SECTION ONE

CONCEPTS AND CLASSES OF DRUGS

1 Concepts of Drugs, Drug Use, Misuse, and Abuse

First the man took a drink, then the drink took a drink, then the drink took the man.

– Recovery movement proverb

This first chapter provides a discussion and clarification of various concepts relevant to drug abuse. Although we attempt clarification of many terms and concepts, it is important to note that there are different substantive distinctions and "fuzzy" boundaries between the concepts. For example, distinctions between drug misuse and abuse, and terms such as *street drugs* or *hard* or *soft drugs* are somewhat ambiguous and perhaps dependent on sociocultural contexts. The chapter begins by providing an overview of a definition of a drug, drug use, and drug action and then distinguishes drug use from misuse and provides terms used to refer to drugs that might be misused.

What Is a Drug and Drug Use?

A drug is a substance that can be taken into the human body and, once taken, alters some processes within the body. Drugs can be used in the diagnosis, prevention, or treatment of a disease. Some drugs are used to kill bacteria and help the body recover from infections. Some drugs assist in terminating headaches. Some drugs cross the blood–brain barrier and affect neurotransmitter function. The varieties of drugs that produce a direct or indirect effect on neurotransmitter function in the brain are of primary interest in this book.

Drugs are processed by the body in four steps, and these drugs also may have various effects on each other when used together. First, "administration" refers to how the drug enters the body (e.g., ingestion [swallowing], inhalation [smoking or vaporous], injection [intravenous, intramuscular, subcutaneous], or absorption [through skin or mucous membranes]). Most classes of drugs are used through several alternative methods. For example, marijuana may be smoked or swallowed. Methamphetamine may be smoked, swallowed, sniffed, or injected. Heroin may be sniffed, smoked, or injected. Depending on the method of administration, drugs generally exert their effects within an hour of intake (e.g., through ingestion) or within minutes or seconds of use (e.g., through injection).

Second, *distribution* refers to how efficiently a drug moves throughout the body. Distribution is influenced by the size of the various drug molecules and their solubility – protein, water, fat bound – among other factors. As a general rule, the rate of entry of a drug into the brain is determined by the fat solubility of the drug (Julien, 2005). The rate of entry is faster

if the fat solubility is greater. Conversely, highly ionized drugs, such as penicillin, penetrate the blood–brain barrier poorly.

Third, *metabolism* refers to the effects (action) of the drug. All drugs that might be misused or abused "feel good" in different ways; for example, the drug user may feel more alert, relaxed, or happy. Almost all drugs that are misused or abused affect mesolimbic reward pathways. However, each drug also may have specific target receptor sites in various brain structures and affect some different neurotransmitter pathways (see Chapter 4 for more detail on the brain). For example, there are concentrations of opioid receptors in the nucleus accumbens, whereas functionally important nicotinic receptors are found in the medial habenula, the superior colliculus, and the anteroventral thalamic and interpeduncular nuclei. Amphetamines mimic the effect of norepinephrine at its receptor sites and significantly impact dopaminergic activity in the mesolimbic reward circuitry. Benzodiazapines (e.g., Valium) are less likely to be a sole drug of abuse (though they are associated with withdrawal symptoms that may last 3 weeks), perhaps because they act primarily on the γ-aminobutyric acid (GABA) neurotransmitter system and not the dopaminergic system (Julien, 2005).

Drugs can have four different types of *interaction effects* when used together (Sussman & Ames, 2001). First, these effects may be additive (e.g., $1 + 1 = 2$; the effects of the drugs simply add together). Second, these effects may be synergic (e.g., $1 \times 1 = 5$; the effects become much, much stronger when the drugs are used together). Third, these effects may be potentiating (e.g., $0 + 1 = 2$; a drug may exert its effects only in conjunction with the use of another drug). Finally, these effects may be antagonistic (e.g., $1 - 1 = 0$; the effects of two or more drugs may cancel each other out).

