# CHAPTER OUTLINE

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Competencies

Upon completion of this chapter, the learner should be able to:

1. Describe current knowledge about the brain and behavior as it relates to the clinical and pharmacokinetics of the major psychopharmacologic agents.

2. Describe the clinical and pharmacologic properties of the major psychopharmacologic agents and the use of these agents in the treatment of mental illness.

3. Apply knowledge about the pharmacokinetic properties of the major psychopharmacologic agents to individualized client care.

4. Explain the nurse’s role in the administration and prescription of psychopharmacologic agents within the treatment regime.

5. Describe the importance of client and family education in the use of psychopharmacologic agents in the treatment of mental illness.

6. Comprehend the nurse’s responsibilities and the ethical issues confronting the nurse in the use of psychopharmacologic agents.

Key Terms

Akathisia: Subjective feelings of restlessness and an inability to sit still resulting from dopamine blockade by certain neuroleptics; part of the extrapyramidal side effects.

Akinesia: A condition characterized by the inability to make voluntary movements.

Anxiolytic: Drug used to reduce anxiety, and is synonymous to the term sedative. Examples include benzodiazepines such as diazepam, lorazepam, and clonazepam.

Cogwheeling: Refers to rigidity or rhythmic contractions noted on passive stretching of muscles, as occurs in Parkinson’s disease.

Dopaminergic Pathway: Nerve fibers in the mesocortical area that project to the cortex and hippocampus regions of the limbic system.

Dystonia: Slow sustained muscle spasms of the trunk, neck, or limb; the result of dopamine blockade from neuroleptic (antipsychotic) medications.

Exponential Kinetics: A pharmacokinetic model in which a constant fraction of a drug is eliminated in a set unit of time.

Extrapyramidal Side Effects (EPS): Involuntary motor movements; and muscle tone side effects that result primarily from dopamine blockade by neuroleptic medications.

Genomics: The study of the human genome sequencing and its contributions to disease and treatment.

Human Genome: The entire genetic information present in a human cell.

Linear Kinetics: A pharmacokinetic model in which a constant amount of drug is eliminated in a set unit of time.

Neuroleptic: Psychotropic medication; major tranquilizers; synonymous with antipsychotic or neuroleptic agent.

Neuroleptic Malignant Syndrome (NMS): A rare and potentially life-threatening syndrome primarily caused by antipsychotic medications and characterized by marked muscle rigidity, high fever, altered consciousness or delirium, tachycardia, hypoxia, hypertension, and diaphoresis.

Neurotransmitters: Nervous system biochemicals involved in facilitating neurotransmission of impulses across synapses between neurons. Examples include serotonin, norepinephrine, and dopamine.

Paradoxical Reactions: A response to a drug that is opposite to what would be predicted by the drug’s pharmacology.

Pharmacodynamics: The study of biochemical and physiological actions and effects of drugs.

Pharmacokinetics: The study of a drug’s absorption, distribution, metabolism, and excretion or elimination.

Pharmacology: The scientific study of chemical formulations (drugs), including their sources, properties, uses, actions, and effects.
He past three decades of research in the neurosciences has dramatically increased our understanding of the neurobehavioral aspects of mental illness to the extent that the 1990s were referred to as the Decade of the Brain and more recent discoveries of the human genome and bioinformatics in 2000. Scientists predict that the discovery of the human genome or human genetic blueprint offers incredible promise for the treatment of diseases, including mental illness. Historically, the advent of the first psychotropic medications in the 1950s significantly changed the treatment of the mentally ill. Part of the role of the psychiatric-mental health nurse has evolved in tandem with the unfolding success of psychotropic medications. The psychiatric-mental health nurse’s knowledge of psychopharmacology and its associated therapeutic agents is a significant factor in contemporary practice. The psychiatric nurse has a critical role in assisting clients to incorporate the psychopharmacologic agents into their efforts to recover and maintain mental health and prevent negative sequel and relapse. In addition, the psychiatric-mental health nurse is responsible for assessing the therapeutic effects of the drugs. Monitoring adverse reactions, knowing therapeutic dosages, documenting administration, and educating the client and family members about the psychopharmacologic agents being used in the treatment regime. At the advanced-practice level in many states, psychiatric-mental health nurses also have prescriptive authority. This chapter presents an overview of current major concepts that relate brain and behavioral response to the major psychopharmacologic agents used in the treatment of mental illness.

Recommended treatments and drug therapies are changed as clinical and scientific findings are made available. In this chapter, we provide the most current information available at the time of this writing about the pharmacotherapeutic agents covered herein. The information provided, however, is not intended to replace sound clinical judgment or individualized client care. Nurses are legally and ethically responsible for being familiar with information such as the action, dosage, adverse effects, and drug interactions of the medications they administer. The reader is advised to check product information before administering any drug, especially new or infrequently ordered drugs. Unless otherwise noted, all information concerning the pharmacokinetic and clinical properties of the psychopharmacologic agents discussed in this chapter is based on adult oral dosages. It is assumed that the student has had a prerequisite to the materials in this chapter’s introduction to pharmacology and the anatomy and physiology of the brain and central nervous system (CNS).

**THE HUMAN GENOME AND PHARMACOLOGY**

Tremendous technological advances in bioinformatics and the human genome or genetic mapping discovery have propelled the study of pharmacology into a new era. Drugs are believed to exert their curative effects by modifying the molecular structure of target proteins in the body. Today’s researchers are bypassing lengthy animal studies and turning to a fast-growing new era of computer science known as bioinformatics. Bioinformatics are being used to fuel scientists’ quest for newer drugs and better targets. Bioinformatic algorithms are being used to help pharmaceutical companies predict the future of proteins encoded by newly discovered genes.

Scientists have conducted the most extensive analysis of the human genetic blueprint, or human genome. This analysis of the human genome sequencing has provided scientists with an access to the 3 billion letters of DNA code arranged...
in 23 chromosomes. These findings have also revealed that the genome is the same from person to person, except those of identical twins who have some differences that make it unique. Virtually every cell in the body, except red blood cells (RBCs), carries a copy of the genome.

Researchers believe that once these genetic sequences are decoded, they will gain a better analysis of the molecules within human cells and dysregulation of vast body functions. Experts also expect these data to usher in an era of medications tailored to people’s unique genetic profiles and provide health care providers the ability to predict, early in life, the risk of disease. Renowned scientist, Francis Collins, submits that understanding the genetic basis of a disease helps predict what protein it produces and provides opportunities to develop a drug to block it. Predictably, the discovery of the human genome has revolutionized medicine and the way drugs are used to fight diseases. Before the human genome discovery, diseases were treated by intervening at the level of symptoms—the final phase in a complex cascade of biochemical processes. Treating symptoms usually involved guessing which medications would work to treat individual people.

In the present era of the human genome discovery, scientists predict that diseases such as cancer and diabetes, obesity, heart disease, Alzheimer’s disease, Parkinson’s disease and mental illness will be treated before symptoms occur. The basis of genomics is the ability to use medication to bolster or neutralize the effects of the person’s proteins with fine precision by destroying unhealthy cells and leaving healthy cells alone. More importantly genomics allow health care providers from the onset to know the best medicine for the individual.

Advances in genomics and bioinformatics are bringing great promise to people suffering from diverse illnesses. Scientists also predict that over the next few years, genome-based drugs will become the accepted standard of care.

THE BRAIN AND BEHAVIOR

The brain is a unique mass of tissue consisting of approximately 10 billion neurons. These neurons coordinate all of a person’s entire behavior by means of unceasing biochemical activity (Ganong, 1999; Gilman & Newman, 1992). The brain’s high metabolic rate enables it to continually process, sort, analyze, integrate, score, and retrieve information from the environment. Because of its energy needs, the brain demands a constant supply of oxygen and glucose, approximately 20 percent of the body’s total needs. These and small amounts of other nutrients (e.g., amino acids, vitamins, and minerals) are provided by a continuous supply of blood, 15 percent of the total cardiac output.

The brain stores energy mainly in the form of glucose, which is used to fuel the ion pump that maintains a resting state or propagates impulses. However, it stores only enough to last about 30 seconds (Ganong, 1999; Gilman & Newman, 1992). Thus, the brain metabolism is quickly and severely altered when cerebral blood flow is compromised.

Behavior is the expression of brain function and represents a complex interplay between the person and the environment. Although certain characteristics of human behavior are universal in nature, many more are specific to the individual. Recent research indicates that genetics and neuroendocrine mechanisms may influence behavior; however, theories arising from this research remain controversial.

NEUROANATOMICAL STRUCTURES RELEVANT TO BEHAVIOR

The brain can be divided into cortical and subcortical structures. The cortical structures (right and left cerebral hemispheres) make up the outer and largest portion of the brain and include the cerebral cortex, or gray matter; the underlying white matter; and the basal ganglia, hippocampus, and amygdala. The subcortical structures include the brainstem, which is made up of the midbrain, the pons, and the medulla; the cerebellum; and the diencephalon, which consists of the thalamus and the hypothalamus (See Figure 2–4). Although each area performs highly specified functions, all areas are connected by an elegant network of nerve pathways that enables the brain to perform complex interactions and associations that result in appropriate psychomotor responses.

Cortical Structures

Cortical structures of the brain consist of the cerebral cortex, which is vastly convoluted, and deep fissures that divide the cerebral hemispheres into several distinct regions, called lobes. Different functions lie within the domain of each area ranging from higher brain functions associated with intelligence and reasoning to vision and perceptions. The role of these regions to psychiatric nursing is vast; they provide for human behaviors and target sites for pharmacologic agents.

The Cerebral Cortex

The cerebral cortex, or surface layer, of the brain (also called the gray matter) is composed almost exclusively of nerve cell bodies. It is divided by gyri (ridges) and sulci (grooves), which greatly multiply the surface area and potential for function. Localized areas of the cerebral cortex either have specific functions or serve as integration areas referred to as association areas (Kupferman, 1991). Association serves as intermediates to assimilate and integrate multiple and diverse sensory stimuli from the specialized cortices. These areas enable the brain to generate complex responses involving more than one behavioral domain.

The Four Lobes and Their Functions

The cerebral hemispheres each have four lobes: frontal, parietal, temporal, and occipital (see Figure 2–4). The occup-
Ital lobes are primarily visual areas. They receive impulses from the retina and interpret visual stimuli for recognition and identification. The occipital areas also connect with the areas of the cortex involved with perception, recall, and optically induced reflexes. The interactions between these cortices provide three-dimensional vision and recognition.

The parietal lobes perform a variety of sensory functions. The anterior portions are specialized in somatic sensation and perception. The more posterior parietal areas integrate visual and auditory stimuli useful for the sense of body position and movement in three-dimensional space.

The temporal lobes perform primarily auditory processing and, on a basic level, detect sound and tone intensity. Wernicke's area, which is responsible for recognition and interpretations of words and letters for speech, is located here. Long-term memory storage areas are thought to be stored in the temporal lobes, as is the ability to add affective perception to experience.

The frontal lobes are vital for cognition. Virtually all other areas of the brain provide information to and receive it from the frontal lobes. These are the areas of highest intellectual function, such as judgment, reasoning, and abstract thinking. The frontal lobes also organize more complicated motor responses and initiate complex voluntary and reflex movements. Psychomotor activity is also generated in the frontal lobes, including the inhibition of emotional impulses. Broca's area, located in the frontal temporal lobe junction, is responsible for speech articulation and lies close to the Wernicke's area. Interaction between speech and hearing centers is the foundation of communication in human beings.

The Association Cortices

Three main association areas lie between the primary functional cortices: the prefrontal motor association cortex, the limbic (affective) association cortex, and the sensory (parietal-temporal-occipital) association cortex (Kupferman, 1991). These association cortices enable a person to assimilate and integrate input from all sensory experiences and formulate effective response patterns such as assessment and problem solving followed by appropriate movement and speech. The prefrontal association cortex integrates sensory and intellectual information as well as correction in the planning of movement. The limbic association cortex adds affective tone to responses, and the parietal-temporal-occipital association cortex processes sensory information to enhance perception and language (Kupferman, 1991).

The Basal Ganglia

The basal ganglia are centralized collections of neuron cell bodies (nuclei) lying within the white matter (see Figure 2–4). These nuclei include the caudate nucleus, the putamen, which are sometimes called the striatum; and the globus pallidus, sometimes called the lenticular nucleus (Ganong, 1999). Their principal function is the modulation of impulses for movement from the motor cortex to provide the smooth sequencing and execution of complex response. They also play a role in some cognitive processes, particularly the caudate nucleus (Ganong, 1999).

The Hippocampus and the Amygdala

The amygdala and the hippocampus are structures generally considered being part of the limbic system; they are often referred to as the limbic lobe (see Figure 9–1 and Figure 10–1). Other structures included in the limbic system are the parahippocampal gyrus and the circulate gyrus. In general, the limbic system has a primary role in the behavioral responses of mood, memory, and learning. Dysfunction in these areas results in the inability to form new memory (Ganong, 1999).

The amygdala, located in the temporal lobes, is composed of many nuclei with connecting tracts to the hypothalamus, hippocampus, cerebral cortex, and thalamus (Ganong, 1999). The amygdala is involved in short-term memory and its conversion to long-term memory. In addition, the amygdala is believed to be involved in learning through assimilation and integration of information from different modalities. It is also involved with the hippocampus in encoding emotional memories. In animal studies, direct stimulation of the amygdala has produced aggressive behavior, suggesting that this structure may play a major role in adding affect to tone to human responses (Ganong, 1999). Recent studies indicate that dysregulation of the hippocampus and amygdala may play a role in exaggerated stress responses found in various anxiety disorders such as post-traumatic stress disorder (PTSD).

Subcortical Structures

Subcortical structures are located in the lower part of the brain and comprise the brainstem, medulla, midbrain, cerebellum, and diencephalon. Similar to cortical or higher brain regions, these structures play key roles in human behavior and regulation of diverse homeostatic processes including metabolism, sleep, wakefulness, temperature regulation, blood pressure, and motor function.

The Brainstem

The brainstem, which connects the brain to the spinal cord and peripheral nervous system, is composed of the medulla, the pons, and the midbrain, and its reticular formation. These structures have specialized neural and physiological-regulating functions such as regulation of the heart, breathing patterns, and circadian rhythms. The brainstem also contains nuclei (clusters of nerve cell bodies) that secrete important neurotransmitters that influence brain activity and response. Biofeedback mechanisms that measure oxygen levels and blood pressure within the brain maintain the blood flow required for normal brain demands (Ganong, 1999).

The medulla is the origin of adrenergic (adrenaline) pathways that project to the hypothalamus, the locus ceruleus, and vagus nerve (Leonard, 1993). The locus ceruleus, a cluster of neurons located in the pons, is the source of noradrenergic (norepinephrine) pathways projecting to the
spinal cord, cerebellum, and brainstem but largely converging in the thalamus and hypothalamus (see Figure 10–1). The reticular formation is a diffuse network of nuclei known to integrate motor, sensory, and visceral functions but, more importantly, it is involved in regulation of arousal and consciousness. This network is responsive to the presence of norepinephrine, serotonin, acetylcholine, and dopamine—neurotransmitters that mediate brain function on the most basic level (Ganong, 1999).

The midbrain lies between the pons and the diencephalon. Structures in the midbrain include the tectum, the tegmentum, the red nucleus, and substantia nigra. These nuclei synthesize dopamine, a neurotransmitter important in movement and memory. The tectum mediates whole body movements in response to visual and auditory stimuli. The ventral portion of the tegmentum is the origin of a network of fibers known as mesolimbic dopaminergic pathway, which projects to the limbic system. Another set of fibers, the mesocortical dopaminergic pathway, projects to the cortex and hippocampal regions of the limbic system. The substantia nigra gives rise to another set of dopaminergic fibers, associating with the nigrostriatal pathway, between the striatum, the subthalamic nucleus, and the cortex (Leonard, 1993; Ganong, 1999).

The Cerebellum
The cerebellum lies dorsal to the pons and medulla and actually wraps around the brainstem. It resembles the cerebral cortex in that it has distinct lobes and a foliated surface. The cerebellum receives afferent somatosensory pathways from the spinal cord, efferent motor relays from higher cortical areas, and input about balance from the vestibular system of the inner ear. The body integrates all this information to plan and coordinate movement and posture.

The Diencephalon
The thalamus and the hypothalamus must lie in the area called the diencephalon. It is the primary synaptic relay center of the brain for different sensory modalities, including somatic sensation, audition, and visual information. The thalamus distributes sensory information to the sensory cortex and also mediates motor functions by acting as a conduit for information from the cerebellum and the basal ganglia to the motor cortex.

The hypothalamus lies beneath the thalamus, with numerous afferent and efferent pathways to and from the other areas of the brain and the pituitary gland. The hypothalamus plays a vital role in the control of the endocrine system, the autonomic nervous system, and the limbic system through the release of hormones (See Figure 2–4). Functions and activities regulated by the hypothalamus include temperature regulation, eating and drinking (appetite), metabolism, glucose utilization, blood pressure and fluid balance (osmolarity), sexual behavior, and emotional responses.

NEUROPHYSIOLOGY AND BEHAVIOR
All behavior is generated and controlled by the nervous system. Nerve tissue is the most fragile of all tissue types and does not have regenerative and restorative abilities—injury to neurons within the brain and the spinal cord is permanent. Protective bone structures such as the skull and spinal column exist to prevent injury from external sources. Physiological mechanisms exist as well to shield the fragile brain tissue from chemical or mechanical injury. One of these mechanisms is a type of nerve cell called glia, or “nerve glue.” Microglia and macroglia hold the conducting neurons in place and sequester extracellular potassium, thereby protecting neighboring neurons from inappropriate depolarization.

A particular type of glia, the astrocyte, wraps around penetrating capillaries and arterioles to stabilize them but, more importantly, to create a barrier between the blood vessels and the nervous tissue. This blood-brain barrier is impermeable to many substances that circulate in the bloodstream yet are toxic to brain tissue. The blood-brain barrier prohibits molecules of low lipid solubility and strongly ionized agents from leaving the blood and entering the brain tissue. Most drugs do not cross this barrier but neither do large molecular bodies, such as bacteria or blood cells, which would contaminate the neural tissue. Phagocytic microglia act as scavengers to remove by-products and other debris from the brain tissue and are the basis of scar formation in injured brain tissue.

Neurons
The most abundant type of nerve cell is the conducting neuron, which generates and transmits nerve impulses. Dendrites are projections from the neuron cell body that receive impulses from adjacent neurons. The axon, another projection from the cell body, is responsible for impulse propagation to other cells (See Figure 2–3).

Synaptic Transmission
Synaptic transmission, the propagation of electrochemical impulses from neuron to neuron, is the basic mechanism for all nervous system activity. The transfer of ionic charge along the cell membrane of the conducting neuron to the targeting receiving neuron accomplishes this process, known as synaptic transmission. Ion channels (microscopic water-filled tunnels that perforate the cell membrane) open and close, depending on cellular demands, and allow ions such as sodium, potassium, and calcium to diffuse into or out of the cell. As ions flow across the cell membrane, the voltage charge increases to a critical threshold and an impulse is generated. This electrochemical impulse is called an action potential. As the action potential moves toward the end of the axon (terminal button), the voltage change triggers the release of neurochemicals called neurotransmitters from
their storage vesicles into the extracellular space (synaptic cleft). These neurochemicals diffuse across the synaptic cleft and attach to specific receptor sites to initiate the impulse at the next neuron (see Figure 2–4). After the impulse is transferred, some of the neurotransmitters remain in the synaptic cleft and are either broken down by enzymatic processes or reabsorbed into the presynaptic membrane by a process of reuptake. These processes of neurotransmitter degradation of reuptake can be altered by the action of psychotropic medications (Kandel, 1991b; Kolb & Wishaw, 1990). The psychopharmacologic agent may increase or decrease the degradation or reuptake of the transmitter to alter its activity and “normalize” the transmitter levels. This regulation serves to alleviate the symptoms of mental illness.

Neurotransmitters

Neurotransmitters in the brain play an important role in normal function and survival. Many neurological diseases and virtually all medications that act on the nervous system influence the neurotransmitter systems in some way. Neurotransmitters have either excitatory or inhibitory abilities. Only a few have both, depending on the nature of the postsynaptic membrane. Excitatory transmitters generate an action potential in the receiving neuron, whereas an inhibitory neurotransmitter dampens or stops the activity of the receiving neuron.

There are four classes of neurotransmitters: the biogenic amines, acetylcholine, the amino acids, and the peptides (Table 28–1).

Biogenic Amines

The first class of neurotransmitters is known as the biogenic amines, or monoamines. This class is divided into two subclasses: indoleamines and catecholamines. Serotonin is an indoleamine. Dopamine, norepinephrine, and epinephrine are catecholamines.

Indoleamines

Serotonin, also known as 5-hydroxytryptamine (5-HT), is hypothesized to play a significant role in states of consciousness, mood, depression, anxiety, and, possibly, schizophrenia (Leonard, 1993) (see Chapter 9). Its highest concentrations are found in blood platelets and in the gastrointestinal tract. Serotonin is synthesized from the amino acid 5-tryptophan. It is metabolized by monoamine oxidase (MAO) to yield 5-hydroxyindoleacetic acid (5-HIAA), which can be assayed by 24-hour urine collection. Specialized nuclei, the upper and caudal raphe nuclei located within the pons, secrete 5-HT to the serotonergic pathways and their target brain areas: the upper brainstem, the limbic system, and the hypothalamic-pituitary axis (Ganong, 1999; Leonard, 1993) (see Figure 9–1).

