

Chapter 5

Biological Aspects of Alcohol and Drug Use

Introduction

It is now generally acknowledged that there may be several contributing causes for substance use problems and that some of the causes are biological. This point is underscored by the finding that the biological children of parents with alcohol problems, even if reared by adoptive parents without alcohol problems, are at increased risk for such problems when compared with other children. In addition, research has revealed that a congenital (acquired during development in the uterus and not through heredity) vulnerability may exist in a group of persons with alcohol problems.

The nervous system is a major site of action for drugs that are abused. You should have some knowledge of brain and nerve function to understand how drugs produce their effects. You should also know how pharmacological treatments may be utilized for mental illness and for alcohol and drug use disorders.

First, we will briefly review the functional anatomy of the brain, spinal cord, and nerves. Then we will cover the basic principles that govern all drug actions. Important factors that influence the effects of drugs and the consequences of chronic drug use, including tolerance and dependence, will be considered. This discussion naturally leads to a more thorough review of the specific short- and long-term actions of abused drugs and medications that are used for mental illness. The chapter concludes with a short survey of drug abuse complications and evidence for the biological contribution to chronic drug problems.

The Central Nervous System

Organization

Drugs can exert their biological effects by interacting specifically with mechanisms responsible for conduction, transmission, and management of information in the brain. Drugs that are likely to be abused have one particular characteristic in common. They act on the nervous system, and the brain in particular, where chemically induced changes adjust mood, level of alertness, perceptions, and thought processes.

The nervous system operates as a control mechanism for many of the body's other systems, helping them to maintain their best possible level of function. Its primary responsibility for regulating body functions such as breathing, blood circulation, sensation, and movement are well known. The nervous system consists of a **central nervous system (CNS)**, which includes the brain and spinal cord, and a **peripheral nervous system**, comprised of sensory and motor nerves. The CNS integrates and coordinates sensation and movement. Some of this activity, like the movement entailed in walking, throwing a ball, or writing, is voluntary while some is involuntary and automatic. These involuntary functions such as the regulation of blood pressure and body

temperature are managed by a special peripheral nervous system called the **autonomic nervous system**. Many substances that are abused directly affect the autonomic nervous system, which has two components, one **sympathetic** and the other **parasympathetic**. When they are stimulated, sympathetic nerves produce an elevation of blood pressure, increase in pulse rate, and a rise in body temperature. Activation of parasympathetic nerves usually produces the opposite results. Drugs like amphetamines and cocaine that enhance sympathetic nervous system activity are called “sympathomimetic” because they mimic the natural actions. Drugs that block the parasympathetic nervous system, like scopolamine, can reduce mucous secretion in the throat and nasal passages and are often found in over-the-counter cold remedies.

The basic functional unit of the nervous system is the nerve cell or **neuron** (see Figure 5.a) which may be thought of in terms of its three main parts:

- (1) the **soma**, or cell body.
- (2) the **dendrites**, or fibers that conduct information toward the soma.
- (3) the **axon**, or nerve fiber that conducts information away from the soma to the axon terminal, where transmission of the information to the next neuron takes place at the **synapse**.

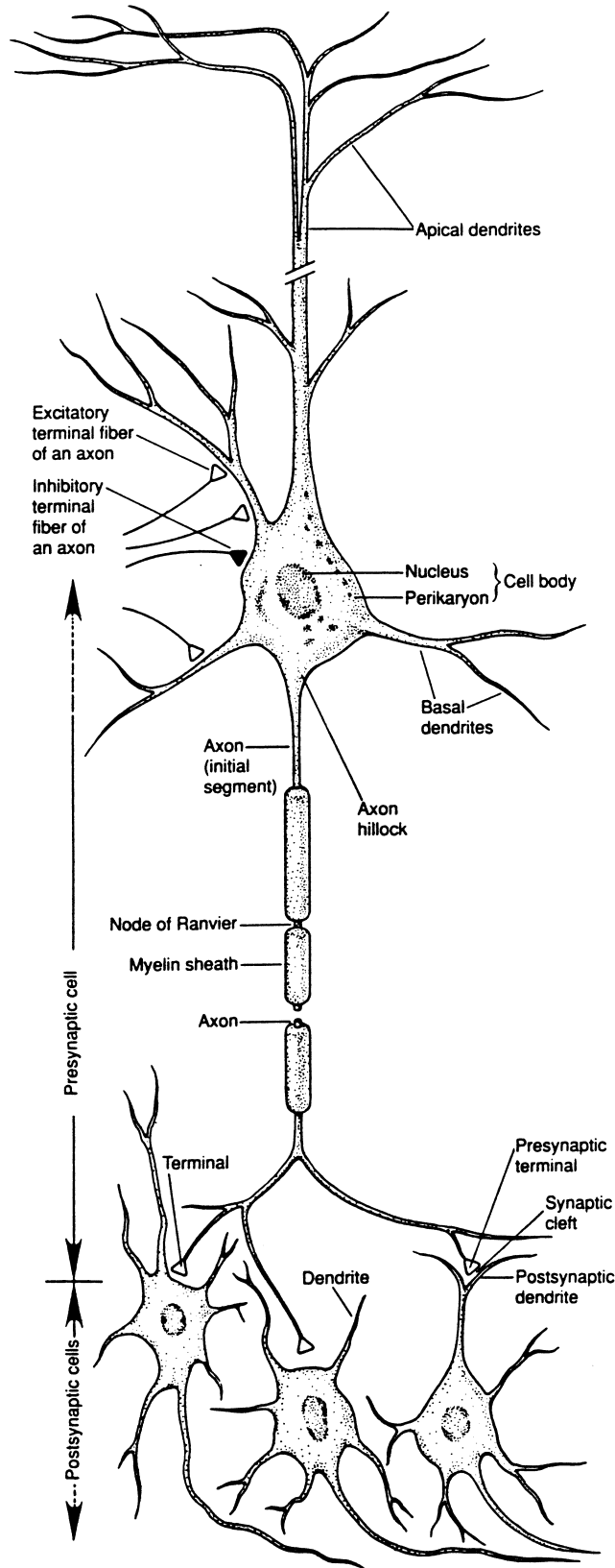


Figure 5.a The Neuron¹

The cell body contains a nucleus, structures to generate energy and manufacture proteins, and other machinery to maintain the healthy function of the neuron. The dendrites are specialized to receive and integrate information that is transmitted at synapses from axon terminals of many other neurons (see Figure 5.b). The synapse is a very important junction, for this site of communication between two nerve cells is where most psychoactive drugs work. All of the structures of a nerve cell are bounded by a continuous cell membrane which, in many ways, is different from membranes of other types of cells in the body. Not only does it look different because of its axon and dendrites, but it acts differently. It is electrically charged (polarized) under normal conditions, like a battery, and it uses this property to integrate incoming signals and conduct them to other places in the neuron.

Most communication of information between neurons is accomplished chemically, by substances called **neurotransmitters**. Neurotransmitters are relatively small and simple molecules that are made from natural materials in the body like amino acids. They are synthesized in the neuron and stored in the axon terminals within sacs referred to as **vesicles**.

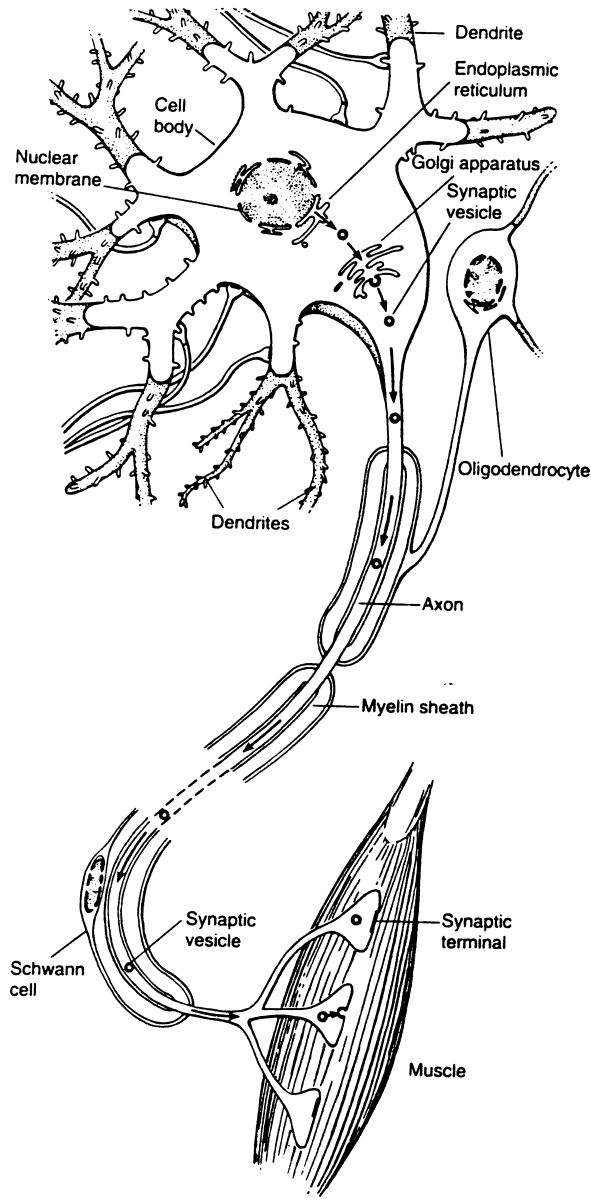


Figure 5.b The Synapse

Each of the neurotransmitters has a unique, three-dimensional structure with negatively and positively charged areas so that it will be attracted to and bind with complementary sites on the neuronal (synaptic) membrane called **receptors**. Examples of neurotransmitters involved with the actions of psychoactive substances include acetylcholine, norepinephrine, epinephrine, dopamine, serotonin, glutamate, and gamma aminobutyric acid (GABA). Some neurotransmitters stimulate postsynaptic cells, while others inhibit their activity. The psychoactive effects of drugs vary according to the types of neurotransmitters involved and their locations in the brain.

The Brain

Different areas of the brain have specialized functions and psychoactive drugs can act upon all of them (see Figure 2.c). In human beings, the **cerebral cortex** makes up about one-third of the total brain mass. It is responsible for higher mental functioning. Problem-solving, creative thinking, and communication are all accomplished by the cortex. Higher-order processing of sensations like sound, sight, smell, and touch takes place here too, along with the control of muscular activity that enables us to react to sensations and act upon our thoughts. Although memory is largely managed in the cortex, another area called the **hippocampus** plays a critical role in the first stage of consolidating new memory. Drugs such as alcohol may interfere with the formation of new memories by their action here.

A group of structures in the brain collectively called the **basal ganglia** lie just below the cortex and are important in coordination of body movements. Some drugs that are abused, and even psychotherapeutic drugs like clorpromazine (Thorazine), can affect this region, causing involuntary movements or muscle rigidity at times. The **thalamus** and **hypothalamus** are located behind and underneath the basal ganglia. These brain structures are involved in the processing of sensory information and controlling vital body functions such as breathing, circulation, and body temperature. The hypothalamus makes certain that all of these functions remain stable in the face of internal or environmental stress.

The **limbic system**, a group of subcortical areas that are linked together, is associated with emotion, and it is here that we believe drugs act to produce feelings of pleasure. Electrical stimulation of these regions in laboratory animals causes reinforcing (“addictive”) behavior. The rewarding properties of cocaine, opioids, and other drugs are thought to have their origin in this “pleasure center.”

