-life require less frequent dosing and produce fewer rebound effects between doses; however, they can accumulate in the body and produce "next-day sedation" effects. Conversely, drugs with a shorter half-life do not accumulate in the body or cause next-day sedation, but they do have rebound effects and require more frequent dosing.

Temazepam (Restoril), triazolam (Halcion), and flurazepam (Dalmane) are most often prescribed for sleep rather than for relief of anxiety. Diazepam (Valium), chlordiazepoxide (Librium), and clonazepam often are used to manage alcohol withdrawal as well as to relieve anxiety.

Side Effects

Although not a side effect in the true sense, one chief problem encountered with the use of benzodiazepines is their tendency to cause physical dependence. Significant discontinuation symptoms occur when the drug is stopped; these symptoms often resemble the original symptoms for which the client sought treatment. This is especially a problem for clients with long-term benzodiazepine use, such as those with panic disorder or generalized anxiety disorder. Psychological dependence on benzodiazepines is common: Clients fear the return of anxiety symptoms or believe they are incapable of handling anxiety without the drugs. This can lead to overuse or abuse of these drugs. Buspirone does not cause this type of physical dependence.

Table 2.6 ANTIANXIETY (ANXIOLYTIC) DRUGS

Generic (Trade) Name	Daily Dosage Range	Half-Life (h)	Speed of Onset
Benzodiazepines			
Alprazolam (Xanax)	0.75–1.5	12–15	Intermediate
Chlordiazepoxide (Librium)	15–100	50–100	Intermediate
Clonazepam (Klonopin)	1.5–20	18–50	Intermediate
Chlorazepate (Tranxene)	15–60	30–200	Fast
Diazepam (Valium)	4–40	30–100	Very fast
Flurazepam (Dalmane)	15–30	47–100	Fast
Lorazepam (Ativan)	2–8	10–20	Moderately slow
Oxazepam (Serax)	30–120	3–21	Moderately slow
Temazepam (Restoril)	15–30	9.5–20	Moderately fast
Triazolam (Halcion)	0.25–0.5	2–4	Fast
Nonbenzodiazepine			
Buspirone (BuSpar)	15–30	3–11	Very slow

The side effects most commonly reported with benzodiazepines are those associated with CNS depression, such as drowsiness, sedation, poor coordination, and impaired memory or clouded sensorium. When used for sleep, clients may complain of next-day sedation or a hangover effect. Clients often develop a tolerance to these symptoms, and they generally decrease in intensity. Common side effects from buspirone include dizziness, sedation, nausea, and headache (Arniel & Mathew, 2007).

Elderly clients may have more difficulty managing the effects of CNS depression. They may be more prone to falls from the effects on coordination and sedation. They also may have more pronounced memory deficits and may have problems with urinary incontinence, particularly at night.

Client Teaching

Clients need to know that antianxiety agents are aimed at relieving symptoms such as anxiety or insomnia but do not treat the underlying problems that cause the anxiety. Benzodiazepines strongly potentiate the effects of alcohol: One drink may have the effect of three drinks. Therefore, clients should not drink alcohol while taking benzodiazepines. Clients should be aware of decreased response time, slower reflexes, and possible sedative effects of these drugs when attempting activities such as driving or going to work.

Benzodiazepine withdrawal can be fatal. After the client has started a course of therapy, he or she should never discontinue benzodiazepines abruptly or without the supervision of the physician (Lehne, 2006).

Stimulants

Stimulant drugs, specifically amphetamines, were first used to treat psychiatric disorders in the 1930s for their pronounced effects of CNS stimulation. In the past, they were used to treat depression and obesity, but those uses are uncommon in current practice. Dextroamphetamine

No alcohol with psychotropic drugs

(Dexedrine) has been widely abused to produce a high or to remain awake for long periods. Today, the primary use of stimulants is for ADHD in children and adolescents, residual attention deficit disorder in adults, and narcolepsy (attacks of unwanted but irresistible daytime sleepiness that disrupt the person's life).

WARNING ⬢ Amphetamines

Potential for abuse is high. Administration for prolonged periods may lead to drug dependence.

The primary stimulant drugs used to treat ADHD are methylphenidate (Ritalin), amphetamine (Adderall), and dextroamphetamine (Dexedrine). Pemoline (Cylert) is infrequently used for ADHD because of the potential for liver problems. Of these drugs, methylphenidate accounts for 90% of the stimulant medication given to children for ADHD (Stahl, 2006). About 10% to 30% of clients with ADHD who do not respond adequately to the stimulant medications have been treated with antidepressants. In 2003, atomoxetine (Strattera), a selective norepinephrine reuptake inhibitor, was approved for the treatment of ADHD, becoming the first nonstimulant medication specifically designed and tested for ADHD.