There are at least three different receptors and a number of subreceptors for 5-HT. Lysergic acid, a commonly abused hallucinogen, is an agonist of 5-HT in that it mimics its actions at receptor sites. The selective serotonin reuptake inhibitors (SSRIs) are potent inhibitors of 5-HT; 5-HT reuptake into the presynaptic cleft, and have a low affinity for cholinergic, noradrenergic, and histamine receptors. SSRIs produce somewhat fewer adverse side effects (Preskorn, 1997; Warrington, 1992). In essence, the efficacy and antidepressant properties of SSRIs stem from their ability to inhibit the reuptake of 5-HT and increase 5-HT in the brain.

Catecholamines

Dopamine. The catecholamine dopamine is perhaps the single most important neurotransmitter, because it affects a large number of neurological functions. Dopamine is largely synthesized in the substantia nigra and the ventral tegmen-tum. It is concentrated in the nigrostriatal and mesolimbic dopaminergic tracts (see Figure 14–1). It is used particularly in the limbic system but also diffusely throughout the brain, and it is believed to play a role in the initiation and execution of movement and regulation of emotional responses. Overactivity of dopamine is hypothesized to play a central role in many symptoms of schizophrenia (see Chapter 14 and Figure 14–1). It also plays a role in the regulation of the endocrine system by altering the hypothalamic to manufacture hormones for storage and release by the pituitary (Leonard, 1993).

Dopamine is synthesized from the amino acids phenylalanine and tyrosine and metabolized by MAO and catechol O-methyltransferase (Leonard, 1993). There are currently six known postsynaptic dopamine receptors: D1, D2A, D2B, D3, D4, and D5 (Ganong, 1999). Each of these receptors may

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<td>Biogenic amines (monoamines)</td>
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<td>Gamma-aminobutyric acid</td>
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exert different dopaminergic influences; thus abnormalities in the dopaminergic system can cause various mental illnesses that respond to different treatments.

**Norepinephrine and Epinephrine.** Norepinephrine is believed to play a role in learning and memory. Neurons in the locus ceruleus and the lateral tegmentum produce norepinephrine and supply the noradrenergic pathways to the cerebral cortex, limbic system, brainstem, and spinal cord (see Figure 11–1).

Norepinephrine is depleted in clients with Alzheimer's disease and Korsakoff's syndrome, contributing to characteristic symptoms of compromised short-term and long-term memory and limited learning ability (see Chapter 16). Norepinephrine is also thought to play a role in mood stabilization, depression, drive, and motivation. Tricyclics, at one time the most commonly prescribed class of antidepressants, act by increasing levels of norepinephrine in the limbic system. Norepinephrine and epinephrine are also secreted by the adrenal glands and play important roles in the arousal of the autonomic nervous system and the stress response (see Figure 11–1).

Norepinephrine is synthesized from dopamine, and it is metabolized in the same manner; however, its distribution in the brain is not as widespread. There are four known norepinephrine receptors in the brainstem and midbrain: alpha-1, alpha-2, beta-1, and beta-2. These receptors appear to provide evidence that norepinephrine plays a key role in blood pressure regulation and skeletal muscle flexion and that it influences the thalamus, hypothalamus, and cerebral cortex (Leonard, 1993).

**Acetylcholine**
Acetylcholine is believed to be the main transmitter responsible for intellectual functioning. It is heavily concentrated in the anterior thalamic nucleus, the septal nuclei, and the association pathways that connect all primary and association areas with the frontal lobe (see Figure 16–1). Acetylcholine transfers the impulses that convey calculations, problem analysis, recognition, learning, and recall. Acetylcholine levels have been found to be low in clients with Alzheimer's disease and other forms of dementia (Kolb & Wishaw, 1990). Also critical to skeletal and cardiac muscle excitation, acetylcholine is released at the motor end plate to initiate the contraction of the muscle fibers. Interference with acetylcholine at this peripheral location is the underlying pathology of myasthenia gravis, a neuromuscular disease characterized by gradual weakness and wasting of muscle.

**Amino Acids**
A third class of neurotransmitters is the amino acids. They include glutamate, aspartate, glycine, and gamma-aminobutyric acid (GABA). **Glutamate and aspartate** are excitatory in nature. They are rapid acting and serve as intermediate neurotransmitters to regulate ionic conditions along the axon membrane before the release of other transmitters in the synaptic cleft. A receptor common to both glutamate and aspartate is the N-methyl-D-aspartate (NMDA) receptor. This specialized receptor records new experiences for learning and future use as memory. NMDA receptors are particularly sensitive to the effects of alcohol and are the first receptors to be destroyed in chronic alcohol use. Glutamate and aspartate also participate in the motor impulses initiated in the cerebellum and the spinal cord.

**Glycine** and **GABA** are inhibitory in nature. Glycine can be found mainly in the corticohypothalamic projection pathway through the reticular activating system in the brainstem. It serves as the impulse modulator for messages going to the spinal cord and the peripheral nervous system. GABA is synthesized from glutamate, and it is present in much higher concentrations throughout the brain than all of the other neurotransmitters described here. GABA pathways exist between the cortex and the hypothalamic-pituitary axis (see Figure 11–1). It serves as the brain's modulator and limits the effects of excitatory transmitters. GABA inhibits neuronal transmission by hyperpolarizing the receptor site to render it less sensitive to continual stimulation. GABA acts in the basal ganglia to regulate sensorimotor impulses for smooth and controlled movement. Low levels of brain GABA predispose a person to convulsions and disorganized sensorimotor function. The choreatic movements that characterize Huntington's disease are associated with a loss of the intrastriatal GABA activity and basal ganglia dysregulation, which contribute to the emergence of the hyperkinetic features of this disease (Ganong, 1999). Benzodiazepines enhance GABA binding to receptor sites and are effective in treating anxiety. Anticonvulsants work in a similar manner to modulate hyperstimulation by their anti-kindling properties and prevent seizures. Perhaps the efficacy of anticonvulsants as mood stabilizers stem from these properties.

**Peptides**
Another class of neurotransmitters, the peptides, is involved in the activation and regulation of response to stress and injury such as pain perception and reflex function. Peptides are produced in the neuronal cell body and are mediated by genetic coding. The actions of enzymes, amino acid residues, and other chemical actions regulate the activity of peptides (Kaplan & Sadock, 1998). Some families of neuroactive peptides are the endogenous opioids, including endorphins and enkephalins. These neurotransmitters are believed to play a role in the modulation of stress, pain, and mood. Substance P is primarily found inafferent sensory motor neurons in the striatonigral pathway and are believed to be at the first synapse of slow pain. High concentrations are found in the nigrostriatal system and the hypothalamus, where it plays a role in neuroendocrine regulation. Dysregulation of Substance P is hypothesized to contribute to symptoms found in Alzheimer's disease and mood disorders (Ganong, 1999).
**Neurotransmitter Action**

Much of the current knowledge about mental illness, neurological diseases, and the medications that treat them is based on the understanding of the role of neurotransmitters in synaptic transmission. Recall that the process of synaptic transmission by axons of neurons is accomplished by an increase in sodium and potassium permeability across the cell membrane. The flow of ions creates an action potential that travels to the end of the axon, where the voltage change triggers the release of neurotransmitters from the presynaptic membrane into the synaptic cleft (Kandel, 1991b; Kolb & Wishaw, 1990) (see Figure 2–4).

The neurotransmitter diffuses across the synaptic cleft to the postsynaptic receptor site on the receiving neuron. The neurotransmitter attaches to each of these chemical structures in a manner similar to a key fitting a lock: the chemical structure makes an exact close fit with the receptor site. Once attached, the neurotransmitter activates the postsynaptic receptor by opening the ion channels, changing the membrane potential, and initiating another action potential at the next neuron (Kandel, 1991b). An excitatory transmitter generates an action potential in the receiving neuron (depolarization), whereas an inhibitory neurotransmitter dampens or prohibits the activity of the receiving neuron (hyperpolarization).

Once the transmitter has performed its function, it must be removed to terminate its action; otherwise, the action potential is abnormally prolonged, inhibited, or exaggerated. The production and release of excess neurotransmitter or the excessive sensitivity of the receptor site to the action of the neurotransmitter also produce an exaggerated effect. For example, excessive norepinephrine secretion could be a cause of anxiety disorders (see Figure 11–1). Conversely, deficient synthesis or insufficient release of the neurotransmitter, or decreased sensitivity of the receptor site produces abnormal results; for example, low dopamine levels could be a factor in depression (Kandel, 1991a). The action of neurotransmitters is ended by one of two mechanisms: reuptake or enzymatic deactivation. The postsynaptic potential produced by almost all transmitter substances are terminated by reuptake, in which the transmitter is rapidly pumped from the synaptic cleft back into the presynaptic terminal bouton. Enzymes (frequently MAO) that metabolize the transmitter accomplish enzymatic deactivation. Acetylcholine, dopamine, and norepinephrine activity are terminated in this manner (Kandel, 1991b).

This description of synaptic transmission is greatly oversimplified. In reality, the surface of receptor sites in any individual neuron may have 2,000 to 3,000 receptor sites that may be highly specialized or that may perform a variety of functions.

Behavior is the manifestation of the combined actions of potentials emerging from masses of neurons in the primary and association areas in the response to a person's thoughts. It stands to reason that many behaviors and neurological symptoms of underlying general medical conditions are a manifestation of disruption to the transmission of processes described earlier. Brain injury from trauma or hypoxia or abnormal cell formation in tumor interferes with normal neural function and metabolism. With aging, the brain undergoes changes more gradually. Its plasticity is reduced as neurons die, and glia becomes more rigid with scar tissue. The blood-brain barrier becomes increasingly permeable, which compromises neural tissue integrity. The overall brain metabolic rate slows, and mentation may become cloudy as transmitter activity becomes sluggish or levels become suboptimal. Brain water is decreased, which lessens the absorbability of neuropharmacologic agents. All of these factors have significant pharmacokinetic implications for the effective treatment of abnormal neural processes present in mental illness.

**PHARMACOKINETIC CONCEPTS**

The efficacy of pharmacologic agents parallels its ability to reach appropriate concentrations at sites of actions. It is crucial for the psychiatric nurse to understand major concepts associated with general principles of pharmacologic actions and drug efficacy.

**Pharmacology**

Pharmacology is the scientific study of chemical formulations (drugs), including their sources, properties, uses, actions, and effects. Two areas of concern for the psychiatric-mental health nurse are pharmacodynamics and pharmacokinetics. Pharmacodynamics refers to the actual biochemical and physiological effects on living tissue that are caused by the interaction of drugs with tissue receptors. In other words, the pharmacodynamic principles focus on what the drug does to the body. Pharmacokinetics, on the other hand, is the study of the absorption, distribution, metabolism, and elimination of drugs. In other words, it is concerned with what the body does with the drug.

Pharmacodynamic and pharmacokinetic concepts are important, because they provide the psychiatric-mental health nurse with an understanding of the relevant properties of psychopharmacologic agents. These concepts also explain the therapeutic properties of drugs, their potential adverse effects, their use in the treatment of mental illness, their interactions with other pharmaceutical agents, and the interactions on human responses. Of recent interest is the potential role that race and ethnicity play in the pharmacokinetics of psychotropic drugs (see the Research Abstract, Ethnicity and Psychotropic Drugs). Pharmacokinetic principles are emphasized in the pharmacodynamic discussions of the psychotropic drugs described in this chapter.
FACTORS THAT INCLUDE DRUG INTENSITY AND DURATION

The first set of concepts is concerned with the general pharmacokinetic effects of psychopharmacologic agents. There are four factors that influence the intensity and duration of drug effect: absorption, distribution, metabolism, and elimination.

Absorption

Absorption is the process by which drug molecules pass from the site of administration into the systematic circulation. Absorption is affected by route of administration (e.g., oral, intramuscular, or intravenous), drug formulation, and such factors as food and antacids in the case of oral administration.

Distribution

Distribution is the movement of the drug from the site of administration throughout the body and dilution in body fluids. The volume of distribution is an indicator of the degree of distribution a drug undergoes. A drug with low volume is limited to intravascular space. Medium distribution means the drug appears in most extracellular fluid, and high distribution means drug concentration occurs inside...
the cell and body fats. Factors that affect the body-fat-water ratio such as age, sex, and weight also affect drug distribution (Janicak & Davis, 2000).

**Metabolism**

*Metabolism* is the formulation of active and inactive metabolites through the conversion of a drug into a new, usually less active and more water-soluble compound and also by-products or waste products. The enzyme system is responsible for metabolism of most drugs and it is located in the endoplasmic reticulum of the liver (known as the microsomal fraction). Other areas of metabolism are the epithelium of the gastrointestinal tract, the kidneys, the lungs, and the skin. The first-pass effect refers to the site of the initial drug metabolism. As mentioned, the liver is the principal organ of drug metabolism. However, some drugs (e.g., clonazepam and chlorpromazine) are metabolized in the intestine. Thus the intestinal metabolism can contribute to first-pass effect. First-pass effects, then, may limit the bioavailability of orally administered drugs such that alternate routes may be needed to be used to achieve the desired therapeutic blood levels (Janicak & Davis, 2000).

**Elimination**

*Elimination* is the removal of the drug, drug by-products, and inactive metabolites from the body, usually through urine or feces, perspiration, and respiration (Janicak & Davis, 2000).

**Steady State, Half-Life, and Clearance**

There are three important concepts in the pharmacokinetics of drugs: steady state, half-life, and clearance.

**Steady State**

*Steady state* is the condition that occurs when the amount of drug removed from the body equals the amount being absorbed. The steady state is important because it represents the amount of drug required to achieve the desired therapeutic effects. Not all drugs have linear kinetics (a linear relationship between dose and plasma concentration) in steady state. Linear kinetics is a pharmacokinetic model in which a constant amount of a drug is eliminated in a set unit of time. It depicts the relationship between a drug’s absorption and elimination necessary to a steady state. In linear kinetics, the drug half-life is *dose dependent*.

For certain drugs and for most drugs in large doses, however, the relationship is nonlinear. In this model, called exponential kinetics, the half-life of a drug is independent of dose. For example, this occurs with imipramine (Tofranil) in older adults and in the long-term use of carbamazepine (Tegretol) or chlorpromazine (Thorazine). Caution is required, therefore, in increasing dosages into the upper range of acceptable prescribed dosages or using these drugs in special populations, such as older adults or clients with comorbid illnesses, in whom the likelihood of toxicity is high (Janicak & Davis, 2000).

**Half-Life**

A drug’s half-life is the time in hours needed for the amount of drug in the body (as measured by plasma concentration) to decrease by one half, or 50 percent. The half-life of a drug is important for predicting the length of time necessary for the drug to be totally eliminated from the body. Drugs with long half-lives have slow rates of egress from the body. This information is useful, for example, when the advanced-practice psychiatric nurse is waiting for one antidepressant to be eliminated from the body before starting another. Such is the case when switching from treatment with a monoamine oxidase inhibitor (MAOI) to an SSRI. For untoward effects to be avoided, drugs with short half-lives, such as the benzodiazepine triazolam (Halcion), may require tapering off of the dose rather than abrupt discontinuation (Kaplan & Sadock, 1996). The half-life of a drug is also important for determining the time required for achieving the stable concentration (or steady state) of a drug. In general, drugs require four to five half-lives to achieve steady state. Knowledge about the drug’s half-life is also important for determining the frequency of dosing. Drugs with short half-lives require more frequent dosing. Drugs with long half-lives can be administered in a once-a-day dose.

**Clearance**

*Clearance* is the volume of blood in millimeters per minute from which all of the drug is removed per unit of time. Clearance determines the magnitude of the steady-state concentration and therefore the dosage required achieving the desired steady state of a drug. Drugs that are efficiently eliminated by renal excretion and hepatic metabolism require higher dosage regimen than do those that are inefficiently eliminated.

**Protein Binding**

Another important factor in understanding the pharmacokinetic properties of drugs is *protein binding*. Once the drug is absorbed into the vascular system, protein molecules transport it, usually albumin, to the site of action (Janicak & Davis, 2000). The plasma proteins are generally unable to exit the vascular beds because of their molecular size. Similarly, protein-bound drugs are unable to exit unless they are freed from their binding sites. The stronger the binding site, the slower the freeing of drugs, resulting a longer duration of action. As the drug is metabolized, more of the drug is released from the binding sites. Occasionally, two or more drugs compete for the same binding sites. When this occurs, the drug with the strongest affinity for the binding site displaces the other drug. When this interaction occurs, the displaced drug usually produces a toxic effect because a large concentration is free in the vascular bed (Janicak & Davis, 2000).
Active Metabolites

Active metabolites play an important role in pharmacokinetics. With the exception of lithium, most of the psychopharmacologic agents produce active metabolites during the process of metabolism. In general, metabolites are more water soluble than the parent compound. The half-life of a metabolite is equal to or longer than that of its parent compound. The cyclic antidepressants, the antipsychotics, and some anxiolytics have major active metabolites. These drugs may require a longer time to reach a steady state. Therefore, active metabolites complicate conclusions about the clinical effects of psychopharmacologic agents based solely on serum levels and steady-state phenomena (Janicak & Davis, 2000).

CULTURAL CONSIDERATIONS

The field of pharmacogenetics has exploded over the past 5 years. Findings from current research indicate that most of the genes governing the expression and function of enzymes that modulate the metabolism of psychotropic agents have been sequenced and differentiated (Lin & Smith, 2000; Lawson, 1999). Researchers have discovered that common mutations at the genetic and cellular levels are responsible for cross-ethnic variations in the response to psychotropic medications. In addition, these findings indicate that gene-encoding proteins (e.g., transporters and receptors) modulate and mediate the action of neurotransmitters and target sites of various psychotropic drugs. Extensive data also show that pharmacokinetics—absorption, distribution, metabolism, and excretion—modulate the fate and nature of most medications and that culture and ethnicity substantially affect the variability of metabolism and drug responses (Lin & Smith, 2000; Lawson, 1999).

As previously mentioned the P-450 enzymes, which recently have been studied extensively, seem to control the rate-limiting stages in the metabolism of most psychotropics. Interestingly enough, the activity of these enzymes is greatly modulated by genetic polymorphisms (e.g., number of alleles [alternative forms of a gene] and gene frequencies), whose distribution varies considerably among ethnic groups (Moldin & Gottesman, 2000). Recent gene studies indicate that some individuals’ enzyme systems are nonfunctional (poor metabolizers), less-efficient functioning (intermediate metabolizers), and enhanced action (extensive metabolizers). The extensive metabolizer group is further broken down into normal functioning and ultrarapid metabolizers (Lin, Smith, & Ortiz, 2001; Nelson, 1999). An important clinical implication for psychiatric nurses is linking culture to the client’s response (e.g., poor, desired, adverse reactions), rather than assuming that a poor response is a nonadherence problem. Other clinical issues include the necessity of increasing or decreasing the drug because the client is an ultrarapid or poor or ultra metabolizer. Overall, the role of culture and ethnicity on gene expression is complex and interesting. Understanding the influence of culture and ethnicity on client responses throughout treatment planning enables the psychiatric nurse to appreciate their significance in all areas of care, including psychosocial and other biological interventions. Psychiatric nurses need to assess the client and family’s perception of mental illness and the role of medication. Issues regarding psychoeducation concerning desired and adverse drug reactions along with psychosocial interventions play key roles in medication adherence. (See the Research Abstract, Symptomatology and Medication Monitoring for Public Mental Health Consumers: A Cultural Perspective). By linking culture and ethnicity to client responses, the psychiatric nurse can develop a more holistic and individualized plan of care that enhances the client’s response to pharmacologic and other treatment modalities.

RESEARCH ABSTRACT

SYMPTOMATOLOGY AND MEDICATION MONITORING FOR PUBLIC MENTAL HEALTH CONSUMERS: A CULTURAL PERSPECTIVE


Study Problem/Purpose

To examine the impact of cultural factors, stressors, moderators, medication monitoring, and psychiatric symptoms in consumers with severe mental disorders.

Methods

A cross-sectional analysis of data from a longitudinal research project conducted in Ohio. The population (n = 199) comprised consumers of community-based services within a public mental health system.

Findings

Demographics, such as age, gender, and race, were associated with indicators of medication monitoring. Culture was found to be a significant facet in the symptoms presentations and in the ability to monitor medications.

Implications for Psychiatric Nurses

Psychiatric nurses need to assess their clients’ cultural needs during the initial assessment and throughout treatment to determine individual needs and preferences.
PSYCHOPHARMACOLOGIC THERAPEUTIC AGENTS

Compelling evidence of the role of intricate biological, genetic, and neuroanatomical influences on signs and symptoms of psychiatric disorders explains the significance of pharmacologic agents in promoting mental health. Psychiatric nurses play pivotal roles in symptom management and facilitating an optimal level of functioning in the client with a mental disorder. The following section provides an overview of pharmacologic agents and their role in providing hope and a quality of life for clients and their families experiencing various psychiatric disorders.

Medication Administration

Historically, the responsibility of the nurse regarding medications was limited to the principles of medication administration, specifically, the correct drug to the correct client in the correct dose by the correct route at the correct time (Sullivan, 1991). The nurse needs to follow facility protocol for medication administration procedures. As with any client treated on inpatient or outpatient settings, documentation and reporting of procedures must be followed with the client with a mental disorder. Although these basic principles are essential, much more is required if the therapeutic purpose is to be attained.

Presently, psychiatric nurses must be able to integrate basic and complex principles into their understanding of medications; client responses, both desired and adverse; and recognize the role of families and health teaching into appropriate treatment planning. Psychiatric nurses play key roles in making accurate diagnoses, prescribing a plan of care that includes pharmacologic and nonpharmacologic treatment planning, and monitoring client responses. Understanding the effects of various pharmacologic agents involves knowing actions of specific agents and promoting safe and appropriate care for clients with assorted mental disorders and medical conditions.