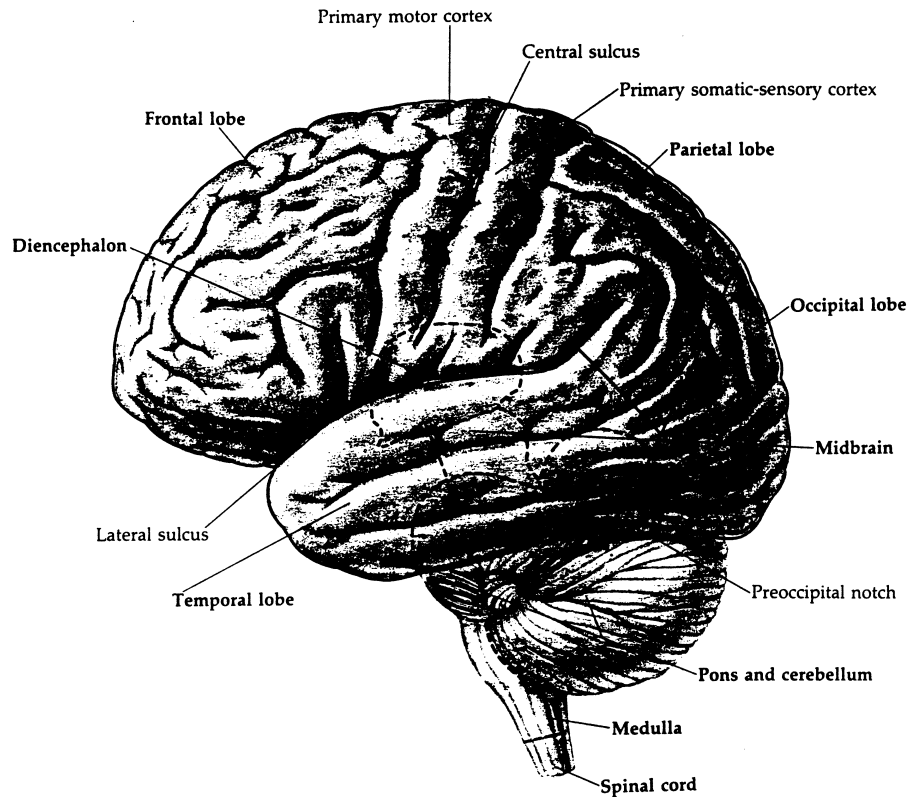


Figure 5.c The Brain

The state of arousal, or general level of central nervous system excitability, is a function of structures in the lower part of the brain collectively referred to as the **brain stem**. The **midbrain** region contains neurons that use serotonin selectively to decrease the excitability of higher centers, while the **pons** has a concentration of nerve cells that do the opposite, using norepinephrine. Drugs that alter serotonin or norepinephrine in the brain modulate the state of arousal in predictable ways. The lowest part of the brain, just above the spinal cord, is the **medulla**, a region that maintains the basic drive and rhythms of essential functions, like breathing and blood pressure. The cerebellar cortex, or **cerebellum**, is a small globe-like structure that overlies the medulla and pons. It takes care of equilibrium, coordination, and mobility. If the cerebellum is disturbed by drugs such as alcohol, barbiturate, and inhalants such as some glues or paint thinners, a person's stance, gait, and gross movement would be affected.

Principles of Drug Action

Common Sites and Mechanisms of Drug Action

As already noted, the neuronal membrane is special. It is always primed for action and has many unique receptors, or binding sites for chemical substances that are made in the body (like neurotransmitters) and drugs. Most of the drugs we discuss in this manual have the ability to intensify, accelerate, diminish, slow down, or even block neuronal function by interfering with synaptic communication. They do so mainly through binding to membrane receptors or by

modifying the normal process of neurotransmission. Some drugs, like ethanol, have widespread actions on nerve membranes that may not be mediated directly by receptors, while others, like caffeine and steroids, can bypass receptors entirely and have internal effects on cell function.

Dose/Effect Relationship

Because they work through specific membrane receptors which are limited in number, most drugs show a relationship between the dose used and the effect achieved. It is not a straight-line relationship, as might be expected, but rather an “S” shaped one (as shown in Figure 5.d). This means that, at the bottom end, it takes a certain amount of drug to activate enough receptors just to get the system going and, at the top end, when all of the available receptors have been activated, adding more of the drug will not increase the magnitude of the effect any further.

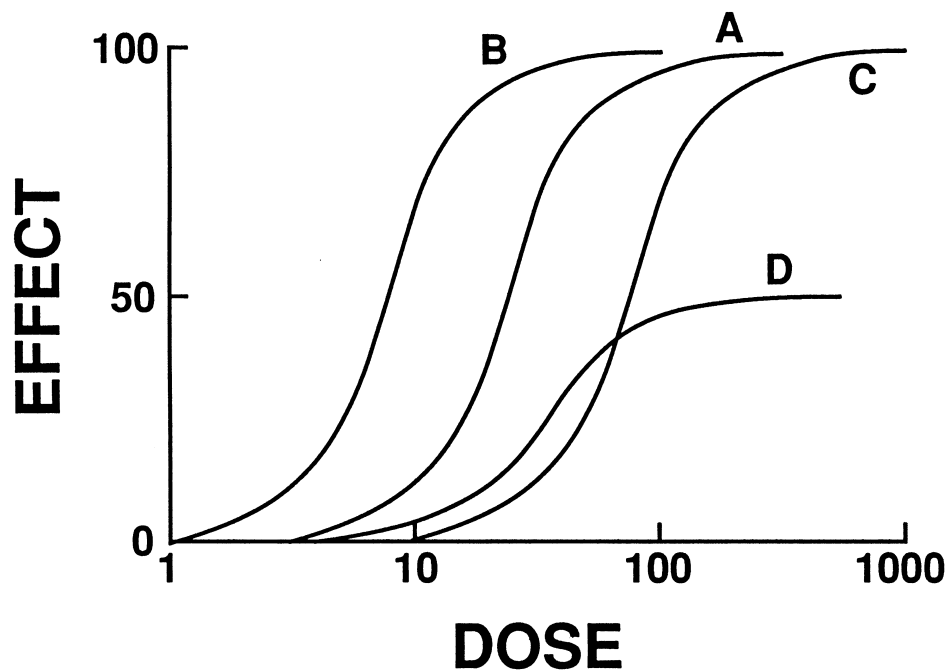


Figure 5.d Dose/Effect Curve

Some drugs within a class seem to produce more of an effect at a particular dose than others do. We refer to these as more potent than the others; that is, they are *relatively* stronger. They bind to the same receptors with greater **affinity** (that is, they like them better). However, it is very important to realize that the maximum effectiveness, or **efficacy** of all these drugs in this class is the same. In other words, they will all produce the same maximum effect *at some dose*—it will just take a higher dose for some than others.

Agonists are chemical substances that produce specific pharmacological effects; **antagonists** are chemical substances that can bind to the same receptors, but do not produce the effects. In fact, if an antagonist is given in the presence of an agonist, it may compete with the agonist for binding sites and diminish the agonist drug effects. It follows naturally then that the blocking effect of a competitive antagonist can always be overcome by raising the dose of the agonist.

Among the many drugs available today, we now also have **partial agonists** that do not produce the full effect expected of the agonist, and **mixed agonist/antagonists** that share some of both properties. The advantage of these mixed agents is that at a low dose they are usually agonistic, but at a higher dose they limit their own effectiveness. There are important examples of this group in the opioid or “narcotic” drug class such as pentazocine (Talwin) and buprenorphine (Temgesic).

Passage of Drugs Through the Body

To effect behavior, psychoactive drugs must be transported from outside the body to the brain. Thereafter, they are removed from their sites of action in the brain, degraded, and eliminated. This transit requires four processes: **absorption, distribution, metabolism, and excretion**. By absorption, we mean the process that occurs when a drug moves across membrane barriers into the bloodstream. In other words, drugs that are consumed by mouth, like alcohol or Valium[®], must be taken up across the stomach and intestinal linings into the capillaries. Drugs that are snorted, like cocaine powder and heroin, have to be absorbed across the linings of the nose and throat. And drugs that are smoked or otherwise inhaled, like crack cocaine (or freebase), have to move across membranes in the lungs.

This last process—inhalation—is the fastest. Inhaling a drug such as crack cocaine greatly minimizes the process of absorption so much so that its effects are experienced faster than if cocaine powder dissolved in water had been injected intravenously.

Drugs that are fat soluble (“lipid loving” or **lipophilic**) have a distinct advantage over those that are water soluble; the rate and degree to which they are absorbed and get into the tissues are greater because cell membranes are largely composed of lipids. All psychoactive drugs tend to be lipophilic, and so they move easily and quickly into the brain.

After a drug enters the bloodstream, it distributes throughout the body. But first it has the opportunity to bind with proteins in the blood itself, such as albumin. This process ties up a certain amount of the drug, making it unavailable to the brain, because only the drug molecules that are freely dissolved in the blood can move into other body tissues. The molecules that are bound to the blood proteins are let go as the free molecules move out of the blood. This operates like a slow-release mechanism to extend the period of drug action. Drugs like Valium[®] are very highly bound to blood proteins, so they can have a long duration of action and a slow tapering off.

The same characteristics that make drugs easily absorbed also help them to move out of the blood and into the brain and other tissues rapidly. When drugs pass into tissues like muscle or fat, they can bind to proteins there or just dissolve in the lipid. This will further prolong the drug’s stay in the body. A common example that many people are aware of is that of tetrahydrocannabinol (THC), the active agent in marijuana, which is so lipophilic that it can remain in body fat for weeks.

The normal process of distribution will also take the drug to the liver and kidney, the chief organs of metabolism and excretion. The liver has a large number of specific enzymes that break down drug molecules into inactive metabolites. In fact, with every passage of blood through the liver (even from the very beginning) drug molecules are removed and metabolized. Because some people have a high capacity for drug metabolism, they will break down the drug faster and require a larger dose than others to get the same effect. In addition, the metabolic rate can change

over time. For many drugs, the development of **tolerance** (decreased effectiveness) is due to a progressively increasing rate of metabolism.

Not only are drug metabolites typically inactive, but they are also more easily excreted in the urine. The kidney filters blood constantly and drug molecules pass into the urine. Because they are fat soluble, many drug molecules normally escape back into the blood before the urine is completely formed and leaves the kidney. The metabolites are more water soluble than fat soluble, so they remain in the urine as it moves into the bladder and out of the body. Many drugs can be excreted by routes other than the urine, including the sweat, exhaled air, and feces. Although more than 90 percent of it is usually metabolized, alcohol is a drug that can be lost through all of these as well as the urine. The fact that approximately 0.5 percent of blood alcohol is regularly exhaled provides the basis for the indirect Breathalyzer[®] measurements of blood-alcohol levels.

Rate of Drug Loss

From the moment a drug is taken, by whatever route, it is in the process of being eliminated (by metabolism or excretion). This central concept governs the rate at which a drug will accumulate in the brain, as well as the rate of its loss from the body. It even affects the maximum concentration that is achieved, along with the actual dose or amount taken, of course! A drug that is metabolized faster or excreted at a greater rate is going to have a shorter stay in the body and a lower peak concentration in the brain than another drug that is given at the same dose. One example of this is the comparison between the tranquilizers Serax[™] and Valium[™]; Serax[™] is eliminated much faster than Valium[™].