Fourth, *elimination* refers to the breakdown and excretion of drugs from a body. Drugs are excreted in time primarily through sweating or urination, involving the skin and kidneys. Drugs have measurable and differential distribution and elimination half-lives (i.e., the amount of time it takes for half of the drug to reach sites of action and be eliminated from the body). For example, nicotine, when smoked in a cigarette, has a 9-minute distribution half-life (very fast) and a 2-hour elimination half-life. Marijuana, when smoked, has a similar distribution half-life, but it also has a 28- to 56-hour elimination half-life, which involves complex metabolic processes. Nicotine is metabolized mostly through the liver, whereas tetrahydrocannibinol (THC; the active ingredient of marijuana) may be stored and released slowly from various bodily organs. As a general rule, regular interval dosing can result in a relatively steady blood level concentration of the drug that is reached after approximately six elimination half-lives (see Julien, 2005).

Overdoses

Overdosing refers to taking enough of a drug such that functioning is grossly impaired and even survival may be jeopardized. Regarding drug use action, there are doses that produce the intended effect for a percentage of drug users (i.e., effective dose) and a dose that will kill the drug user (i.e., lethal dose). Different means of administration, time for distribution, time for action, time for elimination, and context factors may affect the effective-to-lethal dose relation. Overdosing often refers to reaching a near-fatal dose but not always; it may also mean loss of function such that special care is needed (Figure 1.1).

Overdosing tends to result in admissions to emergency rooms. About 31% of emergency room visits in the United States are due to the combined use of alcohol and other drugs.

Figure 1.1. Drug addiction.

Of those individuals admitted for overdoses, approximately 30% are admitted because of cocaine use, 18% because of marijuana use, 17% because of use of benzodiazepines, 17% because of use of narcotic drugs (14% because of heroin use), 6% because of amphetamine or methamphetamine use, and the remainder are admitted because of use of drugs such as Tylenol or Advil, selective serotonin reuptake inhibitors (SSRIs), and sedatives (see discussion in Levinthal, 2005).

An overdose is less likely to occur if a drug is used in the same location (known as "behavioral tolerance"). Physiological tolerance for a drug involves adjustment in bodily organs to the presence of the drug (metabolic tolerance; e.g., faster metabolism of alcohol in the liver with repeated alcohol intake) and neural adaptations to a drug (cellular tolerance; postsynaptic receptors may become less sensitive to a drug and presynaptic sites may manufacture less of an endogenous ligand [naturally occurring neurotransmitter] to compensate for the introduction of the drug that mimics its effects; for a drug that blocks transmission, an increased number of receptor sites may be manufactured or an increased amount of the endogenous ligand may be supplied), which also may effect the lethal dose. Of course, regular use of drugs can lead to physical dependence (i.e., physical and/or psychological withdrawal symptoms occur when drug use is stopped abruptly). Craving the effects a drug produces can be referred to as "psychological dependence," which is affected by neurobiological processes (e.g., associative learning processes; for discussion, see Weiss, 2005; for review, see Franken, 2003).

What Are Drugs of Misuse?

Drug use really implies only that one has taken a drug into the body and that the drug will go through the four steps of processing. However, the whole idea of problematic drug use stems

from the perception that drug use can lead to negative or undesired consequences. There are at least three terms that may be applied to use of a drug: use as appropriate, directed, or prescribed. Use as appropriate implies that there are no specific directions for frequency and quantity of use. However, one generally learns bounds of frequency and quantity of use that generally do not lead to undesirable consequences. For example, drinking one or two alcoholic drinks in a sitting over the course of several hours is unlikely to result in negative effects (e.g., obvious intoxication, depending on the context, or accidents). Use as directed connotes that there exists instruction on use frequency and quantity. Over-the-counter drugs provide such instructions. Finally, for drugs that require a physician's approval, a prescription is provided that also describes the active or safe frequency and quantity of use. If a drug is used inappropriately, not as directed, or not as prescribed, one might say that the drug is being misused. Of course, one might use too little of a drug for it to be effective. Arguably, that would be an example of drug misuse. However, most drugs that affect neurotransmitter function are said to be misused when they are used too often and/or at too high a quantity. Higher drug use may lead to danger (e.g., toxicity, intoxication), whereas lower than recommended use probably will not.