Antidepressants

Depression is a common, disabling illness with enormous social and economic consequences; it is estimated that 18 to 23 percent of women and 8 to 11 percent of men experience at least one serious depression in their lifetime (see Chapter 9). Untreated, depression can be a dangerous illness; approximately 15 to 20 percent of clients with a primary affective illness (depression or bipolar disorder) die from suicide (Mann, Watermaux, Haas, & Malone, 1999). Historically, depression has been described as either endogenous or exogenous. Endogenous depressions were assumed to result from biological alterations and thus treatable with medications. Reactive or exogenous depressions were thought to occur in reaction to an environmentally caused event, such as the loss of a family member or a job. These depressions were “worked through” and not treated with medication. This dichotomy is currently generally rejected. The decision to use medication is now based on the severity of the presenting symptoms and not on presumed causality.

Antidepressants, as their name suggests, are medications prescribed to treat depression. In addition, antidepressants are used in the treatment of dysthymia; anxiety disorders, including obsessive-compulsive disorder, panic disorder, PTSD; somatoform disorders; eating disorders; and childhood enuresis. Like the antipsychotics, most antidepressants have been categorized by their chemical structures. The newer antidepressants are being categorized by their chemical actions. The clinical and pharmacokinetic parameters of the antidepressants are presented in Table 28–2.

**Heterocyclics**

The largest group of antidepressants can be described as heterocyclic, indicating their common structural characteristic: carbon rings. The most familiar type of antidepressant is a subgroup of the heterocyclic compounds called tricyclic antidepressants, or TCAs, so named because of the three carbon rings that characterize all the medications in this subclass. Maprotiline (Ludiomil) is considered a tetracyclic. Clomipramine (Anafranil) is an effective antidepressant, which is the first-line drug of choice in the treatment of obsessive-compulsive disorder. This drug may be useful in the treatment of the depressed client with marked obsessive features. It also shows promise to clients experiencing chronic pain, other anxiety disorders, and phobias (Kaplan & Sadock, 1996).

**Mechanism of Action.** Until recently, the heterocyclics were thought to work by inhibiting the presynaptic reuptake of norepinephrine (a catecholamine) and 5-HT (an indoleamine). Currently, however, several other hypotheses are being advanced. One approach focuses on the slower adaptive changes in norepinephrine and 5-HT systems and reregulation of an abnormal receptor-neurotransmitter relationship. It is thought that this regulatory action speeds up the client’s natural recovery process from a depressive episode by normalizing neurotransmission efficacy (Facts and Comparison, 1993). One specific reregulation hypothesis is the down-regulation theory, which suggests that depression occurs concomitantly with increased norepinephrine activity. According to this theory, antidepressants promote a down-regulation of activity by decreasing beta-adrenergic receptor sensitivity to norepinephrine (Hollister, 1989).

The heterocyclics are equally effective clinically, and many have similar metabolic pathways. These drugs are often divided into subgroups according to potency and reactions (Kaplan & Sadock, 1996). As an example of grouping by secondary properties, the TCAs are grouped into secondary and tertiary amines. Secondary amines are considered activating antidepressants, whereas tertiary amines are considered sedating antidepressants. Thus, an activating secondary amine, desipramine (Norpramin), may be a useful choice for the client whose depression has retarded (slowed) her mental and physical activity, whereas imipramine (Tofranil), a commonly used tertiary sedating amine, may be a better choice for an agitated client who is not sleeping well.
### Clinical and Pharmacokinetic Parameters of Antidepressant Medications

<table>
<thead>
<tr>
<th>GENERIC NAME</th>
<th>BRAND NAME</th>
<th>DOSAGE RANGE (MG/DAY)</th>
<th>HALF-LIFE (HOURS)</th>
<th>ONSET OF CLINICAL EFFECTS</th>
<th>ELIMINATION PERIOD AFTER LAST DOSE</th>
<th>AMINE BLOCKING ACTIVITY*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tertiary Amines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>Elavil</td>
<td>75–200</td>
<td>31–46 (18–44 for nortriptyline)</td>
<td>2–4 weeks for all tertiary amines</td>
<td>≥ 2 weeks for all tertiary amines</td>
<td>NE (2), 5-HT (4)</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Anafranil</td>
<td>75–300</td>
<td>19–37</td>
<td></td>
<td></td>
<td>NE (2), 5-HT (5)</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Sinequan, Adapin</td>
<td>75–300</td>
<td>8–24 (desmethyl)</td>
<td></td>
<td></td>
<td>NE (1), 5-HT (2)</td>
</tr>
<tr>
<td>Imipramine</td>
<td>Tofranil</td>
<td>75–200</td>
<td>11–25 (12–24 for desipramine)</td>
<td></td>
<td></td>
<td>NE (2), 5-HT (4)</td>
</tr>
<tr>
<td>Trimipramine</td>
<td>Surmontil</td>
<td>75–200</td>
<td>7–30</td>
<td></td>
<td></td>
<td>NE (1), 5-HT (1)</td>
</tr>
<tr>
<td><strong>Secondary Amines</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxapine</td>
<td>Asendin</td>
<td>150–300</td>
<td>8–30 (30 for 7-hydrox and 8-hydrox)</td>
<td>2–4 weeks for all secondary amines</td>
<td>2–4 weeks for all secondary amines</td>
<td>NE (3), 5-HT (2), DA (2)</td>
</tr>
<tr>
<td>Desipramine</td>
<td>Norpramin</td>
<td>75–200</td>
<td>12–24</td>
<td></td>
<td></td>
<td>NE (4), 5-HT (2)</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>Aventyl</td>
<td>75–150</td>
<td>18–44</td>
<td></td>
<td></td>
<td>NE (2), 5-HT (3)</td>
</tr>
<tr>
<td>Protriptyline</td>
<td>Vivactyl</td>
<td>20–40</td>
<td>67–89</td>
<td></td>
<td></td>
<td>NE (4), 5-HT (2)</td>
</tr>
<tr>
<td><strong>Tetracyclic</strong></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Maprotiline</td>
<td>Ludiomil</td>
<td>75–300</td>
<td>21–25</td>
<td>3–7 days</td>
<td>2 weeks</td>
<td>NE (3), 5-HT (1)</td>
</tr>
<tr>
<td><strong>Trazolopyridine</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Trazodone</td>
<td>Desyrel</td>
<td>50–600</td>
<td>4–9</td>
<td>1–4 weeks</td>
<td>2 weeks</td>
<td>5-HT (3)</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>Serzone</td>
<td>300–600</td>
<td>3.5–5</td>
<td></td>
<td></td>
<td>5-HT₂ (3), NE (1)</td>
</tr>
<tr>
<td><strong>Bicyclics</strong></td>
<td></td>
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</tr>
<tr>
<td>Fluoxetine</td>
<td>Prozac</td>
<td>20–80</td>
<td>2–5 days (7–9 days for norfluoxetine)</td>
<td>1–4 days</td>
<td>4 weeks</td>
<td>NE (1), 5-HT (5)</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Paxil</td>
<td>20–50</td>
<td>5–21</td>
<td>Up to 8 weeks</td>
<td>2 weeks</td>
<td>NE (1), DA (1), 5-HT (5)</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Zoloft</td>
<td>50–200</td>
<td>24</td>
<td>Up to 8 weeks</td>
<td>2 weeks</td>
<td>NE (1), DA (1), 5-HT (5)</td>
</tr>
<tr>
<td><strong>Aminoketone</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion</td>
<td>Welbutrin</td>
<td>200–300</td>
<td>8 days (4 weeks for active metabolites)</td>
<td>1–4 weeks</td>
<td>2 weeks</td>
<td>NE (1), 5-HT (1), DA (1)</td>
</tr>
</tbody>
</table>

*NE, norepinephrine; DA, dopamine; 5-HT, serotonin. 0 = none, 1 = very weak, 2 = weak, 3 = moderate, 4 = strong, 5 = strongest.
Side Effects, Dosage, and Drug Interactions. Heterocyclic antidepressants usually take 2 to 4 weeks to have any significant antidepressant effect. Side effects, however, can occur within 24 hours and can continue throughout the course of treatment. A comparison of the relative degree of side effects for the antidepressants is presented in Table 28–3. Some side effects are beneficial to the client; for example, sedation is a benefit to a client suffering from insomnia. More frequently, however, side effects such as dry mouth, constipation, orthostatic hypotension, blurred vision, and impaired sexual arousal (erectile function and orgasm) are annoying at best and can seem debilitating at worst. To a person already suffering from depression these side effects can seem like too great a burden to bear. The nurse is in an excellent position to listen and offer hope by pointing out that the side effects will lessen and may disappear with time, whereas the antidepressant effects will increase.

It may take longer than 4 weeks to find the optimum dose of an antidepressant. Although 70 percent of clients respond positively to the first antidepressant prescribed, it is not unusual for a client to have to switch to another medication. This can be discouraging for the client. Again, the nurse can provide needed encouragement and perspective during this period. All these medications can cause side effects to some degree in all clients. The associated symptoms of adverse effects of the antidepressants are presented in Table 28–4.

Other possible side effects from heterocyclics include the following:

- Risk of seizures: All heterocyclics can lower the seizure threshold and must be used with caution in clients with a history of seizures. Moreover, maprotiline and clomipramine, even at therapeutic levels, have been associated with seizures in clients without a history of seizures.

![Table 28–3](image_url)

### Table 28–3

<table>
<thead>
<tr>
<th>MEDICATIONS</th>
<th>ANTICHOLINERGIC EFFECTS</th>
<th>SEDATION</th>
<th>ORTHOSTATIC HYPOTENSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline (Elavil)</td>
<td>***</td>
<td>***</td>
<td>**</td>
</tr>
<tr>
<td>Clomipramine (Anafranil)</td>
<td>***</td>
<td>***</td>
<td>**</td>
</tr>
<tr>
<td>Doxepin (Adapin, Sinequan)</td>
<td>**</td>
<td>***</td>
<td>**</td>
</tr>
<tr>
<td>Imipramine (Tofranil)</td>
<td>**</td>
<td>**</td>
<td>***</td>
</tr>
<tr>
<td>Trimipramine (Surmontil)</td>
<td>**</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Amoxapine (Asendin)</td>
<td>***</td>
<td>**</td>
<td>*</td>
</tr>
<tr>
<td>Desipramine (Norpramin)</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Nortriptyline (Aventyl, Pamelor)</td>
<td>**</td>
<td>**</td>
<td>*</td>
</tr>
<tr>
<td>Protriptyline (Vivactil)</td>
<td>***</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Maprotiline (Ludiomil)</td>
<td>**</td>
<td>**</td>
<td>*</td>
</tr>
<tr>
<td>Trazodone (Desyrel)</td>
<td>*</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Nefazodone (Serzone)</td>
<td>**</td>
<td>**</td>
<td>*</td>
</tr>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>*</td>
<td>0</td>
<td>*</td>
</tr>
<tr>
<td>Fluvoxamine (Luvox)</td>
<td>*</td>
<td>0</td>
<td>**</td>
</tr>
<tr>
<td>Paroxetine (Paxil)</td>
<td>*</td>
<td>0</td>
<td>*</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>*</td>
<td>0</td>
<td>*</td>
</tr>
<tr>
<td>Citalopram (Celexa)</td>
<td>*</td>
<td>0</td>
<td>*</td>
</tr>
<tr>
<td>Bupropion (Wellbutrin)</td>
<td>**</td>
<td>**</td>
<td>*</td>
</tr>
<tr>
<td>Venlafaxine (Effexor)</td>
<td>**</td>
<td>**</td>
<td>*</td>
</tr>
<tr>
<td>Mirtazapine (Remeron)</td>
<td>*</td>
<td>**</td>
<td>*</td>
</tr>
</tbody>
</table>

0, minimal or no sedation. * low; ** moderate; *** high incidence of adverse effects.
• Psychiatric disorders: Tricyclic and heterocyclic antidepressants can induce a manic episode in clients with bipolar I disorder with and without a prior diagnosed manic episode. These drugs may also exacerbate psychotic disorders. Therefore, it is practical to begin with a low dose in these clients and monitor them for signs of mania or psychosis, or consider another antidepressant.

• Cardiac effects: Caution must be used when administering heterocyclics to clients with cardiovascular disease. In high doses, TCAs may produce arrhythmias, sinus tachycardia, flattened T waves, and depressed ST segments and QT intervals. Because the result of these arrhythmias prolongs conduction time, preexisting conduction defects contraindicate the use of these antidepressants.

• Risk of overdose: Drug overdoses with these agents can be lethal, especially when combined with alcohol. Because the risk of suicide is also a consideration with depressed clients, until stabilized, they should not be given more than 1 week’s supply at a time. In addition, because of the prolonged half-lives of these agents, particularly with overdosing, the risk of cardiac arrhythmias is high, requiring cardiac monitoring in the intensive care unit for 3 to 4 days after the overdose attempt (Kaplan & Sadock, 1996).

• Metabolites: One of the breakdown products of the antidepressant amoxapine (Asendin) is loxapine (Loxitane). Because loxapine is an antipsychotic, it carries the risk of extrapyramidal side effects (EPS) and tardive dyskinesia (TD). Many prescribers are reluctant to prescribe this medication for this reason.

### Table 28–4

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>COMMON SIDE EFFECTS</th>
<th>LESS COMMON SIDE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Orthostatic hypotension, tachycardia</td>
<td>Palpitations</td>
</tr>
<tr>
<td>Central Nervous</td>
<td>Drowsiness, weakness, fatigue, dizziness, tremors</td>
<td>Confusion, disturbed concentration, decreased memory, electrocardiographic changes</td>
</tr>
<tr>
<td></td>
<td>Maprotiline: headaches, restlessness</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluoxetine: headaches, insomnia, anxiety, sexual disturbances</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bupropion: agitation, headache, confusion, involuntary movements, ataxia, insomnia, seizures</td>
<td></td>
</tr>
<tr>
<td>Neurological</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autonomic</td>
<td>Dry mouth, blurred vision, constipation, urinary retention</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluoxetine: excessive sweating</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Maprotiline: nausea</td>
<td>Vomiting, nausea, diarrhea, flatulence</td>
</tr>
<tr>
<td></td>
<td>Trazodone: vomiting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluoxetine/sertraline: nausea, diarrhea, weight loss, dry mouth</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bupropion: nausea, vomiting, abdominal cramps, constipation, dry mouth</td>
<td></td>
</tr>
<tr>
<td>Allergic</td>
<td></td>
<td>Skin rash, pruritus, urticaria, photosensitivity, edema</td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
<td>Pharyngitis, rhinitis, sinusitis</td>
</tr>
</tbody>
</table>
Heterocyclics have the potential to produce the following:

1. Increase serum levels with concomitant use of fluoxetine (Prozac) or cimetidine (Tagamet)
2. Decrease therapeutic blood levels for some smokers
3. Increase pressor response to norepinephrine and intravenous epinephrine
4. May reduce the serum levels with concomitant use of birth control pills through induction of hepatic enzymes

**Selective Serotonin Reuptake Inhibitors (SSRIs)**

SSRIs have become the first-line treatment of major depression because of the favorable side effect profile and efficacy. As their name implies, SSRIs potently and selectively inhibit the neuronal reuptake pump of 5-HT in the synaptic cleft and increase 5-HT transmission with little effect on the reuptake of norepinephrine or dopamine. SSRIs share this property with TCAs. Fortunately, their actions avoid the vast actions of TCAs, including blockage of histamine, cholinergic, and alpha, adrenergic receptors, and their adverse effects (Kaplan & Sadock, 1996; Preskorn, 1997). Thus their action appears to be more specific and their side effect profile more narrow. Examples of SSRIs include fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), citalopram (Celexa)—primarily used to treat major depression, anxiety disorders, impulsive control disorders, and eating disorders. Fluvoxamine (Luvox), another SSRI, has shown efficacy in the treatment of obsessive-compulsive disorder (see Table 28–2).

The SSRIs have diverse structures. Paroxetine, for example, is a phenylpiperidine derivative, whereas sertraline is a naphthaleneamine derivative. The efficacy of paroxetine and sertraline for the management of major depression has been established by controlled studies of 6 to 8 weeks, principally in outpatient settings (DeVane, 1992; Preskorn, 1997). Paroxetine’s metabolism through the cytochrome P450 (cyp) 2D6 suggests potential drug interactions and dosage adjustments.

**Drug Interactions and Side Effects.** The SSRIs are eliminated by extensive hepatic biotransformation involving the P450 enzyme system, and all are involved in varying degrees in mediating the effects on the metabolism of other drugs (e.g., inhibition of cytochrome P450). Thus, caution should be used with other coadministration of SSRIs and other drugs metabolized by this isoenzyme, including MAOIs, phenothiazines, alprazolam, triazolam, and type IC antiarrhythmics (e.g., flecainide, encainide, and propafenone) or drugs that inhibit this enzyme (e.g., quinidine) (Nemeroff, DeVane, & Pollock, 1996).

SSRIs are generally well absorbed and have a more rapid onset of action than do other classes of antidepressants—1 to 3 weeks, rather than the 2 to 4 weeks suggested for the heterocyclics. Of note, fluoxetine has a significantly longer half-life (e.g., 2 to 3 days; metabolite norfluoxetine, 7 to 9 days) than do most other antidepressants, which means that it will take much longer to clear out of the client’s system on discontinuation of the medication. It is recommended for all the SSRIs that an MAOI not be used concomitantly and that at least 5 weeks should lapse between discontinuation of an SSRI and initiation of treatment with an MAOI because of potential life-threatening drug interactions (i.e., 5-HT syndrome, hypertensive crisis). Similarly, at least 2 weeks should be provided from the discontinuation of MAOI therapy and the initiation of therapy with an SSRI (Kaplan & Sadock, 1996).

The side effect profile for SSRIs differs from those of the heterocyclics and MAOIs. Common side effects include restlessness, insomnia, nausea, diarrhea, headache, dizziness, dry mouth, and tremor; ejaculatory delay may also occur in males. Unlike most other antidepressants, fluoxetine does not stimulate the appetite or cause carbohydrate craving. On the contrary, there is some evidence that SSRIs decrease appetite and can lead to weight loss initially. The SSRIs rarely appear to affect the electrocardiogram and have only minimal cardiovascular effects (Kaplan & Sadock, 1996).

The SSRIs appear to be much safer in overdose than other antidepressants and are not potentiated by alcohol. These features are attractive when one is prescribing to a population with a higher than average risk of suicide. Finally, the SSRIs need less dosage titration than do the heterocyclic or MAOI antidepressants. In general, this makes them easier to prescribe and easier to take.

A potential problem that can arise for clients taking medications that affect serotonin is called *serotonin syndrome*, a condition of serotonergic hyperstimulation. Various combinations of medications can cause it, but it most commonly results from the combination of MAOIs with serotonergic agents. These serotonergic agents include L-tryptophan (an amino acid precursor of 5-HT) as well as fluoxetine, clomipramine, and paroxetine. The possibility of serotonergic syndrome provides additional rationale for the waiting period between antidepressant therapies involving MAOIs.

Classic features of 5-HT syndrome are changes in mental status, restlessness, myoclonus, hyperreflexia, diaphoresis, shivering, and tremor. Obviously, though, these symptoms are not specific to 5-HT syndrome. Careful observation of clients on medications and an understanding of 5-HT syndrome enable the nurse to be alert to this possibility. The treatment of choice is to discontinue the involved medications and provide supportive measures.

**Dopamine-Norepinephrine Reuptake Inhibitors (DNRIs)**

Bupropion (Wellbutrin) is a unicyclic antidepressant that is unrelated to heterocyclic antidepressants or MAOIs. This drug is metabolized to hydroxybupropion. As its name implies, bupropion is a dopamine-norepinephrine reuptake inhibitor (DNRI) whose primary action involves inhibiting the reuptake of norepinephrine and dopamine. Major uses for bupropion include the treatment of major depression and attention-deficit hyperactivity disorder. It has a favorable side effect profile, and it is often used as a first-line drug for the treatment of major depression (Kaplan & Sadock, 1996; Marangell, Yudofsky, & Silver, 1999). The
most common side effects of bupropion include headache, anxiety, diaphoresis, and gastrointestinal disturbances. The incidence of seizures is 0.4 percent, which is four times that of major antidepressants. Nurses must administer bupropion with extreme caution to clients with a history of seizure disorders or who are taking medications that lower the seizure threshold (e.g., antipsychotic agents) and history of eating disorders. Combining bupropion with an MAOI is potentially dangerous and must be avoided (Kaplan & Sadock, 1996).

**Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)**

Venlafaxine (Effexor), is a structurally novel compound that blocks the reuptake of norepinephrine, 5-HT, and, to a lesser degree, dopamine. At lower doses this antidepressant is a potent 5-HT reuptake inhibitor. Higher doses of venlafaxine act as a potent norepinephrine inhibitor. The once-daily dosing and prolonged duration of absorption of venlafaxine extended release (XR) offer the advantage of enhancing client compliance, facilitating administration, and improving the side-effect profile. Primary uses for venlafaxine include major depression, chronic pain syndromes, generalized anxiety disorder, and attention-deficit hyperactivity disorder (Ellingrod & Perry, 1994; Hackett, 2000). Common side effects of venlafaxine are similar to SSRIs and include headache, early stimulation, gastrointestinal disturbances, nervousness, ejaculatory disturbances, anxiety, sleep disturbances, and modest dose-related hypertension. Venlafaxine should not be combined with MAOIs because of the risk of 5-HT syndrome (Kaplan & Sadock, 1996). Venlafaxine can be a beneficial antidepressant if titrated properly to avoid adverse effects.

**Serotonin Modulators**

Trazodone (Desyrel) and nefazodone (Serzone) are structurally unrelated to the tricyclics or tetracyclics but they have many similar properties. Trazodone, like nefazodone, is a potent antagonist at postsynaptic 5-HT₂ receptor sites and a weak inhibitor of 5-HT reuptake. These features are postulated to enhance 5-HT₁₄ neuronal transmission. Common clinical indications of trazodone and nefazodone are major depression, sleep disturbances, and premenstrual dysphoric syndrome. Clinical advantages of nefazodone include its low incidence of sexual disturbances, its sleep normalization properties, and its anxiolytic effects (Goldberg, 1995).