The rate at which most drugs are lost is controlled by their metabolism in the liver, and this is generally proportional to their blood concentration. That is, the greater the amount of drug, the faster the body will try to break it down. From this notion we get the concept of **half-life**, which, simply stated, is the amount of time it takes to eliminate half of the drug present in the body. In other words, 50 percent of the drug will be lost in the first half-life, 25 percent (or half of the remaining drug) in the second half-life, and so on. We generally think of 4 half-lives as sufficient time to remove enough drug to terminate all of its effects. (How much drug actually remains after 4 half-lives?) If a drug such as cocaine has a half-life of one hour, then it will be substantially eliminated from the body in four hours (traces that linger on for a day or so can be detected in the urine).

A small number of drugs don't follow this half-life rule (what we call a "first-order" process) because the body doesn't have enough of the specific enzymes needed to do the job. These drugs are eliminated at a slower rate—one that is *time-*, and not *concentration-*dependent (what we call a "zero-order" process). The most important example of this drug group is alcohol. A drinker will not lose the alcohol faster if he drinks more; it will simply take him longer. That is, if he metabolizes about one drink an hour, he will take five hours to get rid of five drinks and ten hours for ten drinks.

When people use drugs repeatedly, the substance builds up in the body. Doctors take advantage of this fact, and their knowledge of half-lives to design a dosing schedule (that is, the dose amount and the frequency of administration) that will result in a stable therapeutic blood level or plateau. People who abuse drugs often do the same thing to achieve their "recreational" level. Drinkers tend to consume a lot at first, or "load" themselves, and then taper off to a point at which they are just replacing what their body is losing. Crack cocaine users may do the same, but

the half-life is so brief that they don't seem to be slowing down. Of course, if the drug is used at a much faster pace, and the body can't remove it fast enough, then dangerously toxic levels may accumulate. "Chug-a-lug" contests result in alcohol poisoning with coma and respiratory depression, overdoses of heroin also stop breathing and cause shock, and excessive cocaine may result in seizures.

Individual Factors That Modify Drug Effects

It is probably obvious by now that the biological effects of a drug (agonist) are determined by the type of drug, its dose, efficacy, and how often it is used. But there are other factors that can modify the effects of a psychoactive drug greatly. These include the physical and mental status of the person, as well as their mental set and even the environment. Biomedical factors include body size or composition, gender, age, disease, and genetics.

Body size, composition. The importance of body size or composition can be appreciated now in terms of the absorption and distribution of drugs with different fat and water solubilities. For example, an obese person who smokes marijuana (a very fat-soluble substance) would use more than a thin person to get the same effect, not only because he is much larger but also because a lot of the drug is going into his abundant adipose tissue instead of his brain. A substance like alcohol, that is water soluble, poses a different problem for the same obese person. If we compare his consumption with that of a lean man of the same weight, then he would have a higher blood-alcohol level with the same number of drinks because his water space is comparatively smaller and alcohol does not go into fat tissue.

Gender. Body size and composition are also relevant when we consider gender because, on the average, women have a higher percentage of body fat than men. They also tend to be smaller, and they do not appear to have certain gastric enzymes that men have to begin the breakdown of alcohol in the stomach. The net result is that women are generally more sensitive to alcohol (and other drugs) than men.

Age. Age is an important factor in drug action. While young and middle-aged adults have adequate, stable systems to break down and eliminate drugs, children and elderly adults frequently have much less capacity. An extreme case is the fetus which, while in its mother's womb, can be exposed to high drug concentrations that it can not deal with. Young children are sensitive because their livers and kidneys are not yet fully developed, while the elderly have lost some of the function that they once had, and are more sensitive to drugs for that reason.

Disease. Disease can also have a major influence on the effect of a drug, especially when it impairs the brain, cardiovascular system, liver, or kidney. If brain function is affected, then a psychoactive drug can exaggerate the problem. For example, if an elderly woman with dementia drinks alcohol, she may become extraordinarily confused. Or, if an alcoholic man with liver failure consumes even a small amount of alcohol, it may have a profound depressant effect. A person with high blood pressure may be at great risk for a stroke if he uses methamphetamine (speed, ice, crank).

Genetics. Genetic factors affect how a person's body will function. Logically, then, they will contribute indirectly to the drug effect. People inherit different metabolism abilities, and so while one person may break down alcohol at a rate of one drink per hour, another may take two hours. Genetics also has a lot to do with the actual brain effect of a drug. In other words, neuronal function is more sensitive in some people than in others.

Other very important determinants of drug action in a person who has been using a **psychotropic** (mood/mind altering) drug for some time are the degree of **physiological** and **psychological dependence**, as well as **tolerance**. Physiological dependence represents the body's attempt to correct itself in the face of "invasion" by a foreign substance (the drug) that is disturbing its function. The body compensates for the disturbance in a variety of ways. The net result is an *apparently* normal condition but, in the case of an alcoholic, the brain's inherent level of excitability is increased to offset the depressant effect of alcohol.

Psychological dependence reflects the collection of emotional, cognitive, and behavioral changes that drive the individual to sustain his or her lifestyle. Compulsion and craving are key manifestations of this. And tolerance, as noted before, is the need for increasing amounts of drug to obtain the same effects with repeated use. When a person who has developed dependence on alcohol or another addicting drug stops using it for some reason (because of a personal decision, illness, or incarceration, for example), the dependent state will show itself as a withdrawal or abstinence syndrome. This condition is usually very disturbing to the individual—physically and emotionally. The specific signs and symptoms of withdrawal depend on the type of drug that is used. In general, if a person is dependent on alcohol or another depressant substance, then the withdrawal would be expressed as excitation—both psychological and neurological. For example, this person might experience increased anxiety, shaking, motor tremors, and even convulsions. On the other hand, someone who suddenly stops using cocaine or another stimulant would become depressed during withdrawal. They would appear lethargic, unmotivated and, in a growing number of cases, suicidal. The intensity of a withdrawal syndrome is usually related to the degree of dependence, which is a function of how long, how frequently, and how much of the drug has been used.

Drug Testing

The term **drug testing** generally refers to a quantitative assessment of how much drug is present in the body. There are a number of different measures, and each has its pros and cons. The most common tests are those obtained from body tissues or by-products, including blood samples, exhaled air, urine, stomach contents, feces, hair, and nails. The tests are all invasive to some extent, and therefore considered an imposition. Unfortunately, better quality data are obtained with tests that violate the individual's privacy or person.

Blood tests are the most accurate, but also the most invasive, so they are usually reserved for more extreme circumstances like auto accidents and criminal incidents. The information derived from breath testing can be a very good estimate of drug level in the blood, and this technique is relatively harmless. However, the approach is limited to the few drugs that are excreted from the body in exhaled air, like alcohol.

Restrictions also apply to drug measurements made in samples of stomach contents or feces, and they are most often employed with adults in cases of medical or legal interest. Gastric drug levels are frequently used when gross intoxication is suspected, while fecal quantities may be of interest when a question arises as to how long a drug has been in the body. The latter approach has been utilized in the special case of the newborn, where meconium drug levels may give a good idea of what drugs an infant was exposed to in the womb (the baby's first stool is called "meconium"). Hair and fingernail samples may be of some benefit for similar purposes in the adult. Because these tissues "trap" drugs as they grow, they can provide an indicator of drug use weeks and even months in the past.

The most commonly used drug test is the urine test. The reasons probably have more to do with convenience and acceptability than quality of the data. It's important to realize that urine is an excretory product that accumulates over a variable period of time, and so the actual urine drug concentration may not bear any relationship to either blood level or functional impairment. What it does say is simply that a drug may have been used at some time in the past.

There are some technical aspects that must be appreciated in order to correctly interpret urine drug-screen data. The first is that while screening tests are very *sensitive*, they are not very *specific*. In other words, it is possible to detect extremely low levels, but exactly what is being detected is not always certain. For this reason, responsible testing programs always include follow-up, confirmatory tests of the same sample using the more expensive, but also more accurate technique of gas chromatography with mass spectrometry (GCMS). In fact, this method is considered the "gold standard" and is allowable in court as absolute evidence of drug presence.

Because they are so sensitive, all test procedures use artificial "cutoff" levels to define the absence or presence of a drug. If the cutoff is set too high, there is a risk of increasing the number of false-negative test results. That is, a drug which is present isn't being detected. And the opposite can occur if the cutoff is fixed too low. Obviously, both situations violate the basic purposes and would be counterproductive for either prevention or treatment.

Drug Interactions

Because all psychoactive drugs act in the same place—the brain—and because they employ many of the same mechanisms to get there (and back), there is a great likelihood of interaction between psychoactive drugs. In the simplest case, similar effects of two drugs can add up. Both alcohol and Valium[®] are depressant drugs and, when used at the same time, will produce depression that is at least equal to the sum of their effects. The same is true for the stimulation produced by cocaine and amphetamine.

There are also more complicated ways that drugs interact. For example, when drugs that are metabolized by the same liver enzymes are used together, they will compete with each other, and so the metabolism of both will slow down, resulting in higher drug levels. We see these effects with barbiturates like Seconal[®]. It's interesting, too, that if these same drugs are used repeatedly, they will stimulate the liver to make more of the enzyme. Of course, this will have the opposite effect on other drugs; that is, they will be less effective because they will be broken down faster. Another way that drugs commonly interact is by competing for binding sites on blood proteins. You recall that some drugs, such as Valium[®], are bound to a very large extent, and it is only the free form that can move into the brain. If a second drug is used that binds to the same sites, then it will displace some of the Valium[®], making its free concentration rise quickly. When that happens, the depressant effect intensifies and can become toxic (or even lethal).

Drugs That Are Abused

Overview

Before delving into the specific pharmacologic effects of drugs that are abused, we should consider some general concepts. Perhaps the best place to start would be with some practical definitions. In general, drugs are chemical substances that alter biological function. In other words, they speed up or slow down, intensify or diminish the activities of cells, organs, or the entire body. (Note that they do not make the body do anything it cannot already do!)

Psychoactive agents are drugs that act on the central nervous system (brain and spinal cord) to alter thought processes and emotions. Some psychoactive drugs affect mood and mind, but do not produce abuse and dependence, for example, the antipsychotic medication Thorazine[®]. Others, called psychotropic drugs, have a high potential for abuse and dependence. Psychotropic drugs of different kinds will elevate or depress mood, sharpen or dull thought processes, and alter the perception of reality. One property they all have is a “rewarding” influence—an unconscious, drug-induced drive to continue using. Most psychotropic drugs fit in one of four categories, based on their pharmacologic character: **depressants, stimulants, opioids (narcotics), and hallucinogens**. Drugs within any one of these classes are very much alike, and because they produce the same type of tolerance and dependence, they are often substituted for one another by the chronic user. If tolerance develops for one drug in a class, it develops for all of them. Likewise, if someone is dependent on one drug in a class, then another can be used to block withdrawal. This is not true for drugs in different categories. For the sake of discussion, some drugs that don’t clearly fit in one of these classes can be referred to as a group of “others.”

Depressants

Drugs in this class include sedatives, hypnotics, and tranquilizers that you would typically think of, such as Seconal[®], Halcion[®], and Valium[®]. But first and foremost they include ethanol—or beverage alcohol—in all of its various forms. Unfortunately, many lay people believe that alcoholic beverages are innocuous; they do not see them as pharmacologic agents. For this reason, and because alcohol is by far the most extensively abused, we begin our consideration of drugs with alcohol.

Ethanol. Ethyl alcohol has been known for its beverage value since the beginning of recorded time. The earliest substances consumed were natural fermentation products of honey, fruits, and grains in the form of wines and beers. The discovery of distillation enabled the manufacture of more concentrated beverages like fortified wines and liquors.