WARNING ⬢ Methylphenidate

Use with caution in emotionally unstable clients such as those with alcohol or drug dependence because they may increase the dosage on their own. Chronic abuse can lead to marked tolerance and psychic dependence.

WARNING ⬢ Pemoline

Can cause life-threatening liver failure, which can result in death or require liver transplantation in 4 weeks from the onset of symptoms. The physician should obtain written consent before the initiation of this drug.

Mechanism of Action

Amphetamines and methylphenidate are often termed *indirectly acting amines* because they act by causing release of the neurotransmitters (norepinephrine, dopamine, and serotonin) from presynaptic nerve terminals as opposed to having direct agonist effects on the postsynaptic receptors. They also block the reuptake of these neurotransmitters. Methylphenidate produces milder CNS stimulation than amphetamines; pemoline primarily affects dopamine and therefore has less effect on the sympathetic nervous system. It was originally thought that the use of methylphenidate and pemoline to treat ADHD in children produced the reverse effect of most stimulants—a calming or slowing of activity in the brain. However, this is not the case; the inhibitory centers in the brain are stimulated, so the child has greater abilities to filter out distractions and manage his or her own behavior. Atomoxetine helps to block the reuptake of norepinephrine into neurons, thereby leaving more of the neurotransmitter in the synapse to help convey electrical impulses in the brain.

Dosage

For the treatment of narcolepsy in adults, both dextroamphetamine and methylphenidate are given in divided doses totaling 20 to 200 mg/day. The higher dosages may be needed because adults with narcolepsy develop tolerance to the stimulants and so require more medication to sustain improvement. Stimulant medications are also available in sustained-release preparations so that once-a-day dosing is possible. Tolerance is not seen in persons with ADHD.

The dosages used to treat ADHD in children vary widely depending on the physician; the age, weight, and behavior of the child; and the tolerance of the family for the child's behavior. Table 2.7 lists the usual dosage ranges for these stimulants. Arrangements must be made for the school nurse or another authorized adult to administer the stimulants to the child at school. Sustained-released preparations eliminate the need for additional dosing at school.

Side Effects

The most common side effects of stimulants are anorexia, weight loss, nausea, and irritability. The client should avoid caffeine, sugar, and chocolate, which may worsen these symptoms. Less common side effects include dizziness, dry mouth, blurred vision, and palpitations. The most common long-term problem with stimulants is the growth and weight suppression that occurs in some children. This can usually be prevented by taking "drug holidays" on weekends and holidays or during summer vacation, which helps to restore normal eating and growth patterns. Atomoxetine can cause decreased appetite, nausea, vomiting, fatigue, or upset stomach.

Client Teaching

The potential for abuse exists with stimulants, but this is seldom a problem in children. Taking doses of stimulants after meals may minimize anorexia and nausea. Caffeine-free beverages are suggested; clients should avoid chocolate and excessive sugar. Most important is to keep the medication out of the child's reach because as little as a 10-day supply can be fatal.

Disulfiram (Antabuse)

Disulfiram is a sensitizing agent that causes an adverse reaction when mixed with alcohol in the body. This agent's only use is as a deterrent to drinking alcohol in persons receiving treatment for alcoholism. It is useful for

Table 2.7 DRUGS USED TO TREAT ATTENTION DEFICIT HYPERACTIVITY DISORDER

Generic (Trade) Name	Dosage
Stimulants	
Methylphenidate (Ritalin)	Adults: 20–200 mg/day, orally, in divided doses Children: 10–60 mg/day, orally, in 2–4 divided doses
Sustained release (Ritalin-SR, Concerta, Metadate-CD)	20–60 mg/day, orally, single dose
Transdermal patch (Daytrana)	Adults and Children: 15 mg patch worn for 9 hours per day
Dextroamphetamine (Dexedrine)	Adults: 20–200 mg/day, orally, in divided doses Children: 5–40 mg/day, orally, in 2 or 3 divided doses
Sustained release (Dexedrine-SR)	10–30 mg/day, orally, single dose
Amphetamine (Adderall)	5–40 mg/day, orally, in divided doses
Sustained release (Adderall-SR)	10–30 mg/day, orally, single dose
Pemoline (Cylert)	Children: 37.5–112.5 mg/day, orally, single dose in the morning
Selective Norepinephrine Reuptake Inhibitor	
Atomoxetine (Strattera)	0.5–1.5 mg/kg/day, orally, single dose