Major side effects of these antidepressants include sedation, nausea, and blurred vision. A major concern about trazodone is the side effect of priapism—it is the only antidepressant associated with this adverse reaction. Trazodone is also associated with orthostatic hypotension and changes in cardiac conduction. A major concern about nefazodone is an increase in liver enzymes. Nurses must avoid administering nefazodone with triazolam (Halcion), and alprazolam because it produces a substantial increase in plasma levels of these compounds (Kaplan & Sadock, 1996).

**Norepinephrine-Serotonin Modulator**

Mirtazapine (Remeron) is a novel antidepressant whose primary efficacy stems from its ability to facilitate 5-HT and norepinephrine transmission. This antidepressant is the first of a new class of agents that are presynaptic alpha-2 adrenergic receptor antagonists as well as 5-HT₂ and 5-HT₄ antagonists. Structurally, mirtazapine is a tetracyclic compound unrelated to TCAs. However, like TCA antidepressants, this antidepressant possesses varying degrees of anticholinergic, antihistaminic, antiadrenergic, and dopamine reuptake blocking properties and are responsible for a wide range of side effects. It is a member of a class known as piperazinoazines and is unrelated to any known class of psychotropic agents. Major clinical implications for mirtazapine include depression and some anxiety disorders (Kehoe & Schorr, 1996; Marangell et al., 1999). Mirtazapine has also been shown to shorten sleep latency and deepen sleep, which is useful in treating insomnia associated with depression (Falkai, 1999; Thase 1999).

Common side effects of mirtazapine include sedation, weight gain, and dizziness. Other side effects include anticholinergic effects, hypertension, increased serum lipid levels, and agranulocytosis. Few drug interactions have been reported between mirtazapine and other agents; however, caution should be used when combining it with other CNS depressants and MAOIs (Kehoe & Schorr, 1996).

Despite the efficacy of the SSRIs and newer-generation antidepressants, 10 to 30 percent of clients experiencing depression fail to respond to these therapies, and 12 to 25 percent respond but have recurrent depressive episodes (Schweitzer, Tuckwell, & Johnson, 1998).

**Monoamine Oxidase Inhibitors (MAOIs)**

MAOIs are no longer considered first-line treatment for depression because of the improved tolerability and safety of new-generation antidepressants. Developed and prescribed in the early 1950s, the MAOIs were the first effective antidepressants as well as the first drugs that gave neuropharmacologists an opportunity to study the relationship between neurotransmitters and mood (Kennedy, McKenna, & Baker, 2000). MAO is an enzyme that catalyzes the breakdown of various amines, including epinephrine, norepinephrine, 5-HT, and dopamine. Inhibition of MAO results in an increased concentration of these amines in the synaptic cleft. Thus, the MAOI antidepressant effects are thought to result from the increased availability of CNS norepinephrine and 5-HT (Kaplan & Sadock, 1996; Marangell et al., 1999). MAOIs are also useful in the treatment of personality disorders, hypochondriasis, agoraphobia with panic attacks, PTSD, pain syndromes, obsessive-compulsive disorder, and phobias. The clinical and pharmacokinetic parameters are presented in Table 28–5.

**Side Effects, Dietary Precautions, and Drug Interactions.**

As Table 28–6 indicates, the side effects of MAOIs are similar to those produced by the heterocyclics. The most trou-
blesome common side effect is orthostatic hypotension. Furthermore, MAOIs, when combined with tyramine-rich food or some medications, can cause a hypertensive reaction, a potentially life-threatening condition. Tyramine is a monoamine present in some foods such as chocolates, beer, and aged cheeses. Because MAOIs prevent the body from breaking down this monoamine, tyramine can provoke the release of norepinephrine from endogenous stores in the body, causing an increase in blood pressure (Kennedy et al., 2000). Most hypertensive reactions are quite mild, with a 20 to 30 mm Hg rise in systolic blood pressure accompanied by headache, flushing, or sweating. An undetected severe reaction, although rare, can result in a cerebrovascular accident (CVA). The fear of hypertensive crisis prevents many prescribers from using any medication from this class.

The general advice that can be given regarding dietary precautions with MAOI therapy is that any food subjected to fermentation during its processing or storage may be rich in tyramine and thus may present the risk of a hypertensive crisis. Foods that are very high in tyramine include cheeses such as Camembert, cheddar, Emmenthaler, and Stilton; meats such as fermented sausages (bologna, pepperoni, salami, and summer sausage); fish (especially herring); overripe fruits such as avocados; and Chianti wine. Other foods that have vasopressors and should be used in moderation include beers, wine, chocolate, and coffee.

Some drugs must be avoided as well. Phenylethylamine compounds, including amphetamines, phenylpropanolamine, ephedrine, phenylephrine, and related stimulants; decongestants; and bronchodilators all may provoke severe reactions in clients treated with MAOIs. The narcotic meperidine (Demerol) must be avoided. Persons taking MAOIs must also avoid concomitant use of heterocyclics and SSRIs. There must be an antidepressant-free period when the client stops an MAOI before beginning another class of antidepressants, and vice versa (Kaplan & Sadock, 1996). Any nurse involved in health education is urged to consult a more detailed source. The list of foods and medicines to avoid can appear intimidating to both the prescriber and the client. This probably explains why MAOIs are rarely initially prescribed as first-line treatment for depression. However, it should be emphasized that these can be very useful medications, especially in clients with serious, difficult-to-treat, or refractory depression. Many clients are willing to live with the prescriptions if they can experience relief from depression.

### Mood Stabilizers

Historically, lithium has been recognized as the drug of choice for the treatment of bipolar disorders. Contemporary research suggests that other drugs, specifically anticonvulsants agents such as valproic acid (Depakene) and carbamazepine (Tegretol) are more effective than lithium in the treatment of...
acute mania and rapid-cycling episodes. In general, these drugs are referred to as mood stabilizers because of their ability to stabilize the mood despite the etiology (Table 28–7).

**Lithium**

Lithium is a naturally occurring alkali metal that shares some characteristics with other monovalent cations such as sodium and potassium. In 1949, Cade, in Australia, was the first to report the therapeutic effects of lithium to treat mania. However, lithium was not approved for use in the United States until 1970 because of reported severe and sometimes fatal cases from uncontrolled use as a substitute for sodium chloride. Lithium is used to treat acute hypomanic or manic episodes and recurrent affective disorders. Table 28–8 presents the clinical and pharmacokinetic parameters of lithium.

**Mechanism of Action.** Lithium remains one of the most effective treatments for depression and mania in bipolar I and II disorders (Tondo, Baldessarini, Hennen, & Floris, 786).

### Table 28–7

**Clinical and Pharmacokinetic Parameters of Mood Stabilizers (Antimanic Agents)**

<table>
<thead>
<tr>
<th>GENERIC NAME</th>
<th>BRAND NAME</th>
<th>DOSAGE RANGE (MG/DAY)</th>
<th>HALF-LIFE (HOURS)</th>
<th>ONSET (DAYS)</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>Eskalith</td>
<td>Acute: 1800</td>
<td>21–30</td>
<td>5–14 days</td>
<td>2 weeks</td>
</tr>
<tr>
<td></td>
<td>Lithobid</td>
<td>Maintenance: 900–1200</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topiramate</td>
<td>Topamax</td>
<td>Maintenance: 400–1300</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Lamictal</td>
<td>Maintenance: 300–500</td>
<td>29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Depakene</td>
<td>1200–2500</td>
<td>5–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divalproex sodium</td>
<td>Depakote</td>
<td>1200–2500</td>
<td>5–20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Seventy to ninety percent of clients with “typical” bipolar illness respond to lithium (Kaplan & Sadock, 1996). Although lithium has been shown to have mild antidepressant properties, it is not as effective as antidepressants. Sometimes it is used to treat schizoaffective disorders, often in conjunction with an antipsychotic agent. Lithium is also useful in preventing recurrent depressive episodes and as an adjunct to antidepressants in the treatment of major depression when the illness is partially refractory to antidepressants alone. Lithium has also been found to be effective in the treatment of aggressive or impulsive behaviors.

### Table 28–8

**Adverse Effects Associated with Lithium Therapy**

<table>
<thead>
<tr>
<th>PLASMA LEVEL (MEQ/L)</th>
<th>COMMON SIDE EFFECTS</th>
<th>LESS COMMON SIDE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.5</td>
<td>Initial treatment: fine hand tremors, polyuria, mild thirst, transient and mild nausea, and discomfort Afterwards: fatigue, acne, electrocardiographic changes, hypothyroidism</td>
<td>Twitching, muscular weakness, restlessness, dry mouth, and thinning hair</td>
</tr>
<tr>
<td>1.5–2.0</td>
<td>Diarrhea, vomiting, nausea, drowsiness, muscle weakness, lack of coordination (may be early signs of toxicity)</td>
<td></td>
</tr>
<tr>
<td>2.0–3.0</td>
<td>Giddiness, ataxia, blurred vision, tinnitus, vertigo, increasing confusion, slurred speech, blackouts, incontinence, fasciculation, myoclonic twitching, hyperreflexia, hypertonia</td>
<td></td>
</tr>
<tr>
<td>&gt;3.0</td>
<td>Seizures, arrhythmias, hypotension, peripheral vascular collapse, stupor, spasticity, coma</td>
<td></td>
</tr>
</tbody>
</table>
Lithium is less effective than other antimanic agents in the treatment of rapid-cycling bipolar disorders. Researchers speculate that membrane transport systems and ion channels play key roles in the regulation of intracellular lithium. Lithium is a monovalent cation with intricate physiological and pharmacologic effects by the brain. By virtue of the ionic properties, it shares other monovalent and divalent ions such as sodium, magnesium, and calcium. Its transport across the cellular membrane enables it to modulate an array of enzymatic processes (Lenox, McNamara, Papke, & Manji, 1997).

Although lithium may cross cell membranes and replaces sodium in support of a single-action potential, it cannot replace the action of sodium in the sodium pump and therefore cannot maintain cellular membrane potential. Lithium's effect on transmembrane ion pumps can possibly alter the distribution of sodium, potassium, and calcium ions. However, these effects appear to occur at higher than therapeutic concentrations of lithium (Jefferson & Greist, 2000).

Other evidence suggests that lithium's effects are caused by its action on the second-messenger system. One of the second-messenger systems involves lithium's inhibition of receptor-mediated activation of adenyl cyclase. Because this effect occurs at lithium levels outside the therapeutic concentration levels, it is an unlikely mechanism. However, the inhibition of adenyl cyclase may contribute to some lithium toxic effects, such as an increase in urine concentration and antithyroid effects. Lithium blocks the ability of neurons to restore normal levels of the membrane phospholipid phosphatidylinositol 4,5-biphosphate (PIP2) after it is hydrolyzed post activation of receptors. PIP₂ is hydrolyzed into two second messengers: diacylglycerol and inositol 1,4,4-triphosphate (IP₃). IP₃ acts to release calcium from intracellular stores, which sets off a cascade of events in many cellular processes. Because the IP₃ cannot cross the blood-brain barrier, the brain must regenerate its own IP₃. Depletion of PIP₂s from cells may reduce the responsiveness of neurons to muscarinic cholinergic, alpha-adrenergic, or other stimuli. Thus, lithium could modulate the hyperactive neurons that contribute to the manic episode (Jefferson & Greist, 2000).

**Effects, Side Effects, and Compliance.** When used to treat acute hypomanic or manic episodes, lithium can begin to be effective within 1 to 2 weeks, but it may take as long as several months to stabilize the mood totally. Anti-psychotics and benzodiazepines are often used to manage the behavioral excitement and psychotic symptoms during the early stages of lithium therapy (Leonard, 1993). Lithium is used for maintenance therapy, with the goal of decreasing the severity and frequency of affective episodes. Even with regular lithium, some clients can experience symptoms, periods of distress, and unpleasant side effects (Tondo et al, 1998).

About 20 to 30 percent of clients discontinue lithium therapy on their own (Facts and Comparisons, 1993). The reasons vary. Some clients deny their need for lithium because they deny they have an illness. Some stop taking it after the episode is resolved, believing that prophylactic use of the medication is unnecessary. Others like the feeling of being high during a manic episode, and others report that lithium decreases their creativity and productivity. Finally, some clients stop taking lithium because of its side effects. The nurse needs to assess clients' reasons for discontinuing medication before lecturing or educating them about compliance.

The common side effects of lithium can include polydipsia, polyuria, tremor, gastric irritation, diarrhea, sexual disturbances, a lack of spontaneity, and weight gain. Many of these side effects appear only in the first days. However, though possibly transient and clinically benign, these side effects can be so bothersome to clients that they stop taking the drug. Sometimes, reducing the dose or using a slow-release form or medications such as propranolol (Inderal) or primidone (Mysoline) may be given to alleviate lithium-induced tremor. Coarser, more severe tremors may be caused by lithium toxicity. Clinically adverse cardiovascular reactions are rarely seen in lithium at therapeutic levels, although serious cardiovascular effects can occur in overdose (Jefferson & Greist, 2000).

A second category of side effects may result from either chronic administration of an inappropriately high dose or acute overdose of lithium (see Table 28–8). These toxic reactions usually occur at normal serum levels higher than 2 mEq/L, although they can occur at serum levels, especially in older adults. Gastrointestinal symptoms may appear, followed by CNS depression, which can include somnolence, sluggishness, ataxia, dysarthria, seizures, increased muscle tone, and increased deep tendon reflexes. At serum levels of 3 mEq/L or higher, cardiovascular collapse can occur. Changes in the client's status in such areas as decreased serum sodium levels, use of diuretics, decreased renal function, and pregnancy can result in the accumulation of lithium and result in toxicity (Facts and Comparisons, 1993; Jefferson & Greist, 2000; Leonard, 1993).

The kidneys excrete lithium almost entirely. Thus, effective regulation of lithium depends in part on the sodium and fluid balance of the body. As an example, sodium depletion can lead to marked lithium retention and possible toxicity. Conversely, high levels of lithium can lead to sodium excretion. Because diuretics affect kidney action, they can also affect lithium levels. Thiazide diuretics commonly cause increased levels of lithium by decreasing clearance; this can happen quite quickly. Potassium-sparing diuretics may also cause moderate increases in lithium levels over time. Osmotic drugs and carbonic anhydrase inhibitors such as an acetazolamide (Diamox) can decrease lithium levels by increasing excretion (Jefferson & Greist, 2000).

Long-term lithium therapy can have serious consequences for clients. It can cause a decrease in thyroid hormone. Transient and mild disturbances in thyroid function testing are common during early treatment. Women and clients with preexisting thyroid abnormalities are at risk of
this thyroid-related complication. Researchers submit that lithium impedes the secretion of hormone from the gland. Approximately 4 percent of clients taking lithium develop hypothyroidism and require supplemental hormone replacement treatment, such as levothyroxine (Synthroid). Because hypothyroidism mimics depression, the clinician needs to consider both possibilities (Jefferson & Greist, 2000).

The second serious adverse reaction that can occur with long-term lithium therapy is permanent structural changes in the kidneys. These changes result in chronic tubulointerstitial nephropathy. Because both the thyroid and renal changes are potentially serious side effects, several guidelines need to be followed:

1. Thyroid and renal studies must be performed before lithium is prescribed, and then it must be ordered on a regular follow-up basis.
2. Regular lithium levels must be obtained.
3. The client should be always maintained on the lowest effective level of lithium.
4. Because dehydration may increase renal damage, adequate fluid intake must be maintained.
5. Clients and family members must be educated about conditions that increase the risk of lithium toxicity, including sodium diet restrictions, profuse sweating, or diarrhea and vomiting.

Nonsteroidal anti-inflammatory drugs (NSAIDS) such as ibuprofen (Motrin), naproxen (Naprosyn), diclofenac (Voltaren), ketoprofen (Orudis), and celecoxib (Celebrex) can increase lithium levels. Risk factors for adverse reactions to these agents include high doses, older age, and renal impairment (Jefferson & Greist, 2000).

Finally, an encephalopathic syndrome similar to neuroleptic malignant syndrome has occurred in a few clients treated with an antipsychotic and lithium. Although rare, the possibility of this syndrome increases the necessity of monitoring clients for neurological toxicity (Jefferson & Greist, 2000).

**Dosage and Toxicity.** Lithium is available as a carbonate (pills, tablets, or Eskalith) and as a citrate (liquid). It is usually ordered two or three times a day, although some prescribers believe a once-daily dosing is effective. Lithium has a rather narrow range of effectiveness; too little lithium has little therapeutic value, but only a little too much can produce toxicity. Because of this narrow range, clients need to be well educated about signs of toxicity. It is for this reason also that clients on lithium are required to have serum lithium levels obtained. Initially, these are required frequently as the correct dosing regimen is sought. When stable, lithium levels are required every 1 to 3 months. The lithium levels need to be determined 12 hours after the client’s last dose to be interpreted correctly. Although values may differ among laboratories, the usual therapeutic range is 0.5 to 1.5 mEq/L. When clients with bipolar disorders do not respond to lithium or cannot tolerate it, other agents can be used (Jefferson & Greist, 2000).

All medications, including lithium and various anticonvulsants that have been documented to be effective agents for clients with bipolar disorder, are potentially teratogenic. Llewellyn, Stowe, and Strader (1998) suggest that the treatment plan for women with bipolar disorder, who are of reproductive age or potential, should include several strategies, regardless of the antimanic agent:

1. Assess and document the client’s birth control method.
2. Order a pregnancy test.
3. Document informed consent regarding the risks for pregnancy exposure.

**Nonresponding Clients.** Although lithium is considered the mainstay of pharmacologic intervention for most clients with bipolar disorders, it is recognized that some clients with classic bipolar disorder and a significant number of clients with bipolar variants do not respond to lithium therapy. This subgroup of nonresponders may include those with rapid-cycling bipolar disorder (four or more affective episodes per year), schizoaffective disorder, or dysphoric or mixed mania (defined as a state that simultaneously has both manic and depressive features); older adults; and those with manias arising from underlying general medical conditions, such as CNS diseases, conditions caused by strokes, tumors, traumatic brain injury, and infections. It is also evident that some persons whose symptoms are controlled with lithium cannot tolerate its short- or long-term side effects.

**Anticonvulsants**

The three most common alternatives to lithium for the treatment and prophylaxis of bipolar I disorders are carbamazepine (Tegretol), valproic acid (Depakene), gabapentin (Neurontin), and topiramate (Topamax). Like lithium, these agents exert some antidepressant effects prophylactically, but they are not effective as primary agents for treating major depression.

**Valproic Acid and Its Derivatives**

This group includes valproic acid, its sodium salt valproate, and divalproex sodium (Depakote). Regardless of the form, the dosage is expressed as valproic acid equivalents. Valproic acid is prescribed as an anticonvulsant and has been found effective in the treatment of a host of mental illnesses such as bipolar disorder, anxiety and psychotic disorders, withdrawal and dependence, TD, agitation associated with dementia, and borderline personality disorder (Davis, Adinoff, & Petty, 2000). Its mechanism of action remains unclear, but it is thought to be a GABA-ergic drug. The mechanism of action may also involve the monoamines, specifically by enhancing serotonergic and reducing dopaminergic function. The results of valproic acid’s actions on these neurotransmitters is believed to be the basis of its efficacy in exerting antimanic effects, particularly in the treatment of bipolar disorder I in the acute manic phase (Keck, McElroy, & Strakowski, 1998).
As with lithium and valproic acid, serum blood monitoring is necessary. The most common side effects of valproic acid are the gastrointestinal disturbances, which can be reduced by using the enteric-coated divalproex sodium preparation. The most serious adverse reactions include hepatic failure, pancreatitis, and endocrine disturbances, although the incidence is low. Children younger than 2 years of age and clients with severe seizure disorders accompanied by mental retardation are among the higher-risk groups for serious adverse side effects (McElroy, Pope, & Keck, 2000). Hence, liver function tests are necessary before initiating valproic acid medication. The nurse can review with the client the potential signs and symptoms of liver failure (malaise, weakness, lethargy, facial edema, anorexia, jaundice, and vomiting) as well as monitoring for them throughout treatment. A complete blood count, including platelets, is also recommended because thrombocytopenia has been reported. These diagnostic tests, along with valproic acid serum levels, need to be performed regularly while the client is on valproic acid.

Initial treatment with valproic acid may be associated with drowsiness, tremor, and nausea. Other side effects of this medication include hair loss, weight gain, and headache. As previously mentioned, pure valproic acid is very poorly tolerated by clients; the enteric-coated form is preferred. Valproic acid’s most significant drug interactions involve its effects on other anticonvulsants; otherwise, it has few significant drug interactions.

Overall, valproic acid is well tolerated and its entericoated form, divalproex sodium (Depakote) is more easily tolerated than valproic acid. Because of valproic acid’s tendency to inhibit hepatic enzymes, there is a possibility for increases in the levels of other medications. It is also highly protein bound and may displace other highly bound drugs from protein-binding sites. Although both valproic acid and carbamazepine are prescribed as single-agent medications, it is not unusual to see both of them used in combination with lithium. As is true of lithium, both carbamazepine and valproic acid are dangerous in overdose and are contraindicated during pregnancy. Because valproic acid and carbamazepine are anticonvulsants, neither should be stopped abruptly because they may precipitate status epilepticus.

Carbamazepine

Carbamazepine is prescribed for a host of conditions, including seizure disorder, trigeminal neuralgia, phantom limb pain, alcohol withdrawal, and resting leg syndrome (see Table 26-7). An unlabeled indication is neuronal diabetes insipidus (Facts and Comparisons, 1993). Carbamazepine has also been found to exert potent antimanic effects. It has recently been used for treating intermittent explosive behavior disorder, which is associated with undiagnosed temporal lobe epilepsy. Although its exact mechanism remains unknown, there has been a focus on carbamazepine’s ability to inhibit kindling. Kindling refers to a neurophysiological response that eventually produces a progressive sensitization of a neuron. Some researchers link kindling to mood disorders, including bipolar I disorder and major depression (Post & Weiss, 1998).