Today, we have available a wide variety of drinks that range in alcohol concentration from about 2 percent to 75 percent. The typical domestic beer has about 3.8 percent ethanol, while some malt liquors and foreign beers run as high as 6 percent. Wines vary greatly, but are usually in the range of 9 percent to 13 percent ethanol. The concentration of common liquors (or distilled spirits) is referred to in terms of “proof,” which is twice the actual value of alcohol concentration; the proof is most frequently 80 to 90 (40 to 45 percent). Perhaps it is most important to realize that the volume of a *typical* drink runs opposite to the concentration, so that the more concentrated liquors are used in smaller quantities than the less concentrated wines and beers. The net result is that a typical drink of any kind holds about the same total volume of the drug (approximately half an ounce of pure ethanol).

The primary route of administration for ethanol is by mouth—though it is used medically in other ways. Once in the mouth, it can be absorbed immediately. In fact, alcohol is one of the few drugs that is absorbed to any degree *before* it even reaches the small intestine (the usual site of food absorption). Normally, as much as 25 percent of the alcohol consumed is taken up through the stomach, leaving 75 percent to be absorbed in the intestine. Of course, the rate of uptake is much slower in the stomach because of its thick wall. Therefore, retention of the drink in the stomach by eating food (especially fatty food) reduces the total rate of absorption and the rate at which blood and brain levels rise.

As a chemical substance, ethanol is a very simple, small molecule and not particularly lipophilic.

As a result, it dissolves freely in the blood and travels wherever the blood goes, but it does not concentrate in the fatty tissues. This means that people who have a lot of fatty tissue, relative to their lean body mass, will develop higher blood-alcohol concentrations than leaner people of the same weight who drink the same amount. It also means that people do not store any of the drug in their excess adipose tissue. What you see is what you get—and the blood level roughly reflects the brain level.

Alcohol is eliminated from the body mainly through liver metabolism. Because the amount of the most important enzyme used for this breakdown is in limited supply, oxidation of alcohol takes place as a zero-order process—a fixed amount per time period. For most “normal” drinkers, this rate is about three-quarters to one drink per hour. If a person who metabolizes alcohol at one drink an hour consumes two or three drinks in that period, then he will accumulate the drug in his bloodstream (and brain). People who drink excessively over long periods of time stimulate their livers to synthesize secondary enzymes that will help to break down alcohol faster. In addition to metabolism, alcohol is excreted to a limited extent in the urine, sweat, and exhaled air. Because the concentration of ethanol in the air we exhale is relatively constant, this can serve as a measure of the blood level. Instruments like the Breathalyzer[®] are based on this principle.

Alcohol metabolism is interesting for several reasons. One is that complete breakdown of ethanol produces energy for the body like other carbohydrates. The caloric value is 7 calories per gram, or about 84 calories per drink (12 grams). A second important point is that an intermediate metabolite, acetaldehyde, is particularly toxic. If it accumulates, acetaldehyde causes a great deal of bodily discomfort. A biological response, the discomfort may be enough to inhibit the desire to drink, but apparently the motivation is great enough for some to overcome it (see the discussion of this in Chapter 4).

The pharmacologic effects of ethanol are probably known to every living adult in the modern world, but a brief review might be helpful in any case. First, it is important to distinguish these immediate effects from the toxic and pathologic ones, which occur when an overdose is taken or excessive amounts are used for a long time. The “simple” pharmacology relates brain function to various levels of alcohol on board. A small amount of the drug usually arouses or unrestrains people, while increasing levels depress them. In fact, all functions of the brain are affected, including sensation, perception, reflexes, mood, thought, memory, decision making, motivation, motor skills, communication, and interpersonal skills. The ultimate depression is total loss of consciousness (coma). While many people think that these functions remain intact until they hit the “legal limit” of intoxication (0.100 gm/100ml blood), there is nothing magic about this value. Actually, the effects on mood and mind begin with the very first sip. A host of physiological effects occur, including increases in the release of epinephrine and steroids from the adrenal gland, which in turn raise blood sugar and fat levels. Blood flow to the skin increases, and a person could lose a lot of body heat. (Just think about the homeless alcoholic who finds himself outdoors in subzero weather!)

One interesting neurological effect of ethanol is nystagmus, a jerky, side-to-side oscillation of the eyeballs that can be provoked by looking to the side and is used in some municipalities for roadside pretesting of blood levels. Alcohol also has an effect on certain hormones. In men, testosterone is decreased so their sexual function is compromised. In all people, the hormone that restrains urine output is suppressed, leading to excessive urination (diuresis).

Precisely how ethanol does all of these things and more is still a matter for researchers. The current working hypothesis is that because the drug is so small (and undistinguished), it does not

use a single specific receptor, but rather gets into the cell membrane to alter function of various receptors and other elements. Since nerve and muscle cell membranes are most sensitive, they are affected first. The communication (transmission) between neurons is initially enhanced and then it is diminished. A wide array of neurotransmitters is affected, but it appears that norepinephrine is implicated in the arousal, serotonin may be involved with inhibition of function, and dopamine plays a special role in the pleasurable and rewarding effects of the drug.

Repeated, heavy use of alcohol for a period of only a few days can lead to obvious tolerance: The drinker needs to consume more to produce the same effect, and this will continue to grow with chronic use. This pattern also results in physical and psychological dependence on the drug. As long as he or she is drinking, the dependent alcoholic can look relatively normal, but stopping can cause the person to experience *withdrawal*, an abstinence syndrome characterized by intense craving as early as six hours after the last drink. This is rapidly followed by generalized irritability—*anxiety, shaking, insomnia, sweating, stomach cramps, nausea, and vomiting*. The person’s blood pressure goes up and, if he does not get a drink or some other depressant, he will likely show some motor tremor, growing confusion, disorientation, hallucinations, and even seizures of the grand mal type between one and two days after cessation. A small percentage of alcoholics who undergo withdrawal will experience *delirium tremens*, a second type of abstinence syndrome that usually begins about the third day, which is of greater concern medically because the person could die from the severe hyperthermia, dehydration, and cardiovascular stress that accompany the delirium.

The list of pathological consequences that follow chronic, excessive consumption of alcohol is extraordinarily long. This is true because people use such large quantities of the drug to produce the “desired” effects and because alcohol distributes so widely throughout the body. Some of the more common secondary pathologies are presented in Table 5.1 according to the systems involved.

SYSTEM	PROBLEM
GASTROINTESTINAL	Gastritis, Ulcers, Enlarged Liver and Spleen, Pancreatitis, Hepatitis, Cirrhosis, Esophageal varices, Malignancies
NEUROLOGICAL	Peripheral nerve loss, Cerebellar degeneration, Encephalopathy, Dementia, Organic psychosis
CARDIOVASCULAR	Irregular Heart Rhythm, Arrhythmia, Hypertension, Stroke, Cardiomyopathy
BLOOD CELLS	Decreased production, Increased destruction, Anemias, Decreased lymphocyte function, Decreased Immune System function
HORMONES	Testosterone decreases, Estrogen increases, Testicular Atrophy, Gynecomastia, Prolactin (milk ejection) increases, Parathyroid decreases
MUSCULO-SKELETAL	Muscle wasting, bone thinning
METABOLISM	Carbohydrates increase and decrease, fats increase, B Vitamin absorption decreases, Mineral absorption decreases
SKIN	Blotchy spots, Spiders, Itching
REPRODUCTIVE	Male function decreases, Female function variable, Fetal Alcohol Syndrome and Fetal Alcohol Effects
EXCRETION	Kidney failure

Table 5.1 Common Secondary Pathologies By System

Special reference must be paid to one of the most tragic consequences of alcohol abuse, Fetal Alcohol Syndrome (FAS), for it is the leading preventable cause of mental retardation in the United States today. The average incidence of documented FAS is about 2 in 100,000 live births, but it is much higher among certain subpopulations such as Native Americans. Although there

are physical malformations with FAS, the developing brain is particularly susceptible to alcohol exposure. Depending upon the precise time and amount of exposure, profound developmental arrests can produce intellectual, emotional, and behavioral problems.

Treatment of alcoholism frequently involves the limited use of medication. While we do not have any specific antagonists for alcohol, we can use other agents in its class to manage the withdrawal process. The drugs usually employed today are sedatives like Ativan[®], Valium[®], and phenobarbital. Typically, just enough of this depressant is given to block the abstinence syndrome and then it is progressively withdrawn over three to five days. Sometimes, the use of Antabuse[®] is

recommended for adults during the rehabilitation phase of treatment for six months or more. This drug itself is not therapeutic, however, if a recovering alcoholic slips while he has Antabuse[®] in his system, he will get sick because it causes the buildup of acetaldehyde. It is essential to inform the client that Antabuse[®] remains active in the body for a week to ten days and that a drink may cause intense gastrointestinal upset, shortness of breath, heart palpitations, and severe migraine headaches. This ought to discourage drinking, but remember, there is no magic bullet.

Sedatives/Hypnotics. Other commonly abused drugs in the depressant category are the sedatives (tranquilizers) and hypnotics (sleep inducers). Sedatives like Valium[®], Librium[®], Restoril[®], Xanax[®], and Serax[®] are prescribed by doctors to calm the overly anxious patient without putting him or her to sleep, while hypnotics like Nembutal[®], Seconal[®], and Tuinal[®] are ordered to treat severe cases of insomnia. The hypnotic agents have been around somewhat longer than the tranquilizers, and are part of a larger class that includes drugs that are seldom abused like phenobarbital, which is employed medically to control seizure disorders, and Pentothal[®], the rapidly acting agent that anesthesiologists administer before surgery to induce profound sleep.

Sedatives were introduced on the market in the late 1950s as the first truly specific anti-anxiety agents. Because all of these drugs require prescriptions, the only legitimate way an individual can get them is from a physician. Until very recently, doctors were unaware of the full potential these agents possessed for misuse, abuse, and dependence. This is especially true of tranquilizers, which were proclaimed to be among the safest drugs in the world. Indeed, it may have been the impressively wide margin of safety that the sedatives exhibit which lulled doctors into a false sense of security.

Sedative and hypnotic drugs are manufactured and sold in tablet form at a variety of doses. They are taken orally and have to be absorbed into the bloodstream from the intestines before they can be delivered to the brain. Unlike alcohol, most of these agents bind to blood proteins; for example, as much as 95 percent of Valium[®] may be bound, so that only 5 percent is really free to enter the brain at any one time. All of these drugs are lipophilic to some degree, but Valium[®] happens to be especially fat soluble. As a result, it can take effect in a matter of minutes. For the same reason, it stores up in body tissues resulting in a long half-life and prolonged duration of action.

The effects of most sedatives and hypnotics are terminated by metabolism in the liver. This breakdown usually yields inactive metabolites that are easily excreted in the urine. But in the case of Valium[®], Librium[®], and a few others, the breakdown product is still active, and prolongs the drug effects further. This causes the withdrawal syndrome to be long and drawn out as well.

These drugs do not usually produce the initial arousal that alcohol does; rather, they lead straight to depression of mood, motor, and thought processes in a strict, dose-related fashion. These

dramatic effects on the central nervous system are selective, but may be accompanied by decreased respiratory performance and lowered blood pressure when the hypnotics are used. At high doses of Nembutal, breathing becomes slow and shallow, and may stop altogether. Shock is also possible in the toxic person, and an overdose can be fatal.