persons who are motivated to abstain from drinking and who are not impulsive. Five to ten minutes after a person taking disulfiram ingests alcohol, symptoms begin to appear: facial and body flushing from vasodilation, a throbbing headache, sweating, dry mouth, nausea, vomiting, dizziness, and weakness. In severe cases, there may be chest pain, dyspnea, severe hypotension, confusion, and even death. Symptoms progress rapidly and last from 30 minutes to 2 hours. Because the liver metabolizes disulfiram, it is most effective in persons whose liver enzyme levels are within or close to normal range.

Disulfiram inhibits the enzyme aldehyde dehydrogenase, which is involved in the metabolism of ethanol. Acetaldehyde levels are then increased from 5 to 10 times higher than normal, resulting in the disulfiram–alcohol reaction. This reaction is potentiated by decreased levels of epinephrine and norepinephrine in the sympathetic nervous system caused by inhibition of dopamine beta-hydroxylase (dopamine β-hydroxylase) (Cornish, McNicholas, & O'Brien, 2006).

Education is extremely important for the client taking disulfiram. Many common products such as shaving cream, aftershave lotion, cologne, and deodorant and over-the-counter medications such as cough preparations contain alcohol; when used by the client taking disulfiram, these products can produce the same reaction as drinking alcohol. The client must read product labels carefully and select items that are alcohol free.

WARNING ⬢ Disulfiram

Never give to a client in a state of alcohol intoxication or without the client's full knowledge. Instruct the client's relatives accordingly.

Other side effects reported by persons taking disulfiram include fatigue, drowsiness, halitosis, tremor, and impotence. Disulfiram also can interfere with the metabolism of other drugs the client is taking, such as phenytoin (Dilantin), isoniazid, warfarin (Coumadin), barbiturates, and long-acting benzodiazepines such as diazepam and chlordiazepoxide.

Acamprosate (Campral) is sometimes prescribed for persons in recovery from alcohol abuse or dependence. It helps reduce the physical and emotional discomfort encountered during the first weeks or months of sobriety, such as sweating, anxiety, and sleep disturbances. The dosage is two tablets (333 mg each) three times a day. Persons with renal impairments cannot take this drug. Side effects are reported as mild and include diarrhea, nausea, flatulence, and pruritus.

CULTURAL CONSIDERATIONS

Studies have shown that people from different ethnic backgrounds respond differently to certain drugs used to treat mental disorders. The nurse should be familiar with these cultural differences. Studies have also shown that African Americans respond more rapidly to antipsychotic medications and tricyclic antidepressants than do whites. Also, African Americans have a greater risk for developing side effects from both these classes of drugs than do whites. Asians metabolize antipsychotics and tricyclic antidepressants more slowly than do whites and therefore require lower dosages to achieve the same effects. Hispanics also require lower dosages of antidepressants than do whites to achieve the desired results (Woods et al., 2003).

Asians respond therapeutically to lower dosages of lithium than do whites. African Americans have higher blood

levels of lithium than whites when given the same dosage, and they also experience more side effects. This suggests that African Americans require lower dosages of lithium than do whites to produce desired effects (Chen et al., 2002).

Herbal medicines have been used for hundreds of years in many countries and are now being used with increasing frequency in the United States. St. John's wort is used to treat depression and is the second most commonly purchased herbal product in the United States (Malaty, 2005). Kava is used to treat anxiety and can potentiate the effects of alcohol, benzodiazepines, and other sedative–hypnotic agents. Valerian helps produce sleep and is sometimes used to relieve stress and anxiety. Ginkgo biloba is primarily used to improve memory but is also taken for fatigue, anxiety, and depression.

It is essential for the nurse to ask clients specifically if they use any herbal preparations. Clients may not consider these products as "medicine" or may be reluctant to admit their use for fear of censure by health professionals. Herbal medicines are often chemically complex and are not standardized or regulated for use in treating illnesses. Combining herbal preparations with other medicines can lead to unwanted interactions, so it is essential to assess the clients' use of these products.