Side Effects, Toxicity, and Drug Interactions. As with lithium, monitoring serum blood levels are necessary. Carbamazepine can cause aplastic anemia and agranulocytosis. Although the incidence of these adverse reactions is low, a complete blood count, including platelets, reticuloocytes, chemical screen, and electrolytes, is suggested before initiating treatment and should be repeated regularly while the client continues on carbamazepine. In addition, regular testing is also required to check serum levels. The nurse can explain the rationale for this required blood study as well as provide encouragement around the sometimes frustrating need for regular venipuncture. The nurse can remind the client of the importance of reporting any signs and symptoms of possible hematological problems such as fever, sore throat, mouth ulcers, easily bruising, petechiae, or purpural hemorrhage. Any rash needs to be reported immediately.

Initial treatment with carbamazepine may be associated with mild degrees of sedation, tremor, slurred speech, nausea, vomiting, vertigo, ataxia, and blurred vision. The client is encouraged to take carbamazepine with food to decrease any nausea. Generally, these side effects lessen over time. If they persist or worsen, toxicity should be considered, the medication discontinued, and a serum level obtained.

Carbamazepine is a pharmacologically complicated drug with several drug interactions that should be kept in mind. Besides inducing its own metabolism, it induces the metabolism of other drugs. For example, the concentration of antipsychotic medication (especially haloperidol [Haldol]) is decreased when carbamazepine is coadministered. This means that a client with previously well-controlled symptoms may experience a worsening of symptoms when carbamazepine is administered. The nurse can help the client monitor the symptoms during this initial period. Carbamazepine may reduce the effect of birth control pills, and it can cause birth defects. Both the clients and their prescribers need to be aware that a higher dose of birth control pills may be required. Erythromycin can inhibit carbamazepine metabolism and lead to carbamazepine toxicity. Some additional medications that interact with carbamazepine metabolism and lead to toxicity are cimetidine (Tagamet), verapamil (Isoptin), and isoniazid (INH). Conversely, carbamazepine may increase the risk of isoniazid-induced hepatotoxicity (Zarate & Tohen, 2000).

Gabapentin

Gabapentin (Neurontin) is a relatively new anticonvulsant agent currently approved by the U.S. Food and Drug Administration as an adjunct agent for the treatment of partial seizures with and without generalization. Although the exact mechanism underlying its anticonvulsant actions is not clearly understood, its efficacy appears to lie in its effect on a host of important neurotransmitter systems. It potentiates GABA activity, inhibits glutamate synthesis and sodium channels, and reduces norepinephrine and dopaminergic
release. Because of its effect on mood, it has gained attention in psychiatry as a potential treatment drug for bipolar disorders, anxiety disorders, impulsivity disorders, and alcohol withdrawal (Magnus, 1999; Sussman, 2000).

**Side Effects, Toxicity, and Drug Interactions.** Major side effects of gabapentin (Neurontin) include sedation, dizziness, and ataxia, which tend to be transient and occur during early treatment. Lower extremity edema has also been reported. This drug is not protein bound nor does it induce hepatic enzymes. Gabapentin is excreted unchanged by renal excretion, thus it does not require serum monitoring. Major drug interactions include reduction in absorption when gabapentin is taken with antacids and enhanced sedation when taken with other CNS depressants.

**Lamotrigine**

Another anticonvulsant agent, lamotrigine (Lamictal), is also being used to treat treatment-refractory bipolar disorder. Lamotrigine acts at voltage-sensitive sodium channels. Presumably, this effect stabilizes neuronal membranes and modulates the presynaptic release of glutamate and aspartate. Like other antimanic agents, this drug is contraindicated during lactation and pregnancy.

**Side Effects, Toxicity, and Drug Interactions.** Common side effects of lamotrigine include dizziness, ataxia, headache, tremor, depression, somnolence, rash, vomiting, memory disturbances, diarrhea, and rash. One of the most alarming side effects of lamotrigine is a life-threatening rash known as Stevens-Johnson syndrome. Most rashes appear within 2 to 8 weeks of the initiation of lamotrigine therapy, but some occur after long-term treatment. The incidence is considerably higher in pediatric clients, with a reported incidence of 1 in 50 to 1 in 100 (Rzany et al., 1999). Nurses must assess clients for this rash and provide health education about desired and potential adverse drug reactions. Informed consent and health teaching are a necessary part of treatment planning. The rash is also likely to occur during prolonged treatment (e.g., 6 months), and there is an increased risk when this drug is combined with valproic acid. Nurses must instruct the client to discontinue this medication at the first sign of a rash and seek medical attention. High-risk groups for this life-threatening rash include children, women, and those using valproic acid.

Major drug interactions with lamotrigine include those drugs that inhibit the hepatic cytochrome P450 system, including carbamazepine. Serum blood levels are not required with lamotrigine.

**Topiramate**

Recent studies indicate the efficacy of topiramate (Topamax), an anticonvulsant or mood stabilizer in the treatment of bipolar disorders. Topiramate’s efficacy lies with inhibition of sustained repetitive firing and its enhancement of GABA effects. It blocks the adenosine monophosphate (AMP)-type glutamate receptor (MacDonald & Greenfield, 1997). This medication is well tolerated with slow titration. Major side effects of topiramate are CNS related and include sedation, diplopia, cognitive blunting, paresthesias, and a distinct word-finding difficulty in about 15 percent of clients (Blum, 1998). Additional effects include weight loss and formation of kidney stones because of its weak carbonic anhydrase inhibitor properties. Serum monitoring is not required.

A final note about novel anticonvulsant agents used as a mood stabilizer is a brief discussion about tiagabine (Gabitril). Although it is too early to discern its long-term efficacy and side effect profile, this novel mood stabilizer is thought to act by inhibiting GABA into the presynaptic neurons, resulting in increased GABA levels (MacDonald & Greenfield, 1997). It is believed to produce less dose-related cognitive disturbances than older drugs. The most common side effects of tiagabine, like other novel anticonvulsants, are CNS and GI related (Blum, 1998).

**Antipsychotics**

The term antipsychotic or neuroleptic is used interchangeably in this chapter and refers to a group of drugs classified as dopamine receptor antagonists. The efficacy of neuroleptic agents in treating psychotic symptoms lies in their ability to decrease dopamine activity. Researchers submit that psychotic disorders, including schizophrenia, substance-induced and other psychiatric illnesses are linked to increased dopamine activity.

**Typical or Conventional Antipsychotics**

The advent of antipsychotic agents in the early 1950s revolutionized psychiatric care. Many clients who had been institutionalized indefinitely, often in inhumane conditions, were afforded symptom relief. The antipsychotic medications are divided into families based on their chemical structures. These structures also determine the mechanism of action of the medications. The clinical and pharmacokinetic parameters of the antipsychotics are presented in Table 28–9. Table 28–10 lists receptor sites and side effects of antipsychotics.

**Phenothiazines**

Before the advent of atypical neuroleptics, the most commonly prescribed neuroleptics (antipsychotics) belonged to the phenothiazine family. There are three distinct classes in this family. The apipicic phenothiazines include chlorpromazine (Thorazine), promazine (Sparine), and trifluromazine (Vesprin) (Baldessarini, 1996). The apipicic phenothiazines are relatively low in antipsychotic potency and high in sedation effects. The piperidine phenothiazines include thioridazine (Mellaril) and mesoridazine (Serentil). These medications are of medium potency in antipsychotic actions, sedation, and EPS. The third class of phenothiazines is the piperazines. Commonly prescribed medications in this class include trifluphenazine, fluphenazine (Prolixin), prochlorperazine (Compazine), and perphenazine (Trilafon) (Baklessarini, 1996). These medications were once considered to be first-line treatment of schizophrenia and other psychotic disorders. They are considered to be effective in controlling psychotic symptoms with little or no sedation, but they are more likely than atypical neuroleptics to produce acute and chronic adverse reactions, such as EPS and TD.
### Table 28–9

**Pharmacokinetic Properties of Antipsychotics**

<table>
<thead>
<tr>
<th>MEDICATIONS</th>
<th>DOSAGE RANGE (MG/DAY)</th>
<th>ONSET (MINUTES)</th>
<th>DURATION OF ACTION (HOURS)</th>
<th>HALF-LIFE (HOURS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine (Thorazine)</td>
<td>30–800</td>
<td>30–60</td>
<td>4–6</td>
<td>10–20</td>
</tr>
<tr>
<td>Promazine (Sparine)</td>
<td>40–1200</td>
<td>30–60</td>
<td>4–6</td>
<td></td>
</tr>
<tr>
<td>Triflupromazine (Vesprin)</td>
<td>60–150</td>
<td>15–30</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Thoridazine (Mellaril)</td>
<td>150–800</td>
<td>30–60</td>
<td>4–6</td>
<td>9–30</td>
</tr>
<tr>
<td>Mesoridazine (Serentil)</td>
<td>30–400</td>
<td>30–60</td>
<td>4–6</td>
<td></td>
</tr>
<tr>
<td>Acetophenazine (Tindal)</td>
<td>60–120</td>
<td>30–60</td>
<td>4–6</td>
<td></td>
</tr>
<tr>
<td>Perphenazine (Trilafon)</td>
<td>12–64</td>
<td>30–60</td>
<td>4–6</td>
<td>8–21</td>
</tr>
<tr>
<td>Prochlorperazine (Compazine)</td>
<td>15–150</td>
<td>30–60</td>
<td>3–4</td>
<td></td>
</tr>
<tr>
<td>Fluphenazine (Prolixin)</td>
<td>0.5–40</td>
<td>30–60</td>
<td>6–8</td>
<td>14–153</td>
</tr>
<tr>
<td>Trifluoperazine (Stelazine)</td>
<td>2–40</td>
<td>30–40</td>
<td>4–6</td>
<td></td>
</tr>
<tr>
<td>Chlorprothixene (Taractan)</td>
<td>75–600</td>
<td>30–60</td>
<td>4–6</td>
<td></td>
</tr>
<tr>
<td>Thiothixene (Navane)</td>
<td>8–30</td>
<td>Slow</td>
<td>12–24</td>
<td>34</td>
</tr>
<tr>
<td>Haloperidol (Haldol)</td>
<td>1–15</td>
<td>Erratic</td>
<td>24–72</td>
<td>12–38</td>
</tr>
<tr>
<td>Molindone (Moban)</td>
<td>15–225</td>
<td>Erratic</td>
<td>36</td>
<td>1.5</td>
</tr>
<tr>
<td>Loxapine (Loxitane)</td>
<td>20–250</td>
<td>20–30</td>
<td>12</td>
<td>5–19</td>
</tr>
<tr>
<td>Pimozide (Orap)</td>
<td>1–10</td>
<td>Varies</td>
<td>&gt;24</td>
<td>53–55</td>
</tr>
<tr>
<td>Clozapine (Clozaril)</td>
<td>300–900</td>
<td>Varies</td>
<td>4–66</td>
<td></td>
</tr>
<tr>
<td>Risperidone (Risperdal)</td>
<td>2–6</td>
<td></td>
<td>20–30</td>
<td></td>
</tr>
<tr>
<td>Olanzapine (Zyprexa)</td>
<td>5–40</td>
<td></td>
<td>21–54</td>
<td></td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td>50–750</td>
<td></td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

### Table 28–10

**Receptor Affinity for Antipsychotics**

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>D₁</th>
<th>D₂</th>
<th>5-HT₂ₐ</th>
<th>M₁</th>
<th>α₁</th>
<th>H₁</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>High</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Sertindole</td>
<td>Moderate</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>Moderate</td>
<td>High</td>
<td>Low</td>
<td>High</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5-HT₂ₐ: greater blockade in reference to D₂ leads to fewer EPS.
M₁: dry mouth, constipation, blurred vision, urinary retention, memory deficits, and sinus tachycardia.
α₁: orthostatic hypotension, sexual dysfunction, dizziness, and reflex tachycardia.
H₁: sedation and weight gain.
Butyrophenones
A second class of antipsychotic medications is butyrophenones. The most commonly prescribed drug in this class is haloperidol. Haloperidol is considered similar in potency to the phenothiazine piperazines. It is also related to EPS, particularly acute dystonic reactions (Baldessarini, 1996).

Thioxanthenes
A third class of antipsychotics is the thioxanthenes, which includes chlorprothixene (Taractan) and thiothixene (Navane). These medications are chemically similar to the phenothiazines and act in similar manners. Molindone (Moban), an indole, and loxapine are also examples of antipsychotics.

**Mechanism of Action.** All antipsychotic medications just discussed act by blocking the actions of dopamine in the nigrostriatal area of the mesolimbic area of the brain. A comparison of the degree of side effects of the various antipsychotics is presented in Table 28–11. It is currently believed that these medications have an affinity for the subtype dopamine receptors known as D_2 receptors. The nigrostriatal area and the mesolimbic areas of the brain are rich in these receptors. The action in the mesolimbic area is surmised to decrease the psychotic symptoms of hallucinations and delusions. Additional actions of these drugs include decreasing hostility and agitation, increasing organization in thought processes, and decreasing withdrawal behavior owing to high anxiety and sensory overload associated with psychosis.

**Side Effects.** The action in the nigrostriatal area precipitates a cascade of side effects known as extrapyramidal side effects (EPS). These side effects include akathisia, a subjective feeling of restlessness (Table 28–12). Clients experiencing this side effect appear restless and move constantly.

### Table 28–11

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>ANTICHOLINERGIC EFFECTS</th>
<th>SEDATION</th>
<th>EXTRAPYRAMIDAL SYMPTOMS</th>
<th>ORTHOSTATIC HYPOTENSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine (Thorazine)</td>
<td>**</td>
<td>***</td>
<td>**</td>
<td>***</td>
</tr>
<tr>
<td>Promazine (Sparine)</td>
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<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Trifluromazine (Vesprin)</td>
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<td>***</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Thioridazine (Mellaril)</td>
<td>***</td>
<td>***</td>
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<td>***</td>
</tr>
<tr>
<td>Mesoridazine (Serentil)</td>
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<tr>
<td>Acetophenazine (Tindal)</td>
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<tr>
<td>Perphenazine (Trilafon)</td>
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<td>*</td>
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<tr>
<td>Prochlorperazine (Compazine)</td>
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<td>*</td>
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<tr>
<td>Fluphenazine (Prolixin)</td>
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<tr>
<td>Trifluoperazine (Stelazine)</td>
<td>*</td>
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<td>*</td>
</tr>
<tr>
<td>Chlorprothixene (Taractan)</td>
<td>**</td>
<td>***</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Thiothixene (Navane)</td>
<td>*</td>
<td>*</td>
<td>***</td>
<td>*</td>
</tr>
<tr>
<td>Haloperidol (Haldol)</td>
<td>*</td>
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<td>***</td>
<td>*</td>
</tr>
<tr>
<td>Molindone (Moban)</td>
<td>*</td>
<td>*</td>
<td>***</td>
<td>*</td>
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<tr>
<td>Loxapine (Loxitane)</td>
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<td>**</td>
<td>***</td>
<td>**</td>
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<tr>
<td>Pimozide (Orap)</td>
<td>**</td>
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<td>*</td>
</tr>
<tr>
<td>Clozapine (Clozaril)</td>
<td>***</td>
<td>***</td>
<td>rare</td>
<td>***</td>
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<tr>
<td>Risperidone (Risperdal)</td>
<td>*</td>
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<tr>
<td>Olanzapine (Zyprexa)</td>
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<td>**</td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td>*</td>
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</tr>
</tbody>
</table>

* Low; ** Moderate; *** High incidence of adverse effects.
Table 28–12

<table>
<thead>
<tr>
<th>Extrapyramidal Side Effects from Antipsychotic Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACUTE DYSTONIA</strong></td>
</tr>
<tr>
<td>Manifestations</td>
</tr>
<tr>
<td>Painful and frightening to the client</td>
</tr>
<tr>
<td>Rapid-onset oculogyric crisis</td>
</tr>
<tr>
<td>Opisthotonos</td>
</tr>
<tr>
<td>Torticollis</td>
</tr>
<tr>
<td>Crossing legs frequently</td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Onset (days)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Treatment</td>
</tr>
<tr>
<td>Symptoms disappear when antipsychotic is discontinued</td>
</tr>
<tr>
<td>or dosage is reduced</td>
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<tr>
<td></td>
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<td></td>
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</tbody>
</table>

Prevention is essential
It is important to assess for akathisia, because it is often misunderstood for agitation. The importance of assessment is indicated in the accompanying Research Abstract, Identifying Akinesia and Akathisia: The Relationship Between Patient’s Self-Report and Nurse’s Assessment.

Parkinsonian-like or pseudoparkinsonism extrapyramidal side effects include akinesia, which is slowed or no movement. Manifestations of this side effect include hesitant speech; decreased blinking; and a slow, shuffling gait. Clients display a mask-like facial expression not unlike that of a client with Parkinson’s disease. This side effect may contribute to an appearance of flattened or blunt affect. Closely allied to akinesia is dyskinesia, which is an abnormal, involuntary movement disorder. These movements are spastic, tic-like, or tremorous. They are particularly noticeable in the hands, tongue, and nose.

Still another extrapyramidal side effect is dystonia—abnormal tension or muscle tone. Clients with dystonia often appear rigid and exhibit cogwheeling, a deep tremor of the muscles when a limb is moved while in a flaccid state. Clients may also have acute dystonic reactions, which have a rapid onset and are frightening and embarrassing. An acute dystonic reaction usually begins with a tightening of the jaw and thickening of the tongue. If untreated, acute dystonia may progress to impairment of the intercostal muscles and compromised respiration. Other symptoms of acute dystonia are oculogyric crisis (eyes roll back), opisthotonos (neck contracts backward), and torticollis (neck contracts laterally) (Baldessarini, 1996).

**My Experience with Extrapyramidal Side Effects**

“My mouth is so dry. I feel like I can’t swallow. Why is my mouth tight? Why are my eyes so dry? Even when I blink a lot they are still very dry. I do not know why you are giving a medication that makes me feel so bad. I thought that the medication was supposed to make me feel better. I do not hear voices, but I do not like the way I feel. I am having a hard time sitting still and feel like my legs are moving on their own. I feel so jumpy and strange; in fact, it feels like I am not inside my own body. Please give me something to calm me down and make me sit still and feel like a normal person again.”

**RESEARCH ABSTRACT**

**IDENTIFYING AKINESIA AND AKATHISIA: THE RELATIONSHIP BETWEEN PATIENT’S SELF-REPORT AND NURSE’S ASSESSMENT**


It is not uncommon for nurses to question the veracity of client’s reports of symptoms and subjective feelings during psychopharmacological therapy. Michaels and Mumford studied the relationship between patients’ self-report and nurses’ assessment of two important side effects of neuroleptic drugs: akinesia and akathisia. Akinesia was defined as a set of behaviors characterized by motor slowness and stiffness. Akathisia was defined as a subjective, distressing restlessness leading to the inability to relax. There is disagreement among researchers regarding the reliability of self-reports among psychiatric clients. On the other hand, some found clients’ self-reports to be positively correlated with compliance and positive treatment outcomes.

Michaels and Mumford used a convenience sample of 96 community mental health center outpatients receiving neuroleptic drugs. Psychiatric-mental health nurses evaluated these subjects of akinesia and akathisia after training by a physician who was in the process of developing an evaluation tool. The subjects were also given a paper-and-pencil inventory that included self-report of akinesia and akathisia. The data were pulled from the inventory and clustered into scores for akinesia and akathisia. These scores were compared with those from the assessment tool. The patients’ and the nurses’ responses were positively correlated for akathisia ($r = .67$, $p < .001$) and akinesia ($r = .29$, $p < .05$). It was clear that there was closer correlation between patients and nurses on akathisia than akinesia.

On the basis of their findings, Michaels and Mumford recommend that (a) clients’ self-reports should not be ignored and are believable; (b) assessment must include deliberate and active elicitation of symptom-specific subjective responses and systematic objective observations; and (c) an ongoing, supportive educative relationship is critical in sensitizing clinicians to the subtle symptoms of akinesia and akathisia. Observations and self-report work together to provide an accurate clinical picture and identification of these two side effects of neuroleptic therapy.
Antiparkinsonian Agents

EPS are treated with a group of medications known as antiparkinsonian agents (Table 28–13). These agents include benztropine (Cogentin), diphenhydramine (Benadryl), and trihexyphenidyl (Artane), and their mechanism of action is anticholinergic. Amantadine (Symmetrel) is another commonly used antiparkinsonian agent, which acts by dopaminergic mechanisms. Benztropine and diphenhydramine are both well absorbed and therefore act rapidly when administered intramuscularly, making them particularly useful in the treatment of acute dystonic reaction. Clients may be placed on these medications prophylactically, although whether this practice is safe and efficacious is controversial. Table 28–14 presents the symptoms associated with the adverse effects of the medications for EPS.

Other side effects of antipsychotic medications include orthostatic hypotension, sedation, and endocrine and anticholinergic effects (Table 28–15). Endocrine effects are probably caused by the action of the medication on the hypothalamus. Included in the metabolic changes are weight gain, abnormal glucose levels, amenorrhea, and galactorrhea. In addition, men may experience an inability to maintain erections and retrograde ejaculation, and women may experience inhibition of orgasm. Anticholinergic side effects include dry mouth, blurred vision, urinary difficulties, and constipation. The anticholinergic side effects, in particular, tend to decrease over time. However, all of these adverse reactions should be considered for purposes of client and family education.