When sedative/hypnotics are used regularly over a period of weeks, they produce tolerance and dependence, with cross-over effects for each other and alcohol. The person who becomes tolerant to Valium simultaneously becomes tolerant to the other sedatives, hypnotics, and alcohol. That is, he or she will require more alcohol to get high than would have been true before. This tolerance is due to two factors: the brain itself becomes less sensitive and the liver produces more enzymes to break down the drugs. Cross-dependence is similar in that any of these substances will block withdrawal from dependence on the others. This principle is often used in the early treatment or detoxification stage of therapy when Valium, phenobarbital, or one of the other sedatives/hypnotics is substituted for alcohol under medical supervision and then progressively reduced.

The withdrawal syndrome for sedatives and hypnotics is essentially the same as for alcohol if they are terminated abruptly. It is a dramatic hyperarousal characterized by anxiety, insomnia, shaking, disorientation, confusion, high blood pressure, and seizure. The main difference from the alcohol syndrome is timing; the withdrawal problems for hypnotics and sedatives begin later and last longer. The intensity of the withdrawal is primarily a function of how much, how often, and how long the person has been using the drugs. If there is a bright spot in this otherwise gloomy picture, it is that tissue and organ damage is minimal for people who only use sedatives.

Stimulants

Chemicals in the stimulant category are characterized by their ability to increase the user's wakefulness, perception of strength/energy, and sense of well being. They also decrease the user's appetite. In large doses, stimulants may also cause mania, paranoia, and hallucinations. The most commonly misused drugs in this category are cocaine and amphetamines. Other widely used stimulants include caffeine, Ritalin (methylphenidate), and phenylpropanolamine, an over-the-counter decongestant and diet-aid.

Cocaine. Cocaine, the preferred stimulant drug in many communities, is a chemical derived from the leaves of *Erythroxylon coca*, a shrub grown in South America. Chewing of the leaves by Indians in Peru began prior to 500 A.D. Later, coca leaves were exported to Europe, hailed as a marvelous discovery, and used in wine, tea, and other beverages. The pure chemical substance cocaine was first extracted from the plant in 1855, and medical experiments using cocaine were common in the 1880s, including some conducted by Sigmund Freud on the drug's potential therapeutic effects. Early in this century cocaine made its way to the U. S., where it was added to cola beverages, patent medicines, and even chewing gum. The cocaine in cola was removed and replaced by caffeine in 1903.

The Harrison Act of 1914 was the first legal control placed on the sale of cocaine and other drugs in this country. Physicians, dentists, and veterinary surgeons who distributed cocaine were required to be registered. Widespread cocaine use (which was primarily oral at that time) began to decrease as cocaine went underground to be used by "social outcasts." However, cocaine is still employed today by anesthesiologists and otolaryngologists (ENT specialists) for its local anesthetic effects. Because it has vasoconstrictive properties on mucous membranes, it reduces postsurgical bleeding. There was a resurgence of cocaine use in the late 1960s, when cocaine re-

emerged as a glamorous “nonaddicting” drug. The use reached epidemic proportions in the mid-1980s when inexpensive, smokable cocaine known as *crack* became available throughout the U. S.

Cocaine has several routes of administration: oral, intranasal snorting (insufflation), smoking, and intravenous injection. The intensity of cocaine euphoria is directly related to the speed of absorption of the drug. Thus, the faster the absorption, the greater the high. Oral cocaine is broken down in the gastrointestinal tract, so only 30 percent to 40 percent of the drug is absorbed. The reduced amount and slower rate of absorption decrease the subsequent euphoria. Large oral doses, however, can still cause death. Cocaine is absorbed most quickly when it is smoked. The euphoric rush begins about eight seconds after smoking in contrast to 18 seconds after intravenous injections. With either route, the rush subsides to a less pleasurable euphoria in just a few minutes (see Table 5.2). The effect after intranasal use takes 15 to 20 minutes to peak, and the high disappears in about one hour.

Since cocaine is such a strong stimulant, its use is often accompanied by a sedating agent such as alcohol or marijuana, especially at the end of a run. Cocaine is also combined with heroin either at the same time (speedballing) or sequentially. The drug is metabolized by enzymes found in the blood and liver. Only 1 percent of the original dose is excreted unchanged in urine; the rest is excreted in metabolized form. Since cocaine is both fat and water soluble, it rapidly crosses the blood-brain barrier, has its effect, and leaves just as quickly. The urine is free of the metabolites one to three days after moderate use.

ROUTE OF ADMINISTRATION	ONSET OF ACTION	PEAK EFFECT
Oral - chewing, drinking	10 minutes	60 minutes
Intranasal - snorting	3 minutes	15 - 20 minutes
Intravenous injection	18 - 20 seconds	3 - 5 minutes
Inhalation - smoking	8 seconds	1 - 5 minutes

Table 5.2 Onset and Peak Effect of Cocaine

Crack, a smokable form of cocaine (freebase), emerged in the early 1980’s in the United States. This mode of cocaine use quickly was found to be more “addictive” than snorting. The craving that follows crack smoking is more intense. This phenomenon is thought to result from the rapidity and intensity of the effect experienced after smoking it.

There are many effects of cocaine on the human body, but most are due to its impact on neurotransmission in the central nervous system (see Table 5.3). Chronic administration of cocaine, even at low doses, can lead to seizures by a process known as *kindling*, or progressive sensitization. According to the current hypothesis, the user has a lowered seizure threshold because repeated doses of cocaine enhance electrical conduction in the cortex and hippocampus. Stimulation of the midbrain and cortex is responsible for the restlessness, excitement, and the decreased sense of fatigue. The increased respiratory rate, subsequent shallow breathing, and eventual respiratory failure are due to the toxic effect of cocaine on the respiratory center in the medulla. Elevated body temperature results from a direct action on the temperature-regulating center in the hypothalamus.

Cardiovascular consequences of cocaine use are mediated primarily by effects of the drug outside the central nervous system; that is, blocking of norepinephrine re-uptake at sympathetic nerve endings on the heart and blood vessels. Moderate doses of cocaine increase heart rate and force of contraction, as well as elevate blood pressure by causing arteries to constrict. A large intravenous dose can be toxic to heart muscle and cause heart failure. Heart attack is possible even in persons with normal coronary arteries.

SYSTEM	EFFECT
CENTRAL NERVOUS SYSTEM	Euphoria, Grandiosity, Sexual stimulation, Restlessness, Hyperactivity, Irritability, Insomnia, Hypervigilance, Paranoid Ideation, Hyperactive Reflexes, Dilated pupils, Tremor, Seizures, Hallucinations, Delirium, Panic states, Stereotyped behavior, Vertigo, Vomiting, Hyperthermia.
CARDIOVASCULAR	Hypertension, Tachycardia and irregular heart rhythm, Palpitations, chest pain, Cardiac Arrest.
GASTROINTESTINAL	Dry mouth, Vomiting, Abdominal cramps, Anorexia.
RESPIRATORY	Asthma, shortness of breath, Pulmonary Edema.

Table 5.3 Effects of Cocaine Intoxication

The psychostimulant action of cocaine is due to its effect on several neurotransmitters in the nervous system. Dopamine and norepinephrine seem to be the primary neurotransmitters involved. Cocaine blocks the re-uptake of neurotransmitters by presynaptic nerve endings leaving excess neurotransmitter molecules in the synapses. This causes continued stimulation of the postsynaptic neurons. It is the action of dopamine in the brain's "pleasure center" (limbic area) that is responsible for cocaine's great euphoric effect. Cocaine's continuous inhibition of neurotransmitter re-uptake is a double-edged sword; eventually, it leads to desensitization of postsynaptic dopamine receptors and, at the same time, to a depletion of neurotransmitter in the nerve terminal. The rate of neurotransmitter loss exceeds its rate of production, creating a deficit that causes the cocaine user to crash (become severely depressed) and to crave cocaine.

Tolerance occurs rapidly with frequent cocaine use. The individual increases the amount in an attempt to recreate the first "high." A relative deficiency of neurotransmitter occurs later on, which makes the euphoria more and more difficult to attain. When the person stops using, a severe depression occurs, and may persist for months. Abstinence from chronic cocaine use is also characterized by cocaine craving, appetite increase, weakness, sleepiness, and frequently abdominal discomfort and melancholia. Chronic use may cause damage to the liver, heart, and other organs. Intranasal use of cocaine inflames the mucous membranes and can lead to perforation of the nasal septum. Frank paranoid psychosis, and homicidal and suicidal behavior may occur with high doses or long-term use. Compulsive scratching, known as "cocaine bugs," is a common sign of tactile hallucinations that are experienced during intoxication. (Look for some of these signs and symptoms in the vignettes of Chapter 9; see Helen.)

There has been a lot of publicity regarding "crack" babies, but fact must be separated from fiction. Clearly, the use of cocaine by a pregnant woman may have consequences for the baby. Infants exposed to cocaine *in utero* are smaller in overall size, have disproportionately smaller heads, have higher rates of sudden infant death syndrome (SIDS), and certain birth defects. The pregnancy may be complicated by early separation of the placenta and possible stillbirth. Infants have been born after suffering strokes prenatally and, if the mother shares needles, the infant is at a risk for AIDS. It does appear that cocaine-exposed babies are more irritable and difficult to soothe than those who are not exposed to cocaine in the womb, but we do not yet know what the long-term outlook is for these infants.

No effective chemical substitute is available for the treatment of cocaine dependence, such as methadone is for heroin. Most medications used in the treatment of cocaine dependence are aimed at restoring the balance of neurotransmitters. Neurotransmitter stores may be enhanced by giving neurotransmitter precursors (like L-DOPA), or certain antidepressants that increase available neurotransmitters, including Norpramin (desmethylimipramine). Symmetrel (amantadine) releases dopamine from its storage sites and Parlodel (bromocryptine) decreases cocaine craving because it acts like dopamine. However, treatment must extend beyond simple pharmacotherapy, which may be of very limited benefit. Treatment must be long term, as relapse is common in the first eighteen months of abstinence.

Amphetamines. Amphetamines, a family of synthetic psychomotor stimulants, were first discovered in 1887. Methamphetamine, a more potent drug than dextroamphetamine, was synthesized in 1919. These chemicals became popular during World War II, when they were given to servicemen on both sides to reduce fatigue. (It may be noteworthy that morphine was widely used during and after the Civil War and heroin during the Vietnam era.) Subsequent to World War II, these stimulants were used across the country for their euphoric effect as well as their alerting and appetite-suppressing properties. Physicians even prescribed them to treat heroin addiction!

Amphetamine use reached its peak in the 1960s. Despite stringent sanctions, illegal production of dextroamphetamine and methamphetamine continues today because it is inexpensively and simply produced. In Michigan, amphetamines can no longer be prescribed by physicians for weight loss. However, they are used to treat hyperactivity in children (ADD or ADHD) and, rarely, for narcolepsy (a disease which causes the sufferer to fall asleep uncontrollably) and depression.

Smokable methamphetamine known as “ice,” “shabu,” “crank,” and “crystal,” first became popular around 1989 in Hawaii and western parts of the continental U. S. Its popularity is greatest among teens, especially White and Asian-American teens. Like crack, ice is smokable, which makes it more rapidly “addicting” than Dexadrine or Benzadrine.

The route of administration for drugs of this type may be varied. Amphetamines can be taken orally in a white crystalline form or mixed with liquid, snorted, or injected in a saline solution. When taken orally, the peak effect occurs in 2-3 hours, and a large part of the dose is excreted unchanged in the urine for 2-3 days afterward. The effects of one Dexedrine dose can last from 4-6 hours. Methamphetamine-induced effects last approximately twice as long as those for dextroamphetamine. The amphetamines affect various organs as well as the central nervous system. Many of the peripheral and central effects are identical to those of cocaine (see Table 5.4).