SELF-AWARENESS ISSUES

Nurses must examine their own beliefs and feelings about mental disorders as illnesses and the role of drugs in treating mental disorders. Some nurses may be skeptical about some mental disorders and may believe that clients could gain control of their lives if they would just put forth enough effort. Nurses who work with clients with mental disorders come to understand that many disorders are similar to chronic physical illnesses such as asthma or diabetes, which require lifelong medication to maintain health. Without proper medication management, clients with certain mental disorders, such as schizophrenia or bipolar affective disorder, cannot survive in and cope with the world around them. The nurse must explain to the client and family that this is an illness that requires continuous medication management and follow-up, just like a chronic physical illness.

It is also important for the nurse to know about current biologic theories and treatments. Many clients and their families will have questions about reports in the news about research or discoveries. The nurse can help them distinguish between what is factual and what is experimental. Also, it is important to keep discoveries and theories in perspective.

Clients and families need more than factual information to deal with mental illness and its effect on their lives. Many clients do not understand the nature of their illness and ask, "Why is this happening to me?" They need simple but thorough explanations about the nature of the illness and how they can manage it. The nurse must learn to give out enough information about the illness while providing the care and support needed by all those confronting mental illness.

Points to Consider When Working on Self-Awareness

- Chronic mental illness has periods of remission and exacerbation just like chronic physical illness. A recurrence of symptoms is not the client's fault, nor is it a failure of treatment or nursing care.
- Research regarding the neurobiologic causes of mental disorders is still in its infancy. Do not dismiss new ideas just because they may not yet help in the treatment of these illnesses.
- Often, when clients stop taking medication or take medication improperly, it is not because they intend to; rather, it is the result of faulty thinking and reasoning, which is part of the illness.

Critical Thinking Questions

1. It is possible to identify a gene associated with increased risk for the late onset of Alzheimer's disease. Should this test be available to anyone who requests it? Why or why not? What dilemmas might arise from having such knowledge?
2. What are the implications for nursing if it becomes possible to predict certain illnesses such as schizophrenia through the identification of genes responsible for or linked to the disease? Should this influence whether people who carry such genes should have children? Who should make that decision, given that many people with chronic mental illness depend on government programs for financial support?
3. Drug companies research and develop new drugs. Much more money and effort are expended to produce new drugs for common disorders rather than drugs (often called "orphan drugs") needed to treat rare disorders such as Tourette's syndrome. What are the ethical and financial dilemmas associated with research designed to produce new drugs?

KEY POINTS

- Neurobiologic research is constantly expanding our knowledge in the field of psychiatry and is significantly affecting clinical practice.
- The cerebrum is the center for coordination and integration of all information needed to interpret and respond to the environment.

INTERNET RESOURCES

RESOURCES	INTERNET ADDRESS
• Clinical Pharmacology Online	www.clinicalpharmacology.com
• Research Project Relating to DNA, Genetics, and Mental Disorders	Nimh.nih.gov
• U.S. Food and Drug Administration	http://www.fda.gov

- The cerebellum is the center for coordination of movements and postural adjustments.
- The brain stem contains centers that control cardiovascular and respiratory functions, sleep, consciousness, and impulses.
- The limbic system regulates body temperature, appetite, sensations, memory, and emotional arousal.
- Neurotransmitters are the chemical substances manufactured in the neuron that aid in the transmission of information from the brain throughout the body. Several important neurotransmitters including dopamine, norepinephrine, serotonin, histamine, acetylcholine, GABA, and glutamate have been found to play a role in mental disorders and are targets of pharmacologic treatment.
- Researchers continue to examine the roles of genetics, heredity, and viruses in the development of mental illness.
- Pharmacologic treatment is based on the ability of medications to eliminate or minimize identified target symptoms.
- The following factors must be considered in the selection of medications to treat mental disorders: the efficacy, potency, and half-life of the drug; the age and race of the client; other medications the client is taking; and the side effects of the drugs.
- Antipsychotic drugs are the primary treatment for psychotic disorders such as schizophrenia, but they produce a host of side effects that also may require pharmacologic intervention. Neurologic side effects, which can be treated with anticholinergic medications, are called EPS and include acute dystonia, akathisia, and pseudoparkinsonism. Some of the more serious neurologic side effects include TD (permanent involuntary movements) and NMS, which can be fatal.
- Because of the serious side effects of antipsychotic medications, clients must be well educated regarding their medications, medication compliance, and side effects. Health-care professionals must closely supervise the regimen.
- Antidepressant medications include cyclic compounds, SSRIs, MAOIs, and a group of newer drugs.
- The nurse must carefully instruct clients receiving MAOIs to avoid foods containing tyramine because the combination produces a hypertensive crisis that can become life threatening.
- The risk for suicide may increase as clients begin taking antidepressants. Although suicidal thoughts are still present, the medication may increase the client's energy, which may allow the client to carry out a suicide plan.
- Lithium and selected anticonvulsants are used to stabilize mood, particularly in bipolar affective disorder.
- The nurse must monitor serum lithium levels regularly to ensure the level is in the therapeutic range and to avoid lithium toxicity. Symptoms of toxicity include severe diarrhea and vomiting, drowsiness, muscle weakness, and loss of coordination. Untreated, lithium toxicity leads to coma and death.
- Benzodiazepines are used to treat a wide variety of problems related to anxiety and insomnia. Clients taking them should avoid alcohol, which increases the effects of benzodiazepines.
- The primary use of stimulants such as methylphenidate (Ritalin) is the treatment of children with ADHD. Methylphenidate has been proved successful in allowing these children to slow down their activity and focus on the tasks at hand and their schoolwork. Its exact mechanism of action is unknown.
- Clients from various cultures may metabolize medications at different rates and therefore require alterations in standard dosages.
- Assessing use of herbal preparations is essential for all clients.