Another consequence of antipsychotic medications is tardive dyskinesia. Initially, tardive dyskinesia was thought

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### Antiparkinsonian Agents

**EPS are treated with a group of medications known as antiparkinsonian agents (Table 28–13).** These agents include benztropine (Cogentin), diphenhydramine (Benadryl), and trihexyphenidyl (Artane), and their mechanism of action is anticholinergic. Amantadine (Symmetrel) is another commonly used antiparkinsonian agent, which acts by dopaminergic mechanisms. Benztropine and diphenhydramine are both well absorbed and therefore act rapidly when administered intramuscularly, making them particularly useful in the treatment of acute dystonic reaction. Clients may be placed on these medications prophylactically, although whether this practice is safe and efficacious is controversial. Table 28–14 presents the symptoms associated with the adverse effects of the medications for EPS.

### Table 28–13

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Dosage Range (mg/day)</th>
<th>Half-Life (hours)</th>
<th>Onset Oral</th>
<th>Onset Intramuscular</th>
<th>Duration (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dopaminergic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amantadine</td>
<td>Symmetrel</td>
<td>100–300</td>
<td>9–37</td>
<td>4–48 hours*</td>
<td>NA</td>
<td>12–24</td>
</tr>
<tr>
<td><strong>Anticholinergics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benztropine</td>
<td>Cogentin</td>
<td>0.5–6</td>
<td>?</td>
<td>1–2 hours</td>
<td>15 minutes</td>
<td>24</td>
</tr>
<tr>
<td>mesylate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biperiden</td>
<td>Akineton</td>
<td>2–16</td>
<td>18–24</td>
<td>60 minutes</td>
<td>15 minutes</td>
<td>6–10</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Benadryl</td>
<td>10–400</td>
<td>4–15</td>
<td>30–60 minutes</td>
<td>15–30 minutes</td>
<td>4–6</td>
</tr>
<tr>
<td>Procyclidine</td>
<td>Kemadrin</td>
<td>7.5–20</td>
<td>11–12</td>
<td>30–45 minutes</td>
<td>NA</td>
<td>4–6</td>
</tr>
<tr>
<td>Trihexyphenidyl</td>
<td>Artane</td>
<td>1–10</td>
<td>5.6–10</td>
<td>60 minutes</td>
<td>NA</td>
<td>6–12</td>
</tr>
</tbody>
</table>

*Response takes 2 weeks.

### Table 28–14

<table>
<thead>
<tr>
<th>System</th>
<th>Common Side Effects</th>
<th>Less Common Adverse Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Dizziness, drowsiness, blurred vision</td>
<td>Orthostatic hypotension, tachycardia, palpitations</td>
</tr>
<tr>
<td>Central Nervous</td>
<td>Amantadine: anxiety, confusion, irritability, difficulty concentrating</td>
<td>Confusion, headache, disorientation</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Dry mouth</td>
<td>Amantadine: fatigue, insomnia, weakness, visual disturbances</td>
</tr>
<tr>
<td></td>
<td>Amantadine: nausea, vomiting, anorexia, constipation</td>
<td>Amantadine: dry mouth, increased frequency of urination</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Amantadine: urinary retention</td>
<td>Amantadine: skin rash, dyspnea</td>
</tr>
</tbody>
</table>
to occur only after prolonged use of antipsychotics, but current research is showing an increased prevalence of this side effect after short-term administration, particularly in the older adult (Baldessarini, 1996; Morgenstern & Glazer, 1993). Researchers now believe that TD represents a hypersensitivity to dopamine from extended D₂ antagonism by conventional antipsychotic agents. Older adults have a four- to five-time incidence of TD than clients ages 25 to 35 (Tandon, Milner, & Jibson, 1999). The American Psychiatric Association (APA) Task Force on TD estimated an incidence of 5 percent annually of exposure in young adults and 30 percent incidence after 1 year of treatment among older adults (APA, 1992). TD is irreversible and severely debilitating. In addition, there is no known treatment except to decrease antipsychotic medication to the absolute minimal level that will still afford symptom control. The most important factor in treating TD is that the antipsychotic medication should never be abruptly stopped or the symptoms will quickly, and possibly irreversibly, exacerbate. Therefore, it is imperative that the nurse distinguishes these symptoms from those of EPS. Major symptoms of TD begin with orofacial dyskinetic manifestations such as mouth smacking, frequent blinking and frowning, chewing movements, protrusion of tongue, and puffing of cheeks, and later accompanied by limb and truncal movements.

Early detection of TD is essential. The nurse is often involved in routine screening and monitoring of clients for the presence of abnormal movements. Although standard neurological examinations can be used for this purpose, the Abnormal Involuntary Movement Scale (AIMS), designed by the National Institute of Mental Health (NIMH), is more often used (Table 28–16). The client should be screened before any antipsychotic is begun and every 2 weeks to monthly and every 12 months thereafter (APA, 1992). The NIMH shows areas to be screened and includes the examination procedure.

### Table 28–15

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>COMMON ADVERSE EFFECTS</th>
<th>LESS COMMON ADVERSE EFFECTS</th>
<th>MECHANISM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autonomic Nervous</td>
<td>Dry mouth, blurred vision, constipation, orthostatic hypotension</td>
<td>Urinary retention, weight gain, dyspepsia, priapism, priapism, incontinence Tachycardia</td>
<td>Blockage of muscarinic cholinergic receptors</td>
</tr>
<tr>
<td>Central Nervous</td>
<td>Sedation, extrapyramidal symptoms, headache, tardive dyskinesia</td>
<td>Galactorrhea, changes in libido, impotence in men, amenorrhea</td>
<td>Blockage of alpha-adrenoreceptors</td>
</tr>
<tr>
<td>Endocrine</td>
<td></td>
<td></td>
<td>Blockage of dopamine receptors</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Jaundice at 2–4 weeks of medication</td>
<td></td>
<td>Supersensitivity of dopamine</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, vomiting</td>
<td>Diarrhea</td>
<td>Unknown</td>
</tr>
<tr>
<td>Ocular</td>
<td>Photophobia, blurred vision</td>
<td>Miosis</td>
<td>Unknown</td>
</tr>
<tr>
<td>Dermatological</td>
<td>Skin rashes</td>
<td>Urticaria, petechiae, erythema, hyperpigmentation</td>
<td>Unknown</td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
<td>Nasal congestion</td>
<td>Unknown</td>
</tr>
<tr>
<td>Hemic/Lymphatic</td>
<td></td>
<td>Clozapine: leukopenia, may cause agranulocytosis in up to 3% of clients</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Table 28–16

Abnormal Involuntary Movement Scale and Examination Procedure for Evaluating Tardive Dyskinesia

Instructions: Complete examination procedure before making ratings. Asterisk (*) denotes activated movements.

EXAMINATION PROCEDURE

Either before or after completing the Examination Procedure, observe the client unobtrusively, at rest (e.g., in waiting room).

The chair to be used in this examination should be a hard, firm one without arms.

1. Ask the client whether there is anything in his or her mouth (gum, candy, etc.) and, if there is, to remove it.
2. Ask the client about the current condition of his or her teeth. Ask the client if he or she wears dentures.
   Do teeth or dentures bother the client now?
3. Ask the client whether he or she notices any movements in mouth, face, hands, or feet. If yes, ask the client to describe them and to what extent they currently bother the client or interfere with his or her activities.
4. Have the client sit in the chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at entire body for movements while client is in this position.)
5. Ask the client to sit with hands hanging unsupported (if male, between legs; if female and wearing a dress, hanging over knees). (Observe hands and other body areas.)
6. Ask the client to open his or her mouth. (Observe tongue at rest within mouth.) Do this twice.
7. Ask the client to protrude his or her tongue. (Observe abnormalities of tongue movement.) Do this twice.
   *8. Ask the client to tap his or her thumb with each finger, as rapidly as possible for 10 to 15 seconds, first with right hand, then with left hand. (Observe facial and leg movements.)
   *9. Ask the client to stand up. (Observe the client’s profile. Observe all body areas again, hips included.)
*10. Ask the client to extend both arms outstretched in front with palms down. (Observe trunk, legs, and mouth.)
*11. Have the client walk a few paces, turn, and walk back to chair. (Observe hands and gait.) Do this twice.

ABNORMAL INVOLUNTARY MOVEMENT SCALE (AIMS)

Movement Ratings: Rate highest severity observed. Rate movements that occur upon activation less than movements that occur spontaneously.

Codes:
0 = None
1 = Minimal; may be extreme normal
2 = Mild
3 = Moderate
4 = Severe

(Circle one)

<table>
<thead>
<tr>
<th>Facial and Oral Movements</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Muscles of facial expression, e.g., movements of forehead, eyebrows, periorbital area, cheeks; include frowning, blinking, smiling, grimacing.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Lips and perioral area, e.g., puckering, pouting, smacking.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. Jaw, e.g., biting, clenching, chewing, mouth opening, lateral movements.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. Tongue Rate only increase in movement both in and out of, NOT inability to sustain movement.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

(continues)
A rare, but potentially fatal syndrome associated with antipsychotic medication is **neuroleptic malignant syndrome (NMS)**. The exact cause of this syndrome is unknown, but it may be associated with effects on the hypothalamus and medulla. The symptomatology of NMS is similar to that of malignant hyperthermia. This syndrome can occur anytime during treatment with neuroleptics, including the novel antipsychotics. NMS has a rapid onset and constitutes a medical emergency. Symptoms include:

- Hyperpyrexia (up to 107°F)
- Severe muscle rigidity that precipitates elevated blood creatinine phosphokinase (CPK) and white blood cells
- Changes in consciousness (agitation or delirium)
- Elevated or labile pulse and blood pressure
- Profuse diaphoresis
- Incontinence
- Mutism
- Hypoxia
- Myoglobinuria and acute renal failure (in severe cases)

Treatment includes supportive care and symptomatic relief of hyperpyrexia; dantrolene (Dantrium) to decrease muscle rigidity and spasm, fever, and tachycardia; and bromocriptine (Parlodel), a centrally active dopamine agonist (Hsin-Tung & Simpson, 2000).

**Atypical Antipsychotics**

With prevailing evidence for the efficacy and benefit of novel or atypical antipsychotics over traditional neuroleptics, the standard of practice has changed rapidly over the past few years. During the late 1990s, traditional neuroleptics
were considered the first-line treatment for schizophrenia and were considered equivalent to the efficacy of atypical antipsychotics for the treatment of positive symptoms. However, by the turn of the century, the APA as first-line treatment for schizophrenia (Currier, 2000; Ho, Miller, Napolous, & Andreassen, 1999), recommended the atypical antipsychotics. In addition, the advent of the atypical antipsychotics represents an advancement in the treatment of schizophrenia and other psychotic disorders. Historically, treatment of these clients centered on managing their symptoms with little regard for their quality of life. The novel antipsychotics offer the client with schizophrenia an improved quality of life with fewer side effects that interfere with a higher level of functioning. With atypical neuroleptics, symptom relief occurs with fewer EPS, or at doses below those that precipitate EPS. Common atypical agents include clozapine (Clozaril), risperidone (Risperdal), olanzapine (Zyprexa), quetiapine (Seroquel), and ziprasidone (Geodon) (see Table 28–10, Receptor Affinity for Antipsychotics).

**Mechanism of Action.** The efficacy of the newer antipsychotic agents are also associated with their well-documented control of positive and negative symptoms of schizophrenia along with their favorable side effect profile. Pharmacologically, novel antipsychotics differ from traditional neuroleptics. Traditional neuroleptic agents have D2 antagonism without 5-HT2 antagonism, whereas the novel agents are serotonin-dopamine-2 (D2) antagonists. Theoretically, this explains the improved efficacy of atypical antipsychotic agents over conventional agents in the treatment of negative symptoms of schizophrenia. The D2 and 5-HT2A antagonism properties confer a lower incidence of EPS and TD, which are the most troublesome side effects of the conventional antipsychotics. Atypical antipsychotics do not raise prolactin levels, which every conventional agent does. These newer agents are more effective than traditional agents in reducing negative symptoms; improving cognitive, sexual, and mood function; and controlling agitation and aggression. Overall, atypical neuroleptics are more likely to improve the client’s quality of life and function and experience fewer acute and chronic adverse drug reactions seen in traditional antipsychotic agents (Tandon et al., 1999).

**Side Effects.** Atypical antipsychotics, such as olanzapine, clozapine, and risperidone, are not classified as neuroleptics because they generally do not produce neurological side effects. Newer antipsychotic agents tend to have a different side effect profile, with a lower risk of motor symptoms, but often, additional undesired adverse reactions. Despite the lower side effect profile of these agents, nurses must thoroughly assess the client’s response to them and potential side effects. The nursing assessment should include careful observation of the client’s movements and asking her to describe any problems throughout antipsychotic treatment. Common side effects of novel antipsychotic agents include sedation, weight gain, insomnia, orthostatic hypotension, agitation, constipation, hypersalivation, and dry mouth.

Many of the side effects associated with atypical antipsychotic agents are dose related. At high doses they have similar side effect profiles as the conventional agents. Although, there is limited evidence of EPS or TD, clozapine does produce a potentially life-threatening agranulocytosis. Therefore, clients on this medication must comply with routine blood monitoring. The cost of clozapine remains high. However, this medication and others in this family have brought dramatic symptom relief to clients who have been labeled treatment resistant.

**Sedatives and Hypnotic Agents**

**Sedatives** or anxiolytic agents are used primarily to treat anxiety disorders or anxiety-provoking situations. In comparison, hypnotics are used to promote sleep. Sedatives and hypnotic agents offer limited use and are often used as adjunct therapy with other nonpharmacologic interventions such as cognitive behavioral therapy and sleep hygiene. The following section focuses on both groups of drugs.

**Anxiolytics.** An anxiolytic is any medication used to treat anxiety. Whether to treat anxiety is often a difficult and controversial decision. Anxiety is a universal experience, a common response to daily stress and conflict (Antai-Otong, 2000). Psychiatric nurses must assess the distress and disabling effects of anxiety and collaborate with the client and treatment options. Health education is an integral part of treatment planning and must include both pharmacologic agents and nonpharmacologic approaches such as stress management and deep abdominal breathing exercises.

Anxiety manifests psychologically as anything from uneasiness and irritability to a frightful feeling of doom. It can present physically in a variety of autonomic nervous system manifestations: tachycardia, palpitations, irregular heart rhythm, dizziness, tremor, excessive sweating, dry mouth, diarrhea, abdominal pain, or headache. More commonly, it presents with a combination of physiological and psychological symptoms. Anxiety can underlie other psychiatric conditions (e.g., depression) as well as many medical conditions such as endocrine disorders. Clearly, the diagnosis and assessment of anxiety are important and challenging initial tasks. Like other psychiatric conditions, anxiety can be treated with environmental, social, psychological, and nonbiological interventions. These interventions should be considered along with medications (see Chapter 11).

Current nomenclature divides anxiety disorders into three major subtypes: phobic disorders (agoraphobia, social phobia, and simple phobia), anxiety states (panic disorder, generalized anxiety disorder, and obsessive-compulsive disorder), and PTSD.

Benzodiazepines, anxiolytic agents, are the most widely used and prescribed drugs in the world. Other classes of drugs that are used to treat anxiety disorders include antidepressants, antihistamines, barbiturates, propanediols, beta blockers (e.g., propranolol), nonbenzodiazepines (buspirone),
and the antipsychotic drugs (Table 28–17). Although the general use of antidepressants has been discussed, their use in treating anxiety can be considered here. Clients with a history of anxiety are likely, even with optimal medication response, to require long-term pharmacologic intervention. Because prolonged administration of benzodiazepines may be associated with drug dependence, it is particularly important to assess the particular type of anxiety disorder the client has. Some anxiety disorders, such as agoraphobia, panic disorder, and PTSD, often respond well to antidepressants. Buspirone and venlafaxine appear useful in generalized anxiety (Brawman-Mintzer, 2001; Delle Chiaie et al., 1995; DeMartinis, Rynn, Rickels, & Mandos, 2000; Sheehan, 1999).

The antianxiety agents were introduced with the promise that they were effective, safe, and nonaddicting. Experience with benzodiazepines and other antianxiety agents have shown otherwise. They can all produce tolerance, dependence, and withdrawal symptoms.

**Benzodiazepines**

Chlordiazepoxide (Librium), the first benzodiazepine, was marketed in 1960, and diazepam (Valium), 3 years later. Presently, there are more than three dozen benzodiazepines available. They are the mainstays of treatment for anxiety, insomnia, alcohol withdrawal, stimulant drug intoxication, and psychosis. Benzodiazepines are highly effective for the alleviation of acute anxiety and retain at least a portion of their efficacy over time. They are remarkably safe in an overdose situation, although the combination of a benzodiazepine with alcohol or another sedative-hypnotic agent can be hazardous (Ballenger, 2000). Overall, the safety profile of benzodiazepines is unparalleled.

The anxiolytic potency of a benzodiazepine correlates with its affinity for benzodiazepine receptors. The efficacy of benzodiazepines is their ability to modulate the GABA system. GABA is a large neurotransmitter system that constitutes about 30 percent of the cortical and thalamic inhibitory system. Benzodiazepines raise the seizure threshold and increase the frequency and activity of the brain waves. Other sedative-hypnotics, such as barbiturates, also produce these effects. The benzodiazepines, especially diazepam, cause skeletal muscle relaxation. Again, it appears that the GABAergic action of benzodiazepines may at least account for the anticonvulsant and muscle relaxant effects. The effects on other organ systems appear to be minimal (Ballenger, 2000).

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As with all CNS depressants, the most common adverse effects of the benzodiazepines are drowsiness and ataxia. The older adult may be more vulnerable to these reactions, because they usually achieve higher blood and tissue drug levels for a given dose and also because the aging brain is more sensitive to the effects of sedatives. Although complications of benzodiazepines during pregnancy are uncertain, some data indicate that these agents can produce palate abnormalities and should be used with caution during pregnancy (Ballenger, 2000).

Reports of paradoxical reactions, or disinhibition, are not infrequent. An increased tendency to express hostility, rage, or aggression, even in persons with no previous history of these feelings, has been reported with diazepam (Valium), alprazolam (Xanax), and chlordiazepoxide (Librium). Benzodiazepines have well-documented amnestic properties. Certainly, this effect can be used to the client’s advantage. For example, benzodiazepines can be given during painful

### Table 28–17

**Clinical and Pharmacokinetic Parameters of Antianxiety Medications**

<table>
<thead>
<tr>
<th>GENERIC NAME</th>
<th>BRAND NAME</th>
<th>DOSAGE RANGE (MG/DAY)</th>
<th>HALF-LIFE (HOURS)</th>
<th>ONSET (MINUTES)</th>
<th>DURATION (HOURS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Xanax</td>
<td>0.75–4</td>
<td>12–15</td>
<td>15–60</td>
<td></td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>Librium, et al.</td>
<td>15–100</td>
<td>5–30</td>
<td>15–45</td>
<td>Varies</td>
</tr>
<tr>
<td>Clorazepate</td>
<td>Tranxene</td>
<td>15–60</td>
<td>30–100</td>
<td>30–60</td>
<td>by age, illness</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Valium, et al.</td>
<td>4–40</td>
<td>20–80</td>
<td>15–45</td>
<td>and dosage</td>
</tr>
<tr>
<td>Halazepam</td>
<td>Paxipam</td>
<td>60–160</td>
<td>14</td>
<td>30–60</td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Ativan</td>
<td>2–4</td>
<td>10–20</td>
<td>15–45</td>
<td></td>
</tr>
<tr>
<td>Oxazepam</td>
<td>Serax</td>
<td>30–120</td>
<td>5–20</td>
<td>15–90</td>
<td></td>
</tr>
<tr>
<td>Prazepam</td>
<td>Centrax</td>
<td>20–60</td>
<td>30–100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Drugs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buspirone</td>
<td>BuSpar</td>
<td>15–60</td>
<td>2–11</td>
<td>3–4 weeks</td>
<td>?</td>
</tr>
<tr>
<td>Chlormezanone</td>
<td>Trancopal</td>
<td>300–800</td>
<td>24</td>
<td>15–30</td>
<td>6</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Benadryl, et al.</td>
<td>75–200</td>
<td>2.4–4.3</td>
<td>30–60</td>
<td>4–10</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>Atarax, Vistaril</td>
<td>50–100</td>
<td>3</td>
<td>15–30</td>
<td>4–6</td>
</tr>
<tr>
<td>Meprobamate</td>
<td>Miltown, Equinil</td>
<td>1200–1600</td>
<td>6–48</td>
<td>60</td>
<td>6–17</td>
</tr>
</tbody>
</table>
or unpleasant procedures in part because they cause antero-
grade amnesia. However, the untoward effects of amnesia in
regular doses of benzodiazepines must also be assessed.

Tolerance to the sedative effects of benzodiazepines
develops; whether it also develops to the sleep-maintaining
or antianxiety effects is unclear. Although benzodiazepine
drugs have been used recreationally, most clients have not
abused these drugs. The possibility of addiction must be
considered, though, because there are some exceptions.
First, most prescribers believe that these agents should not
be prescribed to clients with substance-related disorders,
except when used as part of a detoxification protocol. Second,
if a client takes more of a benzodiazepine than is
prescribed, this behavior needs to be carefully examined.
Third, it should be recognized that the type of anxiolytic
prescribed, the dosage used, and the duration of the agent's
effect all can affect the possibility of a problem in compli-
ance. As an example, the shorter the half-life of the drug
prescribed, which increases the frequency of dosing, the
greater the risk of dependency and addiction.

Benzodiazepine withdrawal can lead to reactions much
like those observed with other sedative-hypnotic compounds,
such as barbiturates and alcohol. Whereas withdrawal reac-
tions from cessation of benzodiazepine use were once
thought to be rare, clinicians now believe that clients taking
benzodiazepines for long periods, even at standard doses,
are vulnerable to withdrawal reactions if the drug is discon-
tinued abruptly. Therefore, clients need to consult with their
prescriber and taper off the medication gradually.