SYSTEM	EFFECT
CENTRAL NERVOUS SYSTEM	Arousal, Euphoria, Restlessness, Hyperactivity, Anxiety, Irritability, Dilated pupils, Paranoid Ideation/Psychosis, Sexual stimulation, Aggressiveness, Stereotyped compulsive behavior, Appetite suppression, Hyperthermia.
Cardiovascular	Hypertension, Tachycardia and irregular cardiac rhythm, Heart failure, Stroke

Table 5.4 Effects of Amphetamines

The mechanism of action for amphetamines is related to that of cocaine. It appears that they increase the release of dopamine, norepinephrine, and similar neurotransmitters from their

presynaptic terminals. The amphetamines are taken up across the presynaptic membrane and stored in vesicles, causing displacement of the natural transmitters into the synapse. This leads to the increased activation of postsynaptic receptors.

Amphetamine use can be accompanied by wide emotional swings, sleep disturbance, and even toxic paranoid psychosis. The person who develops a psychosis may require treatment with antipsychotic medication on a temporary basis. Needless to say, those who use amphetamines intravenously, and especially those who share needles, are at risk for infections such as hepatitis and HIV. Tolerance to amphetamines occurs rapidly, particularly at high doses. The person requires progressively larger amounts to achieve the same high and appetite-suppressant effects. The tolerance may be due to more rapid metabolism and excretion of amphetamines, as well as a decreasing sensitivity of synaptic processes. Dependence develops in a manner similar to that for cocaine, and it is marked by a profound behavioral depression during abstinence. The medication needed to treat amphetamine dependence is similar to that employed for cocaine dependence.

Opioids

“Opioid” is a term that was coined to include all of the substances that act like the primary active drug we get from the opium poppy, morphine. In addition to the plant extracts morphine and codeine, the class includes heroin (which is chemically modified morphine), other drugs that can be synthesized in a laboratory like Demerol[®] (meperidine), Dolophine[®] (methadone), and Dilaudid[®] (hydromorphone), and substances that the body itself makes called **endorphins**, or **opioid peptides**. An older term that is often used for drugs in this category is “narcotic,” which came from the observation that they can induce narcosis, or sleep, at some dose. The fact that this action is neither specific nor characteristic for normal analgesic doses suggests that the term should no longer be used (although there is little likelihood of this!).

Discovered almost two hundred years ago, morphine is the oldest drug in the class. It really came into its own as a pain killer at the time of the Civil War, when thousands were maimed and left with chronic pain. Introduction of the hypodermic syringe at about the same time, together with a total absence of societal or governmental controls, led to the first acknowledged national drug problem. In fact, it was this problem and the threat of others that spurred on drug control legislation which, after the turn of the century, culminated in the Harrison Narcotics Act.

The obvious “drug of choice” for those people who do abuse opioids is heroin, a drug that is not approved for medical use in the U. S. But it is clear that chronic heroin users will use any and all of the opioids at different times. Because it is so lipid soluble, heroin can be used effectively by various routes, including snorting, smoking, and drinking, as well as injecting under the skin (“skin popping”) or into a vein. Youngsters often start using by snorting or smoking. Most of the other opioids are produced by pharmaceutical companies as tablets or liquids for oral administration. Some users will pulverize the tablets, dissolve the powder in water, and inject it for a more rapid and intense effect. The liquids like codeine and paregoric are often sold as elixirs and syrups which cannot be altered. The methadone that is provided in drug detoxification or maintenance programs is usually dissolved in juice or a flavored drink. Injectable preparations that are employed in hospitals for pain relief are less frequently diverted to the illicit market.

Most opioids bind around 40 percent to serum proteins, distribute widely throughout body tissues, and are metabolized in the liver. The half-lives of the different drugs vary considerably, from about 2-3 hours for Demerol[®] to 15 hours for Dolophine[®]. The effects do not last as long as 15 hours, although chronic use can extend the action due to tissue buildup.

People who take heroin and other opioids on the street do not use them for pain control, but rather for their euphoric property. The psychogenic effects are *biphasic*; that is, first there is an exhilaration (an intense “rush” with heroin), then a floating feeling, after which the person falls into a sleepy “nod.” Libido is diminished in both men and women, and there is very little interest in eating. In fact, the person might get nauseous and light-headed. The drug releases histamine in the bloodstream and, as a result, causes itchy skin reactions. The person may be unaware of the fact that his blood pressure has fallen, heart rate and breathing have slowed, and body temperature is down 2-3 degrees. The drug’s analgesic effect manifests itself, so a wound may not appear to hurt him. If you look into this person’s eyes, you will see a characteristic constriction of the pupils, even in a poorly lit room where they should be large. When an overdose is taken, the loss of consciousness, reflexes, and motor control can be profound. The classic earmarks of opioid toxicity are coma, respiratory depression, and pinpoint pupils.

When someone uses heroin, Dilaudid®, codeine, or any of the opioids chronically, they can develop tolerance along with physical and psychological dependence. The latter is expressed in much the same way as for other abused drugs—characteristic stereotyped behaviors and compulsive desire. Physical dependence on opioids is manifested by a withdrawal syndrome which is different from depressants and stimulants because different mechanisms are involved. It can begin as early as 6, or as late as 12 hours after the last use of heroin (longer for Dolophine®, shorter for Demerol®) and gives the outward impression of a bad flu. Signs and symptoms include anxiety and restlessness, an inability to concentrate, weakness and pain in muscles and joints, abdominal cramps, nausea and vomiting, tearing and nasal discharge, and an increase in blood pressure, breathing rate, body temperature, and pupil size (look into their eyes!). The condition usually takes 3 to 5 days to resolve if the person was using heroin, 8 to 10 days for methadone. Tolerance is characterized by decreasing effectiveness of the same dose of opioid and a requirement for more to produce the same effect.

The immediate and chronic biological effects of opioids are due to actions on specific opioid receptors. These sites are located in strategic places on neuronal membranes in the synapse, where the nerve cells communicate with each other. The prime functions of opioid receptors are to serve the naturally produced endorphins (peptides that are released from neurons like neurotransmitters) and to modify synaptic communication (mainly to decrease it). When heroin or one of the other drugs is used, it gets into the synapse and swamps the receptors, augmenting the normal function. If the drug is used for awhile, the receptors and the neurons they control become less sensitive to the effect. By the same token, the mechanism that is normally controlled by the endorphin changes to compensate for the drug’s constant impact (dependence).

All of the opioids discussed thus far are agonists that have a wide range of actions. Over the years, attempts have been made to make new agents in the laboratory that do not have all of the negative effects. These efforts have not been successful yet, but they have led to the discovery of **opioid antagonists**—drugs that bind to the same opioid receptors without producing any effects. The two agents that are used medically today are Narcan® (naloxone) and Trexan® (naltrexone). Narcan® is only effective by injection, so it is reserved for managing opioid overdose in the emergency room. Its life-saving effect in the clinic looks truly miraculous. Trexan® is effective when taken by mouth and it is much longer lasting than Narcan®. It is used to assist the motivated, rehabilitating client who might be tempted on a momentary impulse to use heroin again.

The treatment for opioid dependence may involve the use of medications. In the detoxification stage, Dolophine® (methadone) can be used to replace and withdraw over about 5 days, in the

same way that Valium[®] is used for the alcoholic. A preferred drug for detoxification today is Catapres[®] (clonidine). Although it is marketed primarily for high blood pressure, experience has shown that it very effectively blocks most of the withdrawal syndrome—and it gets the person off opioids immediately. In this case, Trexan[®] can begin as soon as the detox phase is completed. Dolophine[®] is also used to treat opioid-dependent people in a maintenance regimen. Here, it is assumed that the individual's system has been changed so much that he or she requires endorphin support, in the same way that a diabetic's system needs insulin. Pregnant, heroin-dependent women typically are managed with Dolophine[®] at a dose that decreases during pregnancy to very low levels, although the medication usually is not eliminated entirely.

Pathology that is typically associated with abuse of opioids is not specific to the drugs, but rather the way they are used. As for other injected agents, the chief medical problem is infection due to contaminated needles. Currently, that means a risk for HIV/AIDS and hepatitis B in addition to more common viral and bacterial organisms that can damage the heart and other organs.

Hallucinogens

Hallucinogens make up a category of substances that are capable of giving the user a distortion of objective reality. They have also been referred to as psychedelics, phantastics, and psychotomimetics (mimics psychosis). Drugs in this category include LSD (D-Lysergic acid diethylamide), mescaline, PCP (phencyclidine), psilocybin, and marijuana. While hallucinogens have been used for centuries in the search for spiritual or religious experience, their use peaked in this country in the 1960s.

LSD, Psilocybin, and Mescaline. LSD was synthesized in 1938 from a derivative of a fungus. Because it was thought to have the ability to reveal the unconscious, it was used for a while as an adjunct in psychotherapy. Later, it was thought capable of inducing a state of temporary insanity, a model psychosis. Unfortunately, it was used by the U. S. Army in experiments on abnormal human behavior. The most notorious case involved the placement of LSD in the drink of an unsuspecting career serviceman who had a panic reaction and subsequently committed suicide.

LSD is a very potent chemical. Extremely small doses are all that is required to produce its effects. Taken by mouth, it is rapidly absorbed, metabolized, and excreted in the urine. It has a plasma half-life of about 3 hours, but its effects can last for 8-12 hours. Detection in the urine is rather difficult, since it is used in such small quantities.

The mechanism of action of LSD is complex, but it appears that its impact on the central nervous system is via serotonin. Twenty minutes or so after ingesting LSD, physical signs of sympathetic nervous system stimulation become apparent. They include dilated pupils, elevated body temperature, increased blood pressure, and salivation. Within the next half hour, the user notes changes in sensation—in particular, the perception of space and time is distorted. This is followed by feelings of depersonalization and an out-of-body experience.

Tolerance occurs rapidly with LSD and there is cross-tolerance with mescaline and psilocybin, which produce roughly the same effects at higher doses. Adverse hallucinogen effects consist of psychotic reactions, panic reactions (“bad trip”), and **flashbacks**. A flashback is a recurrence of the drug-induced sensations after not using the drug for weeks and months. It is not due to lingering traces of the drug in the body. However, we do not know what actually does cause the phenomenon. LSD is not apparently toxic; there are no recorded deaths due to LSD use *per se*. No withdrawal syndrome due to cessation of LSD has been described.

Psilocybin is the active psychotropic chemical found in the Mexican mushroom *Psilocybe*. It was used by people in its native habitat for many years in religious rites and ceremonies long before it was introduced to the U. S. drug culture. Pharmacologic effects are dose related, and range from relaxation to sympathetic nervous system activation and hallucination similar to LSD.

Mescaline is derived from the peyote cactus. It has chemical properties similar to LSD and psilocybin, and produces similar psychological effects when orally administered. It also has a history of being used in Native American and Mexican-Indian religious rituals. In fact, its use is sanctioned by the Native American church which was formally established in 1918.

It is thought that the actions of mescaline on the CNS are due to its serotonin-inhibiting effect. The psychoactive manifestations are dose related, with euphoria occurring at lower doses and hallucinations at higher ones. Its sympathomimetic effects include dilated pupils, and increased body temperature, pulse, and blood pressure. Tolerance occurs with repeated use, but more slowly than with LSD. There is no withdrawal syndrome associated with chronic use of the drug, but death may result from toxic seizures and respiratory arrest due to overdose. In extreme conditions, the intoxication with mescaline (and LSD) can be managed with an antipsychotic drug such as chlorpromazine.