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Chapter Study Guide

MULTIPLE-CHOICE QUESTIONS

Select the best answer for each of the following questions.

1. The nurse is teaching a client taking an MAOI about foods with tyramine that he or she should avoid. Which of the following statement indicates that the client needs further teaching?
   a. "I'm so glad I can have pizza as long as I don't order pepperoni."
   b. "I will be able to eat cottage cheese without worrying."
   c. "I will have to avoid drinking nonalcoholic beer."
   d. "I can eat green beans on this diet."

2. A client who has been depressed and suicidal started taking a tricyclic antidepressant 2 weeks ago and is now ready to leave the hospital to go home. Which of the following is a concern for the nurse as discharge plans are finalized?
   a. The client may need a prescription for diphenhydramine (Benadryl) to use for side effects.
   b. The nurse will evaluate the risk for suicide by overdose of the tricyclic antidepressant.
   c. The nurse will need to include teaching regarding the signs of neuroleptic malignant syndrome.
   d. The client will need regular laboratory work to monitor therapeutic drug levels.

3. The signs of lithium toxicity include which of the following?
   a. Sedation, fever, restlessness
   b. Psychomotor agitation, insomnia, increased thirst
   c. Elevated white blood cell count, sweating, confusion
   d. Severe vomiting, diarrhea, weakness

4. Which of the following is a concern for children taking stimulants for ADHD for several years?
   a. Dependence on the drug
   b. Insomnia
   c. Growth suppression
   d. Weight gain

5. The nurse is caring for a client with schizophrenia who is taking haloperidol (Haldol). The client complains of restlessness, cannot sit still, and has muscle stiffness. Of the following PRN medications, which would the nurse administer?
   a. Haloperidol (Haldol), 5 mg PO
   b. Benztropine (Cogentin), 2 mg PO
   c. Propranolol (Inderal), 20 mg PO
   d. Trazodone, 50 mg PO

6. Client teaching for lamotrigine (Lamictal) should include which of the following?
   a. Eat a well-balanced diet to avoid weight gain.
   b. Report any rashes to your doctor immediately.
   c. Take each dose with food to avoid nausea.
   d. This drug may cause psychological dependence.

7. Which of the following physician orders would the nurse question for a client who has stated "I'm allergic to phenothiazines"?
   a. Haldol, 5 mg PO bid
   b. Navane, 10 mg PO bid
   c. Prolixin, 5 mg PO tid
   d. Risperdal, 2 mg bid

8. Clients taking which of the following types of psychotropic medications need close monitoring of their cardiac status?
   a. Antidepressants
   b. Antipsychotics
   c. Mood stabilizers
   d. Stimulants

FILL-IN-THE-BLANK QUESTIONS

Identify the drug classification for each of the following medications.

_____ 1. Clozapine (Clozaril)

_____ 2. Fluoxetine (Prozac)

_____ 3. Amitriptyline (Elavil)

_____ 4. Benztropine (Cogentin)

_____ 5. Methylphenidate (Ritalin)

_____ 6. Carbamazepine (Tegretol)

_____ 7. Clonazepam (Klonopin)

_____ 8. Quetiapine (Seroquel)

SHORT-ANSWER QUESTIONS

1. Explain the rationale for tapering psychotropic medication doses before the client discontinues the drug.

2. Describe the teaching needed for a client who is scheduled for PET.

3. Explain the kindling process as it relates to the manic episodes of bipolar affective disorder.