The U.S. Drug Enforcement Administration (DEA) was created in 1973 to enforce the provisions of the Controlled Substances Act of 1970 (http://www.usdoj.gov/dea/index.htm). The DEA shares concurrent jurisdiction with the U.S. Federal Bureau of Investigation regarding narcotics enforcement matters. The Controlled Substances Act provides the authority and administrative structure to establish scheduling of drugs to avoid hazards to public safety, monitoring of use of different drugs, including manufacture, distribution and labeling, and offences and penalties for violations of the rules the DEA establishes. Some rules also extend to drug paraphernalia. These drug schedules with examples are shown in Table 1.1.

The types of drugs of misuse that this text focuses on are those that are relatively likely to cause negative consequences if used too often or at too high a quantity, that generally tend to readily cross the blood–brain barrier and affect neurotransmitter function, and that in some way achieve a function desired by the drug user. Desired functions of these drugs tend to be described as alterations in arousal, affect, or sensory perception/cognitive experience. Drugs that alter arousal, affect, or sensory-cognitive experience often are referred to by one or more terms.

Terms Used to Refer to Drugs That Might Be Misused

Drugs that affect the central nervous system (CNS) can be classified by the substance from which they are derived, such as *opiates* or *opioids*, or by their effects on the human nervous system, such as *stimulants*, *hallucinogenic drugs*, or *psychotropic drugs* (Julien, 2005). Although there might be overlap in the drugs that each of these terms encompasses, these terms are relatively unbiased. (Certainly, for example, there are exceptions that might be defined across categories; ecstasy may be defined alternatively as a stimulant or a hallucinogen or both.) There are several typologies of classes of drugs that are not purely based on physical qualities of drugs. We briefly discuss five widely applied terms: *street drugs*, *hard or soft drugs*, *illicit drugs*, *designer drugs*, and *club drugs*. We discuss the meaning of these terms and consider the usefulness of such variable drug terminology (see Sussman & Huver, 2006).

Table 1.1. DEA drug use schedules

Schedule and definition	Examples of drugs
Schedule 1: drug has no current accepted medical use, high potential for abuse	2,5-dimethoxyamphetamine, cathinone (constituent of "Khat" plant), GHB, heroin, LSD, marijuana, ecstasy, mescaline, methaqualone, morphine methylbromide, peyote, psilocybin
Schedule 2: drug has current accepted medical use, high potential for abuse	Amobarbital, amphetamine, cocaine, codeine, Demerol, methadone, methamphetamine (speed), morphine, nembutal, opium, oxycodone, phencyclidine, preludin, Ritalin, Seconal
Schedule 3: drug has current accepted medical use, medium potential for abuse	Amobarbital/ephedrine capsules, anabolic steroids, ketamine, Marinol, Paragoric, Tylenol with codeine
Schedule 4: drug has current accepted medical use, low potential for abuse	Ativan, Dalmane, Darvon, Librium, Miltown, Placidyl, Redux, Rohypnol, Valium, Xanax
Schedule 5: drug has current accepted medical use, lowest potential for abuse	Lomotil, Kapectolin PG, Motofen, Robitussin AC (liquid suspensions)

Street Drugs

The term *street drugs* is contained within the Web site of the National Institute on Drug Abuse, has its own heading within the OVID Medline Search Engine, and is commonly displayed in print (e.g., Bartlett & Steele, 2004) and on Web sites (e.g., http://www.streetdrugs.org). With such widespread use, one might expect that this term is well understood and consensually used in one way. However, this is not the case. A literature search conducted by Sussman and Huver (2006) of the use of the term *street drugs* in the popular and scientific literatures resulted in a consensus on seven definitions. The seven different definitions of the term *street drug* based on these sources of information were as follows: (1) all drugs used recreationally, (2) a term implicating violence or other crime (sold illegally; involvement of "pushers"), (3) "street terms" (slang) for drugs that may reveal a subcultural language or indicate drug use combinations (e.g., http://www.whitehousedrugpolicy.gov/streetterms), (4) drugs manufactured unprofessionally (not in official labs), (5) impure drugs, (6) reflecting a street or poor lifestyle, or (7) physically dangerous drugs. These terms are not mutually exhaustive and exclusive.