A group of amphetamine derivatives which includes DOM (dimethoxymethyl-amphetamine), also referred to as STP, and DMA (dimethoxyamphetamine) have hallucinogenic effects at low doses and stimulant effects at higher ones.

Phencyclidine (PCP). Phencyclidine (marketed today for veterinary use as Sernyl) appeared in the 1950s as an intravenous anesthetic. It produced exceptional analgesia without serious side effects and without inducing sleep. When it was used originally as an anesthetic in humans, changes in body perceptions, hallucinations, and temporary psychoses were observed and so human use was stopped. It appeared on the street in the 1960s along with the other popular hallucinogens, and again in the 1970s as “angel dust.” It was mixed commonly in “joints” with marijuana and is still very available in certain areas of this country, particularly along the mid-Atlantic coast. Because it is relatively easy to manufacture, PCP reappears regularly under a host of pseudonyms.

PCP is administered by nearly every imaginable route, but is most commonly taken orally, by inhalation, and by intravenous injection. It can be used, and often is, together with alcohol, barbiturates, opioids, and marijuana. The drug is lipophilic and distributes very widely throughout the body. PCP has a long half-life and is detectable in the urine for several days. Ninety-three percent of its metabolite is excreted in the urine, with about 4 percent excreted through the bowel.

PCP's mechanism of action is not entirely understood. More than one neurotransmitter and receptor system may be involved, including a type of opioid receptor. Effects of PCP are dose related, and within the first 12 hours, the user may experience skin flush, enlarged pupils, delusions, dissociations, amnesia, nystagmus, and behavioral excitement. Blood pressure may be elevated, along with dizziness, nausea, and vomiting. Large doses of PCP will cause seizures, respiratory depression, and heart arrhythmias. Chronic use of PCP can cause a schizophrenic-like syndrome with visual and auditory hallucinations, paranoia, and catatonia. Users develop mood disorders and unpredictable behaviors, becoming self-destructive or harmful to others. Psychotic episodes may last for weeks and even months. PCP withdrawal is characterized by depression. Placental transfer of PCP takes place without any difficulty and drug-exposed infants appear at

birth to have neurobehavioral signs such as irritability, shaking, and increased muscle tone.

Marijuana (marihuana). Marijuana, hashish, and hash oil are products of the hemp plant known as cannabis. One species, *Cannabis sativa*, is grown worldwide. The major psychoactive chemical in cannabis is delta-9-tetrahydrocannabinol (THC). THC is most concentrated in the resin of the flowering tops (sinsemilla); less is found in the leaves. The concentration of THC found in typical marijuana preparations varies from 1 percent to 8 percent. Many factors affect the potency, including the climate, genetics of the plant, and the method and duration of storage. Hashish is a concentrated preparation of resin, and hash oil is an even more concentrated form that can be 50 percent or more pure THC. The marijuana that is available today is more concentrated than the “pot” that was popular in the 1960s and 1970s.

The history of cannabis dates back to China as early as 2737 B.C. It arrived in Europe around 1800 A.D., where it became very popular for its value as a medicament and snuff. However, it attracted little interest in this country until the 1920s and 1930s when an association was made between marijuana and crime. Shortly thereafter, all the states established laws regulating the manufacture, sale, and use of marijuana. In 1937, the Federal Marijuana Tax Act was passed. It didn't ban marijuana, it just taxed every aspect of its production and distribution. The years following were marked by debate over the safety of marijuana use. Nevertheless, its use began to increase in the 1950s and 60s and “decriminalization” of marijuana became a battle cry. Marijuana use peaked in this country in the late 1970s, with 10 percent of high school seniors admitting to daily use.

Marijuana is not approved for therapeutic use, but there are two chemically synthesized oral forms of delta-9 THC (Marinol[®], Cesamet[®]) approved for the treatment of nausea and vomiting that occur with cancer chemotherapy. These preparations also have been used to treat glaucoma, but are no better than conventional glaucoma medications.

Marijuana is usually smoked, so the THC is rapidly absorbed into the bloodstream. After going to the brain, it is carried to the liver where some is metabolized. Sixty-five percent is excreted in the feces, while 35 percent is eliminated through the urinary tract. Since THC is extremely fat soluble and not all of it is metabolized during its passage through the liver, some of it is deposited in fatty tissues of the body where it is gradually released over time. As a result, marijuana (like PCP) has a long plasma half-life of approximately 19 hours. Metabolites may be found in the urine from 3 to 40 days after last use. The drug can be ingested orally, but it takes three times as much to get the same psychoactive effect as by inhalation.

The intoxicating effects of marijuana begin within minutes after smoking and last for 2 to 3 hours. The drug causes euphoria and a dreamlike state, along with changes in time and distance perception. Larger doses may cause distortions of the user's body image, delusions, and hallucinations. There is impaired vision, motor coordination, and acquisition of new information. Even though the subjective effects last only three hours or so, there is impairment of the user's driving ability for up to 24 hours after use. Other acute effects include reddening of the eyes, dry mouth and throat, increased hunger, sleepiness, increased heart rate, and bronchodilation. The mechanism of action of marijuana is not well understood, but probably is mediated through neurotransmission, and may involve a unique receptor.

Most of marijuana's toxic effects are psychological, such as delirium, disorientation, or panic attacks, but cardiac arrhythmias and EKG irregularities may occur, and irritation of the respiratory tract can be extreme. The term “amotivational syndrome” was coined to describe

young people who use marijuana chronically and is characterized by apathy, loss of productivity, fatigue, impairment in concentration, and poor grooming. Whether the association is direct or indirect is not clear, and the syndrome may simply represent depression or a pre-existing condition. However, it does appear that chronic marijuana use causes (temporary) problems with learning.

Marijuana use during pregnancy may have a negative impact on the development of a fetus (decreased head circumference and possible decrease in body weight). Dependence occurs with repeated use of the drug; the abstinence syndrome is characterized by irritability, restlessness, nausea, vomiting, loss of appetite, and sleep disturbance. Most of the symptoms resolve in a few days without medication.

Other Drugs That Are Abused

Inhalants. Drugs in the category of **inhalants** include volatile **solvents** like gasoline, glue, spot cleaners and lighter fluid, aerosol propellants, some anesthetic agents, and **nitrites** that first appeared as “poppers” and “snappers” (fine glass ampules for people with angina heart pain) and have since become available in nasal spray form. These two types of drug work differently. They are only associated by their manner of use—inhalation—and their popularity with teenagers and young adults. (“Glue sniffing,” an older, colloquial term for solvent abuse, covers a wide range of substances from gasoline to nitrous oxide.) All of these act on the brain in a way similar to alcohol, but faster because the absorption is immediate. The person who has inhaled one of these substances initially experiences a euphoric rush and behavioral stimulation, followed by a more lasting depression of mood. In the early phase, the user may be quite impulsive and, lacking judgment, dangerous to himself and others. Tolerance and dependence can develop to these drugs if they are used repeatedly; the pathological consequences can be severe, involving the nervous system, liver, kidney, and heart.

Nitrite abuse produces what is sometimes called a “head rush,” that is, a short-lasting, but profound change in perception, mood, and thought. It seems to be due to an indirect effect on blood flow to the brain rather than a direct action on the brain itself. In fact, nitrites are used medically to relax blood vessels in the heart, but they can do the same thing to cerebrovascular and gastrointestinal muscles. They are popular in the gay community, and are often sold with their paraphernalia in “porno” shops.

Nicotine. Tobacco is used extensively in the U. S. and throughout the world. It is our country’s sixth largest (legal) cash crop and cigarettes are the primary drug delivery system. Each cigarette contains a dose of about one milligram of nicotine, approximately 90 percent of which is absorbed within seconds. Because the drug is lipophilic, it moves around the body very easily and is stored in fatty tissues. The half-life of nicotine in blood is hours long, but the dependent user typically smokes a new cigarette every 20-30 minutes. The pharmacologic effects of nicotine are complex: at first, the smoker experiences stimulation, but after a while there is a sedating or calming effect. Both tolerance and dependence occur with chronic smoking. People familiar with many different chemical dependencies have indicated that the craving and compulsion to use tobacco are among the most intense. However, signs and symptoms of physical withdrawal are not outwardly profound. The medical consequences of smoking are legion, with cancer, pulmonary, and cardiovascular disease heading the list. More than 450,000 deaths each year are directly attributable to smoking tobacco. There is a strong correlation between heavy smoking and heavy drinking of alcohol, and epidemiologic data show that they

increase the pathologic effects of one another.

Caffeine. Caffeine is a legal and seemingly benign substance. Naturally present in coffee, tea, and chocolate, it is added to popular beverages like soda pop. It is also marketed in tablet form to inhibit sleepiness (No-Doz[®] and Vivarin[®]), and many over-the-counter analgesic agents contain some caffeine (check the labels!). Strong coffee is the beverage with the highest drug content. After the beverages or tablets are consumed by mouth, the caffeine is rapidly absorbed. Its stimulant effect begins in minutes, peaks in about a half hour and may last for 2 to 3 hours. But people do develop tolerance and dependence to caffeine, so they may consume progressively more after repeated heavy use. The dependence is characterized by a true withdrawal syndrome that includes, among other things, headaches, muscles twitches, and general fatigue. People who drink a lot of coffee at work during the week sometimes experience headaches on the weekend, when they change their pattern of consumption. Although we think of caffeine as safe, recent medical studies have raised the possibility that it may be detrimental to reproductive and cardiovascular function. An elevated rate of spontaneous abortion has been noted in heavy caffeine drinkers, and males who consume five or more cups of coffee per day are 2.5 times more likely to have heart disease.

Steroids. The abuse of anabolic steroids for the purpose of muscle building grew significantly among the general population during the 1980s. The practice spread from Olympic and professional athletes to those in college and high school, and is controlled today only by strict policies, drug tests, and sanctions. An array of natural and synthetic male hormones are used, including testosterone itself, Dianabol[®] (oral), and DecaDurabolin[®] (injectable). They are typically used in cyclical patterns; that is, one to four months on and an equal period off. For athletes, these off periods may coincide with competitions, when the user will be tested. During the “on” period of the cycle, the user will “pyramid” the dose from low to high and down again; often, the user will “stack,” or add a second and even a third drug to the regimen. This pattern is intended to maximize the anabolic or muscle-building effects of the drugs, while minimizing androgenic (male hormone-related) effects and suppression of the pituitary gland.

It is quite clear that anabolic steroids are not “magic bullets”; they will only enhance muscle development under regular, intensive training conditions. Furthermore, this action is inseparable from the androgenic effects that produce male characteristics such as facial hair growth, voice-deepening, and so forth. Actually, while the female steroid user will become masculinized, the male user will become feminized—with testicular atrophy, decreased sperm production, and breast development. The reason for this is that the liver sees the large concentration of the male sex steroid on top of the body’s normal level and converts the excess to estrogen, the female hormone.

It has only recently come to light that the psychological impact of steroids can be profound, and that they may lead to a true chemical dependency state. High doses of steroids produce hyperarousal, aggressiveness, and even paranoia like the stimulants. The user can be dangerous to him- or herself and others in the toxic state, and if he or she stops using suddenly, will experience a withdrawal syndrome like that of the stimulants. The long-term user is also likely to have medical consequences such as liver disease, bone and joint degeneration, permanent hormonal dysfunction, sterility, and cancer.