Mild symptoms of withdrawal include insomnia, dizziness,
headache, anorexia, tinnitus, blurred vision, and shakiness.
These symptoms may also indicate a returning anxiety. If
these symptoms begin to wane after several weeks, a with-
drawal reaction seems unlikely.

Severe signs of withdrawal may include hypotension, hy-
perthermia, neuromuscular rigidity, psychosis, and seizures.
Short-acting benzodiazepines may have a higher risk of
withdrawal symptoms because longer-acting agents are self-
tapering.

**Buspirone**

Buspirone (BuSpar) is structurally and pharmacologically
unrelated to benzodiazepines. It has no direct effect on
GABA<sub>A</sub> receptors, is not a CNS depressant, and lacks the
sedative action of the benzodiazepines. It is speculated that
buspirone exerts its anxiolytic effect by acting as a partial
agonist at 5-HT<sub>1A</sub> receptors, particularly in the hippocampus
and other limbic structures. It also increases the norepi-
nephrine metabolism in the locus ceruleus. Buspirone does
not appear to produce tolerance or dependence and has
neither anticonvulsant nor muscle relaxant properties. The
most common side effects are dizziness, nausea, headache,
nervousness, lightheadedness, and excitement. Unlike any
of the benzodiazepines, buspirone is effective only when
taken regularly. It takes 1 to 2 weeks to show initial effects;
maximal effectiveness may be reached after 4 to 6 weeks
(Ballenger, 2000).

**Antihistamines**

Because of their sedative effects, drugs that block central
and peripheral histamine receptors (primarily H<sub>1</sub>) are some-
times used to calm anxious clients. Hydroxyzine (Vistaril)
and diphenhydramine (Benadryl) are frequently prescribed
elements of this class. Besides sedation, these medications
also have antiemetic and antihistamine properties. Unlike
most antianxiety agents, antihistamines depress the seizure
threshold and must be used cautiously in clients with
seizure disorders. They have more anticholinergic action
than the benzodiazepines do, which limits their use, partic-
ularly in older adults (Ballenger, 2000).

**Barbiturates**

Benzodiazepines have largely replaced the once popular
barbiturates. There are several reasons for this. First, benzo-
diazepines appear to be more effective than the barbiturates
in treating anxiety. Second, barbiturate overdose can be
extremely dangerous. Third, barbiturates interact pharma-
logically with a greater number of agents.

**Propranolol**

Propranolol blocks beta-noradrenergic receptors in the
peripheral sympathetic nervous system and probably cen-
trally as well. Although drugs specific to beta-1 (cardiac) and
beta-2 (pulmonary) receptors have recently been devel-
oped, propranolol itself blocks receptors competitively and
without discrimination. Propranolol has extensive effects on
the cardiovascular system, the pulmonary bronchi, and car-
bohydrate and fat metabolism. Although propranolol is
probably not as effective an antianxiety agent as other med-
ications, clients with somatic complaints may find it useful.
It should be noted that propranolol has not been approved
for the treatment of anxiety or other psychiatric conditions.
Propranolol is sometimes given to alleviate lithium-induced
tremors (Ballenger, 2000).

**Propanediols**

The propanediols (e.g., meprobamate [Equanil]) were ex-
tremely popular in the 1950s, but controlled studies have
failed to demonstrate their superiority over barbiturates in
the treatment of anxiety. Neither class of drugs is used today.

**Antipsychotics**

The significant negative side effect profile of the antipsy-
chotics, particularly the conventional agents, makes them a
poor choice to treat anxiety. Only when psychosis is the
cause of the anxiety are they considered.

**Hypnotics**

Almost 20 percent of clients who visit physicians complain
of difficulty sleeping, and half of these clients are prescribed
hypnotics. Insomnia is a symptom with diverse causes,
including medical, psychological, and situational. It is important
to search for a specific treatable cause before prescribing a
nonspecific therapy such as a hypnotic. The client’s sleep
behaviors need to be assessed and reviewed; nonpharmacologic interventions, or sleep hygiene measures, should be implemented whenever possible (Greenblatt, 1992; Roehrs, Rosenthal, Koshrek, Mangano, & Roth, 2001). Sleep hygiene measures are practices that promote sleep such as drinking warm milk; taking a warm bath; reading; developing a regular routine for preparing for sleep; and avoiding food or fluids high in caffeine such as chocolates, coffee, tea, or colas (see Chapter 22).

There are many substances, differing widely in their chemical structure, that can be considered sedative-hypnotics in that they produce dose-dependent CNS depression. The more commonly used agents are presented in Table 28–18 and the symptoms of adverse effects of their use are listed in Table 28–19. There can be cross-reactivity between these diverse compounds. For example, a client who has developed tolerance to a benzodiazepine not only will be tolerant to other benzodiazepines but will also be tolerant to barbiturates and other CNS depressants. Abrupt discontinuation of any of these medications is associated with a withdrawal syndrome. All clients, regardless of whether they have a history of a substance-related disorder, who are regularly using small amounts of sedative-hypnotics may gradually develop tolerance and experience a withdrawal syndrome if the drug is suddenly stopped or significantly decreased. Note that the features of withdrawal syndrome (tremulousness, irritability, and sleep disturbance) may be mistaken for the initial target symptoms. The nurse may be able to explore this in a careful interview.

In summary, it is important to remember (1) the need for careful evaluation before any medication is prescribed or administered; (2) the importance of short-term use if these medications are chosen; (3) the relevance of educating the client on sleep hygiene measures.

**Benzodiazepines and Other Hypnotic Agents**

Should a hypnotic (sedative or sleeping pill) be prescribed, the most likely choice would be a benzodiazepine. Examples of major hypnotics or sedatives are flurazepam (Dalmane), temazepam (Restoril), and zolpidem (Ambien), a nonbenzodiazepine but within the same schedule as hypnotics. It is likely that most, if not all, of the benzodiazepines used to treat anxiety could also be used to induce sleep at the appropriate dosage. It is a corporate decision whether to market benzodiazepines as anxiolytics or hypnotics; FDA labeling approval is based almost entirely on information supplied by the manufacturer.

The two major concerns in choosing a benzodiazepine hypnotic are rapidity of onset and half-life. For clients who report difficulty falling asleep, the rate at which the drug achieves its hypnotic effects is important. Two benzodiazepines that have rapid onset are diazepam (Valium) and flurazepam (Dalmane). Benzodiazepines with long half-lives decrease sleep latency (the time required to fall asleep), decrease early morning awakenings, and usually increase the total amount of sleep. However, the trade-off may be daytime drowsiness and related unwanted effects. Over time, their use must be assessed in terms of the benefits for the client (Ballenger, 2000).

The second important consideration is half-life. Benzodiazepines with short half-lives do not accumulate, but they may cause rebound insomnia. Benzodiazepines decrease the length of sleep in stages 3 and 4 and their effect on rapid eye movement (REM) sleep varies, depending on the client, the illness, and the type and dosage of the drug. Rebound insomnia may occur when a benzodiazepine with a short half-life is used on several consecutive nights.

Flurazepam is a long-acting drug that resembles diazepam. Its half-life of 50 to 100 hours means that the blood level on the eighth morning after a consecutive week of nightly flurazepam is likely to be 4 to 6 times that found on the first morning. A long half-life can have positive consequences: it may be useful for clients who are anxious and have rebound insomnia. Rebound insomnia is less likely with long-acting agents. Negative consequences may include morning hangover (residual sedation and impaired cognitive and motor skills). In addition, potential interactions with other sedatives, including alcohol, may be prolonged.

Temazepam (Restoril), with its shorter half-life, may reduce the hangover, but increase rebound insomnia. Zolpidem (Ambien) is a hypnotic that acts at the GABA-benzodiazepine complex, similarly to benzodiazepines, but it is not a benzodiazepine. This short-acting sleep agent does not produce tolerance. Zolpidem is useful to decrease sleep latency, increase total sleep time, and decrease the number of nighttime awakenings. Zaleplon (Sonata) also has a short half-life. It decreases sleep latency but does not increase total sleep time or decrease the number of awakenings. Although zolpidem and zaleplon are structurally not benzodiazepines, the differences are subtle and thus claims to safety and efficacy need to be carefully evaluated over time.

**Other Agents**

The caveats mentioned regarding the prescription of barbiturates for anxiety apply equally to the prescription of hypnotics. Because of problems with tolerance, abuse, dependency, adverse effects, rebound, and the danger of overdose, barbiturates are rarely prescribed. Other agents formerly widely used and now much less frequently prescribed, for many of the same reasons, are chloral hydrate, glutethimide (Doriden), methaqualone (Quaalude), paraldehyde, and bromides.

**Antihistamines**

Sedating antihistamines, many of which are available over the counter, can be effective hypnotics for some adults. Diphenhydramine is probably the most commonly used drug in this class. It may suppress REM sleep, and REM rebound occurs following its discontinuation. Because of its anticholinergic effects, confusion and delirium can develop in susceptible clients, older adults, and persons taking drugs with anticholinergic activity.
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Dosage Range (mg/day)</th>
<th>Onset (Minutes)</th>
<th>Half-Life (Hours)</th>
<th>Duration of Action (Hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcarbromal</td>
<td>Paxarel</td>
<td>—</td>
<td>250–500 bid or tid</td>
<td>15–60</td>
<td>?</td>
</tr>
<tr>
<td>Chloral hydrate</td>
<td>Noctec</td>
<td>0.5–1g</td>
<td>250 tid</td>
<td>30–60</td>
<td>7–10</td>
</tr>
<tr>
<td>Ethchlorvynol</td>
<td>Placidyl</td>
<td>500</td>
<td>100–200 tid</td>
<td>15–60</td>
<td>10–20</td>
</tr>
<tr>
<td>Ethinamate</td>
<td>Valmid</td>
<td>—</td>
<td>500–1000</td>
<td>20</td>
<td>2.5</td>
</tr>
<tr>
<td>Glutethimide</td>
<td>Doriden</td>
<td>250–500</td>
<td>—</td>
<td>30</td>
<td>10–12</td>
</tr>
<tr>
<td>Methyprylone</td>
<td>Noludar</td>
<td>200–400</td>
<td>—</td>
<td>45</td>
<td>3–6</td>
</tr>
<tr>
<td>Paraldehyde</td>
<td>Paral</td>
<td>10–30 ml</td>
<td>5–10 ml</td>
<td>10–15</td>
<td>3.4–98</td>
</tr>
<tr>
<td>Propiomazine</td>
<td>Largon</td>
<td>—</td>
<td>—</td>
<td>10–20</td>
<td>—</td>
</tr>
</tbody>
</table>

**Benzodiazepines**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Dosage Range (mg/day)</th>
<th>Onset (Minutes)</th>
<th>Half-Life (Hours)</th>
<th>Duration of Action (Hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estazolam</td>
<td>Prosom</td>
<td>1–2</td>
<td>NA</td>
<td>30–60</td>
<td>10–24</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Dalmane</td>
<td>15–30</td>
<td>NA</td>
<td>15–45</td>
<td>50–100</td>
</tr>
<tr>
<td>Quazepam</td>
<td>Doral</td>
<td>15</td>
<td>NA</td>
<td>45–120</td>
<td>25–41</td>
</tr>
<tr>
<td>Temazepam</td>
<td>Restoril</td>
<td>15–30</td>
<td>NA</td>
<td>20–30</td>
<td>10–17</td>
</tr>
<tr>
<td>Triazolam</td>
<td>Halcion</td>
<td>0.125–0.5</td>
<td>NA</td>
<td>15–30</td>
<td>1.5–5.5</td>
</tr>
</tbody>
</table>

**Barbiturates**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Dosage Range (mg/day)</th>
<th>Onset (Minutes)</th>
<th>Half-Life (Hours)</th>
<th>Duration of Action (Hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long acting</td>
<td>Phenobarbital</td>
<td>Barbital, Luminal</td>
<td>100–320</td>
<td>30–120</td>
<td>53–118</td>
</tr>
<tr>
<td></td>
<td>Mepobarbital</td>
<td>Mebural</td>
<td>—</td>
<td>90–400</td>
<td>11–67</td>
</tr>
<tr>
<td></td>
<td>Aprobarbital</td>
<td>Alurate</td>
<td>40–160</td>
<td>120</td>
<td>16–40</td>
</tr>
<tr>
<td></td>
<td>Butabarbital</td>
<td>Butisol, Butratan</td>
<td>50–100</td>
<td>45–120</td>
<td>66–140</td>
</tr>
<tr>
<td></td>
<td>Talbutal</td>
<td>Lotusate</td>
<td>120</td>
<td>60–80</td>
<td>15</td>
</tr>
<tr>
<td>Short acting</td>
<td>Secobarbital</td>
<td>Secondal</td>
<td>100</td>
<td>—</td>
<td>10–15</td>
</tr>
<tr>
<td></td>
<td>Pentobarbital</td>
<td>Nembutal</td>
<td>100</td>
<td>40–120</td>
<td>15–40</td>
</tr>
</tbody>
</table>
It is crucial for the psychiatric nurse to understand the influence of age-related pharmacokinetic and pharmacodynamic processes and their impact on side effect profiles and indication for health education. This section focuses on these issues and the role of the nurse in providing safe drug administration, symptom management and drug response monitoring.

### Sedative and Antianxiety Agents
Because the metabolism of benzodiazepines is slowed in the older adult client, these drugs are likely to remain in the body at higher concentrations than they would under comparable conditions in a younger person. Agents that are not recommended owing to active metabolites are chlordiazepoxide, clorazepate, diazepam, halazepam, and flurazepam. Likewise, barbiturates with longer half-lives and meprobamate should be avoided in this age group. Regardless of the antianxiety or sedative changes, their effects on the older adults, especially on their mental status, must be regularly assessed.

### Antipsychotics
The side effects of primary concern in the older adult population are anticholinergic effects, parkinsonian effects, TD, orthostatic hypotension, cardiac abnormalities, reduced bone density, sedation, and cognitive impairment (Masand, 2000). Antipsychotics, especially the conventional agents, with
greater hypotensive and anticholinergic effects such as mesoridazine (Serentil) and thioridazine should be avoided. The novel antipsychotic agents, such as olanzapine and quetiapine, have favorable side effect profiles that make them the first-line treatment for older adults with psychotic disorders (Kaplan & Sadock, 1996).

Children and Adolescents

Indications for the use of psychotropic medications in children and adolescents have been revolutionized for more than a decade. However, the use of these agents in children presents philosophical, legal, and diagnostic problems. A nurse who is working with children who have been prescribed psychotropic medication needs to consider the following points:

• Developmental factors such as age, gender, weight, and physical health play major roles in how children and adolescents react to drugs. Hepatic metabolism appears to be greatest during infancy and childhood, approximately two times the adult rate in prepuberty and equivalent to adult by age 15 (American Academy of Child and Adolescent Psychiatry, 1998). The clinical significance of this premise suggests that younger children might need higher milligram-per-kilogram dosages than older youth or adults (American Academy of Child and Adolescent Psychiatry, 1998; Vitello, 1998).

• Drug pharmacokinetics differ in children and adults. For example, a child’s liver represents a proportionally larger amount of the total body weight; children often metabolize agents more quickly (Gadow, 1991, 1997). Although drug absorption for most medications is similar in children and adults, children tend to have a faster absorption rate and reach peak plasma levels earlier (Bourin et al., 1992). A lower level of protein binding and lower percentage of body adipose tissue result in smaller depots for drug storage, which means quicker onset of action and decreased duration of effect. Therefore, children may often require relatively higher and more frequent doses than adults, but they tend to develop fewer side effects (Waters, 1990).

• When unwanted reactions do occur, they are generally less severe and respond more readily to a decrease or discontinuation of the medication. Children should be systematically and repeatedly questioned about the development of untoward reactions, because they volunteer this information less readily than adults (Coffey, 2000). Most of the untoward effects that children develop are similar to those in adults.

Antipsychotics

Once a diagnosis has been established that indicates the need for a dopamine receptor antagonist, such as the phenothiazines or serotonin-dopamine antagonists, such as olanzapine, an antipsychotic agent may be prescribed or administered. Major indications for these drugs include psychoses, Tourette’s disorder, and self-injurious behaviors. Side effects produced by these agents are similar to those produced in adults. Young clients may be at a higher risk for EPS. It may be safer to initiate therapy with an atypical antipsychotic. If pediatric clients fail atypical agents, then a typical antipsychotic may be tried. Doses are initiated at half the recommended adult dosage and titrated every 3 to 4 days. Because of the potential for weight gain with the agents, encourage low-calorie snacks and exercise. It is recommended to monitor for TD every 3 months by evaluating clients with the AIMS (Findling, Schulz, Reed, & Blumer, 1998)

Antidepressants

Although the FDA has not approved the use of antidepressants in children younger than 12 years of age, the ultimate decision to medicate rests with the physician or advanced-practice psychiatric nurse and parents. Because hepatic metabolism of TCAs is more rapid in children, they may require adult doses of antidepressants. However, the nurse should closely observe as well as closely question young children who are taking antidepressants, because they may not report adverse effects and may develop serious toxicity at relatively low doses. More rapid metabolism may also mean that the therapeutic response may take longer in children than adults.

TCAs have been approved for use in children and adolescents with enuresis, attention-deficit hyperactivity disorders, and depression. Imipramine (Tofranil), desipramine (Norpramine), and nortriptyline (Aventyl) have been studied most extensively in children and adolescents. Major side effects are similar to those in adults, but cardiovascular ones pose the most significant concern. Because of the safety concerns about cardiovascular side effects, TCAs are not the first-line treatment for depression in children and adolescents. Before being placed on a tricyclic antidepressant, Coffey (2000) recommends the following:

• A thorough history of health that includes individual and family history of cardiovascular, neurological and other medical conditions

• Baseline electrocardiogram (ECG) before initiating medication

• Serum blood monitoring with specified parameters

The SSRI antidepressants are being used extensively in the treatment of depression, obsessive-compulsive disorder, panic disorder, and selective mutism. Overall, these agents are the first-line treatment of specified psychiatric disorders in youth because of their reduced risk of cardiovascular toxicity (Coffey, 2000). SSRIs may be more effective, although caution must be used in clients with other psychiatric disorders. With the use of SSRIs, there is the potential for inducing mania and irritability. Whatever agent is chosen, therapy in pediatric population clients should be initiated at half the recommended adult dosage and titrated at a minimum of 2 weeks.
Mood Stabilizers

Mood stabilizers or antimanic agents are used alone or as adjunct medications in the management of bipolar and other psychiatric disorders. Because of the complexity of bipolar disorder and the range of symptoms that fluctuate and cycle between depressions and mania, psychiatric nurses must understand the role of mood stabilizers in symptom management. In addition, they must be able to work with clients and their families and develop holistic treatment planning that integrates these agents with other interventions to facilitate an optimal level of functioning.

Lithium

Although lithium has not been approved by the FDA in the treatment of bipolar disorders in children, it has been used successfully to manage bipolar I and bipolar II disorders. Because the renal clearance of lithium is higher in children than in adults, children and adolescents may require higher doses to achieve therapeutic blood levels. In addition, renal, thyroid, and cardiac function must be monitored regularly (Coffey, 2000).

Valproic Acid (Depakene)

Although the anticonvulsant valproic acid (Depakene) has not been approved by the FDA for the treatment of psychiatric disorders in children and adolescents, recent study results are promising, and, in some cases, it is being used as first-line treatment for bipolar I and bipolar II disorders. Side effects from this drug are the same in children and adolescents as those in adults (Coffey, 2000).

Sedative and Antianxiety Agents

SSRIs are considered the first-line agents for children and adolescents. TCAs and benzodiazepines may be used when the child has not responded to SSRIs. Before initiating TCAs in children and adolescents, the nurse must order or obtain a baseline ECG because of the potential cardiotoxic effects of these agents. Third-line agents would include MAOIs, antihistamines, and beta-adrenergic antagonists. With the pediatric population it is efficacious to implement cognitive-behavioral therapy. Interventions include illness education, support, relaxation training, and parent behavior management training (Velosa & Riddle, 2000).

Older Adults

Although people age 65 and older make up more than 12 percent of the U.S. population, they receive 25 percent of the prescriptions written for psychotropic medications and 22 percent of all other prescriptions. Older adults are more likely to be receiving multiple medications and thus are at a greater risk for drug interactions; psychotropic medications place older adults at particular risk for cardiac effects. Polytherapy that includes psychotropic drugs with antidopaminergic action is the greatest precipitant of adverse reactions. When the older adult experiences changes in mental status functioning, such as confusion, restlessness, irritability, depression, or psychosis, medications should be suspected as the cause. Because of age-related changes older adults are also more likely to metabolize and eliminate drugs slower, thus requiring lower dosages of medications (Grebb, 2000). The following are some of these age-related changes:

- Decreased renal flow, glomerular filtration, and renal tubular secretions of 50 percent by age 80 mean that medication may stay in the body longer.
- Gastric motility is decreased.
- An increased ratio of adipose tissue to lean body mass results in increased retention of fat-soluble drugs, including psychotropics such as sedatives, antidepressants, and antipsychotics.
- Many drugs are bound to plasma proteins, which are synthesized in the liver. With age, there may be fewer plasma-binding sites and fewer drug-metabolizing enzymes, leading to prolonged, sustained serum drug concentrations. In addition, all psychotropic medications (except lithium) bind extensively to plasma albumin. Because albumin levels decrease with age, older adult clients may be more susceptible than middle-aged clients to toxic responses and may thus require smaller doses of medications.
- Decreased liver function limits drug metabolism and contributes to drug accumulation and overdose.
- Cardiac output may decrease with age, delaying circulation time and thus affecting the distribution of drugs to tissue.

An adverse drug effect may be much more significant to an older adult than a younger one. The postural hypotension and dizziness that can be produced by some psychotropics may be merely annoying to a younger person but can predispose an older person to falling.