Recreational drugs are those used for nonmedicinal purposes, in particular, for fun or leisure. This label provides a very wide umbrella as a definition. Several medication and drug guides tend to refer to all recreational drugs as being street drugs (e.g., www.allpsych.com/drugs.html). Many people do use drugs as a form of recreation. However, some people may use drugs, such as methamphetamine, to drive long distances or to lose weight rather than to achieve pleasure (a utilitarian motive; Sussman & Ames, 2001). Yet, many people might refer to methamphetamine as being a prototypical street drug (www.cbc.ca/news/background/drugs/crystalmeth.html) that is used for many purposes (Sussman, Dent, & Stacy, 1999). Thus, it is not clear to what extent this definition is useful.

Illicit drugs are obtained and sold illegally by dealers or sellers on the street (e.g., http://library.thinkquest.org/TQ0310171/street_drugs.htm; Reif, 1999; Smart, Adlaf, & Walsh, 1992). Drug companies, in particular, tend to refer to illicit drugs as being street drugs.

Figure 1.2. Methamphetamine laboratory.

However, there are many exceptions to this definition of the term. In Dutch legislation, possession of cannabis is tolerated (up to 30 g, equivalent to almost 1 oz). Yet cannabis is as likely to be referred to as a street drug in the Netherlands as it is in the United States, where federal laws do not permit its possession, growth, sale, or use (Sussman & Ames, 2001). Some may refer to nicotine and alcohol as street drugs, which is at odds with the current definition but could be consistent with the first (recreational) definition (http://allpsych.com/drugs.html). Glue is legal, but it may be used as a type of inhalant and is commonly referred to as a street drug (http://library.thinkquest.org/TQ0310171/street_drugs.htm).

Many drugs have *street terms* that are applied to them. For example, methamphetamine often is referred to as "speed" and cocaine has been referred to as "Charlie" (http://www.whitehousedrugpolicy.gov/streetterms). Interestingly, street drug terms may serve as valuable diagnostic cues to the mental state and drug history of the drug user (Johnson, Michels, & Davis, 1991). Although street terms often refer to street drugs, it is possible that some street drugs are not labeled with street terms. If so, this definition is flawed. Of course, if all drugs have slang terms, then arguably this definition could refer to any and all drugs.

Drugs manufactured in home laboratories or not by professional companies have been labeled street drugs (e.g., Marshall, 2003). For example, consistent with this definition, "moonshine" (a home-brewed alcoholic beverage) would be an alcohol street drug but Jack Daniels (http://www.jackdaniels.com/age.aspx) would not. However, the "professionalism" with which some drugs that are considered street drugs are produced may make one doubt the value of this definition. For instance, although ecstasy (3,4-methylenedioxymethamphetamine [MDMA]) is manufactured in clandestine laboratories, these laboratories are operated by highly trained staff and can hardly be called "unprofessional," and analyses of MDMA indicate purity of 80% to 90% (Parrott, 2004) (Figure 1.2).

Alternatively, one may mean "not licensed" when referring to "unprofessionally manufactured." Unlicensed manufacturing of a drug would seem to suggest an illicit type of street drug. Conversely, it is interesting to note that 100,000 deaths per year occur from adverse

drug reactions to pharmaceutical (licensed) drugs, a number five times greater than the number of deaths caused by unlicensed street drugs, according to Bartlett and Steele (2004). Moreover, many pharmaceutical drugs are sold on the street. Some people might think of these drugs as street drugs as well (http://www.usdoj.gov/dea/pubs/abuse/4-narc.htm), and many street drugs are "cut" with pharmaceutical drugs.

Impure drugs indicates impurity, adulteration, or dilution in the manufacturing of the drug (e.g., http://www.drugscope.org.uk/resources/faqs/). *Impurities* are substances present in the drug as a natural result of how it was made rather than substances that are deliberately added. *Adulterants* are drugs that are added to mimic or enhance the effects of the drug being offered. For example, sometimes amphetamines have been cut with caffeine or ephedrine. *Diluents* are compounds such as sugars or baking soda that are used to "bulk out" the deal (make more money per assumed quantity of drug). Heroin may vary in purity from 30% to 80% and is often cut with other opium alkaloids, sugars, and sometimes diazepam. Although emergency room physicians treat many patients who have used illegal drugs, little is known about the relative toxicities of the abused drug versus the drug additives. Current thinking and research suggests that additives play only a minor role in the majority of emergencies (Shesser, Jotte, & Olshaker, 1991). This definition may overlap in meaning with the definitions of "unprofessional" or "illicit."