“Look-Alikes.” Look-alikes are common legal drugs such as those found in cold tablets that are made to look like street drugs. For example, a large-dose caffeine tablet or a decongestant drug might be marketed as an amphetamine, or an antihistamine could be sold as a “downer” or

sedative. Obviously, the target for these substances is a uniquely naive group of people, usually young adolescents. The use of “look-alikes” is not without some danger; in fact, some of the substances can be downright hazardous because they have to be used at rather high doses to produce the desired psychogenic effects.

Psychotherapeutic Agents

While psychotherapeutic agents are not frequently misused, they are often encountered in chemical dependency settings for the treatment of mental disorders. A few decades ago, those with mental disorders were often relegated to life in a locked asylum. But the discovery of drugs that could relieve psychotic symptoms helped release many from institutions to a productive life.

Major disturbances of reality testing are referred to as **psychoses**. If the cause is known and involves a lesion in the brain, the psychosis is classified as **organic**. Among those in this class are the toxic psychoses due to alcohol, PCP, or heavy cocaine or amphetamine use. Much of the time, no organic cause of the psychosis can be identified, and so the condition is classified as a **functional** psychosis. Schizophrenia, a common form of functional psychosis, is characterized by delusions, hallucinations, and disordered behavior. Psychotic symptoms are managed with antipsychotic medications such as Thorazine[®], Mellaril[®], Prolixin[®], and Haldol[®]. It appears that abnormalities in neurotransmission play a role in most psychoses and these agents are all known to be dopamine receptor antagonists.

Affective disorders are severe positive and negative mood disturbances. Symptoms of elevated mood, or mania, include rapid speech, excessive motor activity, decreased need for sleep, and racing thoughts. **Depression**, on the other hand, is characterized by symptoms of fatigue, lethargy, loss of the ability to experience pleasure, and insomnia for a minimum of two weeks. Affective disorders that are primary depressive states may be treated with antidepressant medications such as Tofranil[®], Norpramin[®], Elavil[®], or Prozac[®]. Bipolar (manic-depressive) disorders are effectively managed with lithium in many cases. All of these medications appear to exert their action by intervening in the neurotransmitter process. Another important category of psychiatric problems, the primary **anxiety disorders**, includes phobias, panic disorders, obsessive-compulsive disorders, and post-traumatic stress disorders. These problems can sometimes be managed with medication.

It is essential to understand that a totally “drug-free” existence may not be possible for many people with mental illness. In fact, use of a psychotherapeutic medication may be appropriate for the rest of a person’s life. It is also important for the caregiver to realize that none of these psychotherapeutic drugs will “cure” a psychiatric disorder; they will only serve to control the symptoms and allow more normal function. If they do not receive adequate treatment, people with mental illness are at greatly enhanced risk to use street drugs in an attempt to “medicate” their primary mental disorder.

Drug Schedules

The U. S. Congress passed the Comprehensive Drug Abuse Prevention and Control Act of 1970 to regulate the manufacture and distribution of potentially harmful drugs. The law established five **schedules** or drug categories of psychotropic substances according to their potential for abuse, dependency, and existence of an acceptable medical use in this country (see Table 5.5). Penalties for illegal manufacture, distribution, or possession were assigned by drug category. Rules for physician prescribing also varied with drug category. Medications listed in the drug schedules are known as “controlled substances.”

At one time, Michigan led the nation in the diversion of prescription stimulants and opioids. Largely in response to this challenge, a triplicate prescription form was instituted for all Schedule II drugs in August 1989. This “Trip Scrip” creates a paper trail from the physician to the state monitors. When the doctor writes a prescription for a Schedule II drug, he or she does so on a form that makes an original and two copies. The doctor keeps one copy for his or her files and the patient gives the other two to the pharmacist, who retains one copy and forwards the last one to the state.

CATEGORY	MEDICAL USE	POTENTIAL FOR ABUSE	EXAMPLES
I	None	High	Heroin, Designer Drugs, Marijuana, LSD, Mescaline.
II	Yes	High	Cocaine, Methadone, Dextroamphetamine, Methylphenidate, Morphine, Codeine, Secobarbital.
III	Yes	Moderate	Glutethimide, Pentazocine, Tylenol with Codeine.
IV	Yes	Mild	Diazepam, Triazolam, Chlordiazepoxide, Alprazolam, Dextro-propoxyphene.
V	Yes	Low	Elixir Terpin Hydrate with Codeine, Lomotil, Imodium.

Table 5.5 Drug Schedules

Infectious Complications of Drug Use

There are many infectious consequences from using contaminated syringes and needles (“works”), and sharing the works may compound the problem further. Clearly, injecting directly into the veins is most hazardous, but injecting drugs like steroids into muscles, or heroin under the skin (skin popping) also carries significant risk for infection. Infections may be caused by a variety of agents including bacteria, fungi, or viruses. It may be local, such as a festering abscess near the site of the injection, or systemic, in which case the agent will travel through the bloodstream to attack a distant site such as the heart or brain.

Viral Infections

AIDS (Acquired Immuno-Deficiency Syndrome) is a fatal infection caused by the Human Immuno-Deficiency Virus (HIV). When AIDS was first diagnosed in 1981, much publicity was given to the fact that gay men were most likely to contract it, and many lay people believed that only this community would suffer the disease. There is evidence now that intravenous drug users were infected with HIV prior to that time. In any case, during the 1980s the proportion of AIDS cases associated with I.V. drug use increased. Women who use intravenous drugs (HIV-contaminated “works”) or have sexual contact with men who do and become pregnant may give birth to HIV-infected infants.

Viral hepatitis is another serious infection acquired by needle sharing during drug use. The most common type is hepatitis B, but hepatitis C is now being diagnosed. These viruses enter the body through the bloodstream, but appear to cause their major damage in the liver. As with AIDS, the person infected with one of these viruses may appear healthy and have no symptoms for months and even years. About one person in a thousand will die from hepatitis B. In this case, as in HIV, the proportion of hepatitis B infections is increasing among women. Unlike AIDS,

however, a vaccine is available to prevent hepatitis B and this has been added to the list of routine infant immunizations. Michigan law now requires the testing of pregnant women for HIV and hepatitis B.

Other Infections

Types and locations of bacterial and fungal infections are numerous and include small skin abscesses, infections of blood vessels, heart valves, bones, and other organs. When the infection involves a heart valve, replacement with an artificial valve may be required. Debates have arisen regarding the economic realities and ethical constraints in providing such expensive care for HIV-infected, intravenous drug users that require major heart surgery and even cardiac transplantation.

While many serious infections are the direct result of needle sharing among drug users, with the dramatic rise in crack use it has become apparent that any sexually transmittable disease (called STDs, such as gonorrhea and syphilis) including AIDS may result indirectly from drug and alcohol use. There are several explanations for this association of drug use and sexually transmitted diseases. Frequently, sexual activity is exchanged for drugs or money to purchase drugs, increasing the risk of acquiring an STD. Psychoactive drugs cloud decision-making ability and may lessen inhibitions such that sexual activity is more likely to be “unsafe.” Some drugs, like cocaine and amphetamines, are used for their “aphrodisiac” potential; that is, they may be used to enhance the sexual experience.

The Biological Component of Alcohol and Drug Problems

Neurochemical Basis of Addictive Behavior

Years before there was scientific evidence, the notion was introduced that dependence on alcohol is associated with real changes in brain function. Not only did the idea make sense to those with alcoholism, but it helped to define the problem as a “disease”—rather than a “crime”—which health and human services professionals could manage like any other serious health problem. It also served to reduce the stigma, so that recovering alcoholics could regain their self-respect.

For a long time, it was popular to refer to the biological component of the disorder as the “X” factor. The concept prompted scientists to search for neurochemical mechanisms of alcoholism, and much has been learned over the decades of concerted research since then. The investigations have been helped greatly by advances in our general understanding of brain function and by studies in clinical epidemiology and genetics. However, even the staunchest advocates for a biological basis of alcoholism still appreciate the importance of psychosocial and environmental factors in its development.

Evidence for heritability of alcoholism is the foundation for the neurobiological and disease concepts. The idea that some people have a genetic vulnerability or susceptibility is supported by a host of studies on families of alcoholics, identical and fraternal twins, and adoptees who were removed from their biologic-alcoholic home at birth. It should be noted that all of the data are retrospective, and so they cannot prove causality. Furthermore, some of the studies did not support the existence of a genetic link.

The positive studies on families of alcoholics showed that all members of the nuclear family had a probability of being alcoholic that was significantly greater than the general population. For

example, one extensive study in Germany found that the fathers of alcoholics had greater than a 50 percent chance of being alcoholic, while brothers had a probability of about 30 percent. Males in the general population are thought to have a prevalence rate closer to 5 percent.

While these investigations were informative, they did not illuminate the nature versus nurture issue very well, and so others were conducted on differences between twins reared in the same household. The evidence here was supportive in many cases; for example, a Swedish study of alcoholics who were twins found that 54 percent of the identical twins were also alcoholic, while only 28 percent of fraternal twins met the criteria. The elevated rate presumably is attributable to the stronger genetic link. To separate the nature and nurture influence more precisely, a study was conducted in Denmark on sons of alcoholic fathers who were removed from their biologic home at birth for adoption. When they achieved adulthood, 18 percent manifested a dependency on alcohol, compared to only 5 percent in a control population of male adoptees. Interestingly, other sons of the alcoholic fathers who were reared in the alcoholic home also showed about the same propensity to become alcoholic as their brothers (18 percent).

Studies since then have further refined our appreciation for the contribution of biology, including attempts to classify alcoholics based on the degree of genetic versus environmental influence. A proposal was made that two fundamental types of alcoholism exist. One, which is relatively mild, is expressed in both men and women, and is driven strongly by environmental factors. The second is seen most often in men, begins earlier in life, is associated with sociopathic behavior, and is largely determined by genetics. The possibility that multiple forms of alcoholism could exist is attractive and, although the specifics of the two-type hypothesis are somewhat controversial, most researchers believe that the idea of different forms of alcohol problems has merit.

Laboratory studies on animals have provided evidence for a biologic drive in the development of alcohol dependency. But what constitutes a good animal model of alcoholism? Early studies showed that some animals were much more sensitive to the sedative effects of alcohol than others. Later work has focused on the selective preference for drinking alcohol rather than water, and the ability to create genetically homogeneous strains of rats and mice with such preferences. The use of laboratory animals has enabled scientists to explore the possible reasons for “alcoholic behavior” at the level of brain chemistry. In fact, doing so has been most exciting for those interested in identifying the “X” factor.

Unfortunately, the excitement and desire to know may have trapped some people in beliefs that are not supported by current research. One example of this is the notion that “addiction” is due to an endorphin deficiency. Another is the idea that substances produced in the brain from alcohol metabolites, referred to as TIQs or THIQs (for tetrahydroisoquinolines), promote alcoholism. The latter is widely subscribed to because early research demonstrated that administration of TIQs to rats raised their preference for alcohol over water. Although both of these are attractive notions, the evidence to date does not fully support either proposal. For example, neither alcoholics nor sons of alcoholics seem to have unusual levels of either chemical in their bodies under normal conditions.

It is essential that those who are interested and work in the field of substance abuse retain a critical perspective on research. That is, they must listen equally to the evidence that challenges their beliefs as well as that which supports them. We cannot allow ourselves to be drawn into a dogmatic, unquestioning stance founded on belief alone. The very same scientists who have challenged the endorphin and TIQ theories continue their investigation of biological mechanisms

that could explain why certain people are more likely to become alcoholic than others.

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