Many psychotropic medications produce antidopaminergic side effects such as blurred vision, dry mouth, urinary retention, constipation, and tachycardia. Older adult clients, especially those with some underlying cognitive disorder, may also experience an acute toxic delirium secondary to these antidopaminergic effects. Excessive sedation in the older adult client is possible with most psychotropic medications. Over-sedation may not only be mistaken for depression, but may also reduce the client’s personal contact with the surroundings, impair cognitive capacities, and decrease self-esteem. Signs of CNS depression may include ataxia, dysarthria, diplopia, blurred vision, confusion, dizziness, vertigo, nystagmus, muscle weakness, incoordination, somnolence, and (rarely) respiratory depression (Grebb, 2000).

There is also increased risk of cardiac effects from antipsychotics and heterocycles. These risks include tachycardia, increased incidence of premature ventricular contractions, heart block, and atrial and ventricular arrhythmias. Alcohol and drug use must be carefully assessed in the older adult client. The use of these agents significantly complicates prescribing for this population.
**Antidepressants**

The side effects profile of SSRI antidepressants make them the drug of choice for older adult clients experiencing depression and anxiety disorders. The SSRI antidepressants cause fewer troublesome side effects, including anticholinergic and cardiac, and are therefore the first-line treatment for older adult clients. Other antidepressants with lower anticholinergic potential, such as amoxapine, desipramine, and trazodone, are also preferred for this population over more strongly anticholinergic antidepressants such as amitriptyline, doxepin, imipramine, and protriptyline. The MAOIs are useful in that they lack anticholinergic effects, but they can produce significant hypotension. The sedative effects of cyclic antidepressants may be useful in treating sleep disturbances, but they may be problematic in that they produce daytime drowsiness. For older clients it is recommended to use the XR formulation of venlafaxine (because of the potential for hypertension with the regular release) and SR formulation of bupropion (because of the increased risk of seizures).

**Mood Stabilizers**

Valproic acid is the first-line mood stabilizer in the older adult. However, it is contraindicated in clients with hepatic disease or severe hepatic dysfunction. Lithium can be used safely in the older adult client, but it is generally used in lower dosages, maintaining blood levels in the range of 0.4 to 0.6 mEq/L. Even these dosages may produce signs that appear toxic. Diuretics must be cautiously administered because they may cause increased lithium levels or hypokalemia (Grebb, 2000). The dose of lithium may need to be decreased significantly in elderly clients with renal dysfunction.

**Sedative and Antianxiety Agents**

Because the metabolism of benzodiazepines is slowed in the older adult client, these drugs are likely to remain in the body at higher concentrations than they would under comparable conditions in a younger person. Agents that are not recommended owing to active metabolites are chlordiazepoxide, clorazepate, diazepam, halazepam, and flurazepam. Likewise, barbiturates with longer half-lives and meprobamate should be avoided in this age group. Regardless of the anti-anxiety or sedative changes, their effects on the older adults, especially on their mental status, must be regularly assessed.

**Antipsychotics**

The side effects of primary concern in the elderly population are anticholinergic effects, parkinsonian effects, TD, orthostatic hypotension, cardiac abnormalities, reduced bone density, sedation, and cognitive impairment (Masand, 2000). Antipsychotics, especially the conventional agents, with greater hypotensive and anticholinergic effects, such as mesoridazine (Serentil) and thioridazine, should be avoided. The novel antipsychotic agents, such as olanzapine and quetiapine, have favorable side effect profiles that make them the first-line treatment for older adults with psychotic disorders (Kaplan & Sadock, 1996).

**THE ROLE OF THE NURSE**

Pharmacotherapy is an integral aspect of caring for clients with psychiatric disorders. Psychiatric nurses have major responsibilities in administering and ordering various psychopharmacologic agents. Information concerning the purpose, side effect profiles, client preferences, cultural, age-related issues, and health education are pivotal to safe medication administration. Specific roles and responsibilities of the generalist and advanced-practice registered psychiatric nurse will be discussed in this section.

**The Generalist Nurse**

Psychopharmacology today requires that nurses, clients, physicians, pharmacy specialists, and significant others collaborate by designing quality management strategies that promote optimal benefits and minimal harm. Because nurses are most likely to be the primary team members to administer, observe, assess pharmacologic responses, and intervene when appropriate, they must anticipate responses that the medications are likely to produce. In essence, the psychiatric-mental health nurse has a professional responsibility to comprehend basic knowledge of pharmacology and be able to anticipate drug responses, rather than simply reacting to them later (Lehne, Moore, Crosby, & Hamilton, 1998).

The nurse must understand basic processes underlying the client’s symptoms and behaviors and reasons for administering specific psychopharmacologic agents. The initial step in pharmacotherapy involves gathering baseline data and assessing the client’s mental and physical status and capacity for self-care. Assessment information is critical to the client’s safety because it guides the decision to prescribe and evaluate therapeutic and adverse responses to medication (Lehne et al., 1998). Nurses need to assess the significance of the medication to the client related to family sick role issues and concerns about control and stigma. In addition, nurses are ethically and legally responsible for ensuring that the client and significant others have the information necessary for them to make an informed consent regarding the purpose, desired effects, and potential adverse or interactive effects of these agents and to achieve and maintain an optimal level of health (American Nurses Association [ANA], 2000). The nurse is responsible for (ANA, 2000):

- Providing opportunities for the client and significant others to explore their feelings and concerns related to the medications
- Assessing the client health teaching needs and using them as a guide to individualized health education and include information about delayed beneficial or optimal effects
- Collaborating with the client’s health care provider to assess and individualize the client’s medication and treatment needs
TREATMENT ADHERENCE

A major challenge to nurses in psychiatric-mental health nursing practice is medication adherence (Lund & Frank, 1991). Adherence refers to the extent that a client follows treatment recommendations. It also results when clients make informed choices that help them master the challenges. The outcome of clients' nonadherence with a medication regimen is often recurrence or exacerbation of symptoms (relapse) and rehospitalization. Nonadherence relapse rates are estimated to be 50 percent in the first year and 70 percent in the second year after treatment (Malla et al., 2002; Robinson et al., 2002). Factors that contribute to medication adherence and poor treatment outcomes may be partly related to a lack of integration of services, failure to meet the client's needs, and medication side effects. Additional factors include stigma and cultural factors concerning ambivalent attitudes about drugs that often reflect a knowledge deficit about drug treatment for mental disorders. Most researchers submit that enhancing medication adherence during the early course of psychiatric disorders, such as schizophrenia, is likely to have a substantial impact on positive treatment outcomes (Malla et al., 2002; Robinson et al., 2002). Psychiatric nurses must actively involve themselves in coordinating holistic health care that facilitates symptom management and positive treatment outcomes. Clients often believe that taking psychotropic medications deprives them of control over their lives or that these agents are addictive and they will never be able to stop taking them (Kaplan & Sadock, 1998).

Age-related factors also play a role in adherence, particularly in older adults. Approximately 40 percent or more of older adults fail to take their medications as prescribed. Because of the stigma of mental illness and taking medications, some clients may refuse to adhere to medication regimes. Lehne et al., (1998) delineated factors that contribute to nonadherence in older adults:

- failure to refill prescriptions
- failure to follow correct dosing schedule
- forgetfulness
- failure to understand instructions owing to sensory or cognitive impairment
- inadequate finances to pay for medication
- detailed dosing schedules
- side effects
- stigma
- beliefs that drugs are unnecessary or dosage is too much

Another overlooked factor that contributes to compliance is culture. Because culture shapes beliefs and prospects that govern the client's attitudes and responses about medication, compliance may be a serious problem in cross-cultural clinical settings. Primary reasons for ethnic differences stems

The Advanced-Practice Psychiatric Registered Nurse

Advanced practice psychiatric-mental health nurses have even greater responsibilities that extend beyond basic pharmacology. They include prescribing pharmacologic agents and ordering and interpreting diagnostic studies. Other responsibilities require additional expertise and knowledge of diagnosis and treatment of mental disorders and the ability to plan a pharmacotherapy regimen. The client's past history, current mental and physical status, preferences, and outcome-based treatment plan should guide the nurse's role in pharmacology. Explanations regarding the treatment plan should be given to the client and significant others, and their ideas about it should be respected (ANA, 2000; Kaplan & Sadock, 1998).

Educational preparation for the advanced role begins at the master's degree level and progresses through clinical experience, leading to certification as an advanced-practice registered nurse-psychiatric-mental health (APRN-PMH [i.e., clinical nurse specialist, psychiatric-mental health nurse practitioner]). Concerning the use of pharmacologic agents, the role of the certified psychiatric-mental health specialist often includes prescriptive authority. Responsibilities inherent in prescriptive authority involve ordering medications and interpreting relevant diagnostic and laboratory tests. Additional responsibilities of the APRN-PMH with prescriptive authority include seeking to effect desired therapeutic responses and anticipating and minimizing adverse drug interactions.

The inclusion of prescriptive authority in the advanced-practice role is guided by federal and statutory regulations governing prescriptions. The APRN-PMH applies neurobiological, psychopharmacologic, and physiological knowledge of all aspects of the therapeutic process. Of particular significance is the use of this knowledge to make differential diagnoses of mental disorders and medical conditions, develop therapeutic strategies based on clinical indicators, and to treat the mental disorders with pharmacologic agents (ANA, 2000). Health teaching is also an integral aspect of pharmacologic interventions and must focus on educating other nurses and health care providers about pharmacologic agents and consulting about their use and management.
from communication dilemmas and disagreements between the client and nurse (Smith, Lin, & Mendoza, 1993). Nurses need to appreciate the impact of the client's culture, individual needs, and beliefs about health care and integrate them into treatment planning.

The nurse also needs to be mindful of a number of principles of medication use that are important to ensure the desired therapeutic effects. First, no person should be seen as only a medical client or only a psychiatric client. Nurses should afford all clients a comprehensive examination that contributes to making a differential diagnosis of medical, mental, or substance-related disorders. For instance, treating a medical condition such as hypothyroidism may cure a client's depression, whereas treating a psychiatric illness such as depression may improve the client’s irritable bowel syndrome.

Second, psychosocial or alternative options should always be considered first. Crisis intervention, sleep hygiene, counseling, substance-related treatment, and stress management techniques are alternatives to medication.

Third, medications alone are rarely indicated in the treatment of any psychiatric disorder; medication in combination with psychotherapy is almost always more effective than medication alone. Psychiatric illnesses, including depression or anxiety disorders, can be best understood and treated by using a biopsychosocial model.

Finally, the nurse should consider the following points:

• The smallest possible effective dose should be used for the shortest effective period. This principle must be balanced against the knowledge that failure to use an inadequate dosage and to continue medication long enough are significant contributors to treatment failures. As a rule, older adults should be started on lower doses than younger clients.

• Whenever possible, medication dosing should be simplified (i.e., once-a-day dosing). Avoid midday dosing if possible.

• The simpler the drug regimen, the higher the compliance. In most instances, a once-a-day dosing schedule is possible. An obvious exception is lithium; most prescribers believe that its short half-life necessitates more frequent dosing.

• Polypharmacy should be avoided when possible. Combinations of psychoactive drugs generally are not more effective than a single dose (Alpert, Berstein, & Rosenbaum, 1997; Kaplan & Sadock, 1996; Baldessarini, 2001). The more medications a client takes, the higher the risk of side effects she experiences, making compliance more difficult.

• Overall, the safety of using most psychiatric medications during pregnancy and lactation has not been established. The prescriber and the client must carefully assess the use of these medications. The basic rule is to avoid administering any drug to pregnant women, particularly during the first trimester or lactation. The most teratogenic drugs in psychopharmacology are lithium and anticonvulsants such as valproic acid (Depakene) and gabapentin (Neurontin) (Kaplan & Sadock, 1998; Spratto & Woods, 2000). See Table 28–20, Guidelines for Enhancing Medication Adherence.

**Table 28–20**

**Guidelines for Enhancing Medication Adherence**

- Assist client in acquiring knowledge about medications, including actions, precautions, side effects, signs of toxicity, drug interactions, and food and drug interactions.

- Explore client's beliefs about medications and their effects.

- Explain nature of and time span for onset of therapeutic results.

- Help client develop strategies for dealing with common side effects and missed doses of medication.

- Relate medications to the target symptoms associated with client’s illness.

- Explore with client any differing expectations regarding barriers and facilitators for medication compliance and medication effects.

- Provide written and verbal instructions to reinforce compliance.

- Develop strategies to help client incorporate medication taking into daily routine.

- Include family members or significant others in education about client’s medications and illness and their own needs as caregivers.

- Explain complications that can result from use of alcohol and other drugs that can lead to establishment of a maladaptive pattern of coping.

**LEGAL AND ETHICAL ISSUES**

Psychiatric nurses must have a strong commitment to the health of their clients and families concerning medications and other treatment modalities. This process involves initiating treatment planning that protects the rights of
clients and assures safe, culturally-sensitive and holistic health care.

**Client Advocacy**

Another invaluable role of the mental health nurse is *client advocate*. Nurses are first-line advocates for clients receiving psychotropic medications because they often administer the medication and are the first to detect errors, potential drug interactions, or changes in the client’s mental and physical status.

The administration of psychotropic medications presents unique challenges to nurses. Medications themselves are often quite potent, and individual responses are relatively unpredictable. To complicate the matter further, clients have difficulty complying with the medication regimen, giving informed consent, recognizing and reporting therapeutic and adverse effects, and applying psychoeducational material. See Research Abstract, Characteristics of Clients with Schizophrenia Who Express Certainty or Uncertainty About Continuing Treatment with Depot Neuroleptic Medication.

The first and foremost responsibility of psychiatric nurses is client advocacy (ANA, 2000). With respect to pharmacologic interventions, nurse advocacy activities include a strong commitment to the client’s health and overall welfare and well-being. Additional responsibilities comprise actions to protect the client from harm, while taking appropriate actions on behalf of the client to ensure the use of the least restrictive environment. This is particularly salient in ethical dilemmas created by the use of chemical restraints in some situations. (See Chapter 8.)

**Right to Refuse**

As mentioned, obtaining informed consent from the client with a mental disorder can be difficult. Many clients in these

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**RESEARCH ABSTRACT**

**CHARACTERISTICS OF CLIENTS WITH SCHIZOPHRENIA WHO EXPRESS CERTAINTY OR UNCERTAINTY ABOUT CONTINUING TREATMENT WITH DEPOT NEUROLEPTIC MEDICATION**


**Study Problem/Purpose**

To examine factors corresponding to clients’ certainty or uncertainty concerning continuing to use depot neuroleptic medication.

**Methods**

This exploratory study comprised 94 participants from a tertiary care schizophrenic clinic, and researchers used a psychoeducational intervention aid that focused on the risks and benefits of treatment. Participants were also interviewed to elicit their levels of decisional conflict, self-efficacy, and emotional support.

**Findings**

Data from this study showed that 87 percent of the participants opted to continue treatment. About 10 percent expressed uncertainty about continuing treatment with a higher level of decisional conflict, lower levels of self-efficacy, lower expectations from the hospitalization if treatment ceased, along with lower levels of benefits and higher expectations of side effects if treatment continued.

**Implications for Psychiatric Nurses**

Clients often benefit from collaborative relationships with nurses and other clinicians. Efforts to involve the client in treatment planning appear to result in positive client outcomes.
settings, perhaps because of their respective illnesses, their beliefs and culture, or their fears, are reluctant to comply with medication administration. Except in unusual circumstances, a client with a mental disorder has the right to refuse medication. First, a client may have been involuntarily committed to a hospital because she was judged to be gravely disabled and harmful to herself or others. States vary in their statutes regarding medicating these clients against their will, and it is imperative that the nurse be familiar with the laws of the state in which she practices. In addition, in certain cases, a court may order clients to be medicated against their wishes. This usually happens to clients with long histories of noncompliance who have shown clear improvement when their symptomatology is under the control of medication. In clients without such legal support, however, exceptions may still need to be made. For example, in some cases, it may be believed that the client is so severely endangered by her behavior that a life-threatening crisis is imminent. It may be advisable for the nurse to collaborate and consult with the interdisciplinary team and significant others. If a decision is made to medicate a client against her will, it is imperative that documentation be clear, descriptive, and inclusive of other interventions that were tried.

Obviously, assessing the client’s capacity to comprehend information is challenging. However, the nurse also has a legal and ethical obligation to inform the client to the best of her ability to understand what a medication is, what symptoms can be expected to be treated, and its potential risks (ANA, 2000; Kaplan & Sadock, 1998). Information should be provided that will enable the client and family members to recognize signs of symptom remittance as well as adverse effects. Clients and significant others should receive written and verbal information about methods, any contraindications, and particularly any adverse effects that could precipitate an emergency (such as the development of neuroleptic malignant syndrome). See Chapter 8 for an in-depth discussion of the right to refuse treatment.

### Psychoeducation

Marangell et al. (1999) submit that the most effective ways to improve adherence are communication and health education. Interventions such as providing the client with written instructions and verbal communication are particularly helpful when the client is on several medications or has instructions for drug titration.

This notion is consistent with the role of the psychiatric nurse in psychopharmacology. Perhaps one of the challenges most enjoyed by the psychiatric-mental health nurse is the development of creative psychoeducational strategies for medications. Common strategies include medication education groups, Internet sites, printed instructions, and self-medication programs. It is also crucial for the client’s family or significant others to be involved in the educational and treatment process. A frequent problem cited by mental health advocacy groups is that families are often uninformed about the treatment itself and its risks and potential benefits. This process should also be documented (Lund & Frank, 1991). Other factors such as the Internet are making an impact on the mental health consumer’s understanding about mental illness, the role of neurobiology, technological advances, and treatment options.

### Medication Monitoring

A final area of particular interest in the legal and ethical administration of psychotropic agents is medication monitoring. The nurse must be thoroughly familiar with both the expected outcomes of the medication and the potential adverse effects. These include physical, affective, and behavioral sequelae. For instance, the nurse should know which medications would affect blood pressure or sexual function. See Table 28–21 for a list of these medications. Many psychiatric settings use some sort of formalized system of symptom documentation, whether checklists for adverse effects or abbreviated mental status report for affective, motor, and behavioral assessment. It is imperative that the nurse develops excellent assessment skills for this purpose.

### Table 28–21

<table>
<thead>
<tr>
<th><strong>Antidepressants</strong></th>
<th><strong>Antipsychotics</strong></th>
<th><strong>Alpha-Antagonists</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline (Elavil)</td>
<td>Acetophenazine (Tindal)</td>
<td>Doxepin (Sinequan) &gt; 150 mg/day</td>
</tr>
<tr>
<td>Imipramine (Tofranil)</td>
<td>Chlorpromazine (Thorazine)</td>
<td>Trifluoperazine (Stelazine &gt; 5 mg/day)</td>
</tr>
<tr>
<td>Protriptyline (Vivactyl)</td>
<td>Chlorprothixene (Taractan)</td>
<td></td>
</tr>
<tr>
<td>Perphenazine and amitriptyline (Triavil)</td>
<td>Thioridazine (Mellaril)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Haloperidol (Haldol)</td>
<td></td>
</tr>
</tbody>
</table>
SUMMARY

- Recent advances in research on the brain have created a virtual explosion of knowledge of the relationship between the brain and human behavior.
- As a result, health care professionals' understanding of the neurobiological basis of many mental illnesses has been enhanced dramatically, and more efficacious pharmacologic agents for the treatment of mental illness have been developed.
- Technological advances in the study of genetics and human behavior offer promise and hope to clients and their families regarding improved quality of life.
- This chapter has provided the reader with a review of areas of neuroanatomy and neurophysiology related to the pharmacokinetics of psychopharmacologic agents used across the life span.
- Principles of psychopharmacokinetics and pharmacodynamics that are germane to an understanding of the complexity of psychopharmacologic management of mental illnesses have been discussed.
- The nurse's roles in the use and administration of these agents and health education of clients and their families have been described.
- The legal issues related to psychopharmacology and the ethical considerations in the management of pharmacotherapy treatment have been highlighted.

STUDY QUESTIONS

1. The neurological blood-brain barrier is composed of:
   a. histaminic receptors in the stomach
   b. endothelial cells in the small intestine
   c. endothelial cells in the brain
   d. noradrenergic neurons in the brain

2. Which of the following structures is considered part of the limbic system?
   a. The frontal lobe
   b. The thalamus
   c. The pons
   d. The amygdala

3. Parkinson's disease involves a depletion of which neurotransmitter in the basal ganglia of the brain?
   a. Norepinephrine
   b. Dopamine
   c. Gamma-aminobutyric acid
   d. Glycine

4. Which of the following structures associated with the reception of speech is located in the temporal lobe?
   a. Wernicke's area
   b. Broca's area
   c. Korsakoff's area
   d. Hippocampus

5. The concept of drug half-life time is important to determine:
   a. the dosage necessary to achieve therapeutic effects
   b. toxicity
   c. how often a drug needs to be administered
   d. side effects of the drug

6. A client experiencing akathisia most likely displays:
   a. a tremor on resting
   b. orthostatic hypotension
   c. chewing, puffing movements around the mouth
   d. agitation and restlessness

7. Pseudoparkinsonism is caused by which of the following mechanisms?
a. A sudden increase in serotonin in the limbic system
b. A depletion of gamma-aminobutyric acid in the striatum
c. An increase in norepinephrine in the temporal lobe
d. A depletion of dopamine in the basal ganglia nigrostriatum

8. Which of the following is an important issue in using medications in older adults?
   a. Aging alters the ability to metabolize and excrete medications.
   b. Older adults may have difficulty managing a number of medications at once.
   c. Older adults have a higher rate of nonadherence.
   d. Older persons are more susceptible to the cardiovascular effects of drugs.

RESOURCES

Please note that because Internet resources are of a time-sensitive nature and URL addresses may change or be deleted, searches should also be conducted by association or topic.

Internet Resources
http://www.apna.org  American Psychiatric Nurses Association

REFERENCES


**SUGGESTED READINGS**