Street drugs sometimes are implicated as representative of a *street or lower class lifestyle* or as definitive of the drug user, such as street youth (e.g., Ginzler & Cochran, 2003) or homeless drug users (e.g., Deren et al., 2003). In this sense, drug use is integrated into "street life." When one lives "on the street," one may live in, for example, empty buildings ("squats"), on a friend's couch, in a car, or under a bridge (Sussman et al., 1999). Survival may include drug dealing as a means of income or as a means to cope with exposure to the elements (weather) and vulnerability to crime. Drugs used by "street people" vary but may include alcohol, heroin, methamphetamine, crack, cannabis, or glue sniffing. Drugs may be chosen based either on their use as a means of barter or income or because of their relatively low cost. However, many of these types of street drugs have been used at raves or other party or clublike venues composed of relatively wealthy individuals (www.clubdrugs.org). Thus, this definition may provide some descriptive (or literary) value but does not apply to many drug users (although some of these drugs, if abused consistently, may eventually lead individuals into a street life [e.g., see http://www.pbs.org/wgbh/pages/frontline/meth/]).

Sometimes street drugs directly imply *dangerous drugs* (e.g., Cheng, 1999). In this sense, many drugs may be referred to as street drugs because most are facilitative or predictive of accidents or psychotic symptoms and several are predictive of depressed mood, cardiovascular disease, or digestive/excretory difficulties (Sussman & Ames, 2001). Still, street drugs may vary in danger. For example, some people would refer to hallucinogens as street drugs, yet they are perhaps among the relative safe types (even though they are listed in Schedule 1 of the DEA scheme). As with the previous definition, this one has a potential descriptive function and applies to some street drugs but not to the full range of street drugs.

Some of these definitions are used to keep the public image of one entity (e.g., the pharmaceutical industry and the alcoholic beverage industry) apart and "cleaner" than drugs or drug distribution systems that do not fall under their domain of control. Some definitions are used to refer to relative danger. Yet, other definitions appear to imply the

improper or nonlegitimized use of a drug. We might say that a street drug may be defined as any drug that is misused; that is, any drug that may have dangerous consequences and is considered improper to use either intrinsically or in the social context within which it is used.

Hard and Soft Drugs

A distinction is often made between hard and soft drugs. *Hard drugs*, such as heroin, methamphetamine, and crack/cocaine, generally are considered more dangerous and can lead to dependence. The most abused hard drug in the world today is methamphetamine. There are approximately 1.5 million methamphetamine addicts in the United States (see http://www.pbs.org/wgbh/pages/frontline/meth/). Purportedly, the use of hard drugs may result in more immediate negative consequences than that of soft drugs because of their high dependence potential, which may result in increased compulsive drug taking and the perpetration of income-generating crimes as a means of supporting drug use. Hallucinogens also would be considered hard drugs, in spite of the fact that they have no addiction potential. Thus, this supposed difference between hard and soft drugs is not universal across drug types.

The term *soft drugs* is often used to refer to drugs such as cannabis, alcohol, and nicotine, of which use allegedly does not result in as severe a degree of physical dependence and may appear less dangerous in connotation (Jonnes, 1996; Sussman, Rohrbach, Skara, & Dent, 2004). There are at least two problems with this distinction. First, soft drugs are not less dangerous than hard drugs per se. Long-term use of cannabis has deteriorating effects on the nervous system, causes damage to the lining of the lungs, and can cause dependence and addiction (Sussman & Ames, 2001; Sussman et al., 1996). Generally considered as soft drugs – perhaps mistakenly because of their wide availability – alcohol and nicotine are both highly addictive and dangerous. Alcohol is the most widely used drug in Western society (and the world). Approximately 14 million Americans meet the criteria for alcohol abuse or alcoholism and heavy drinking is related to a number of cancers and liver and heart damage. Alcohol is estimated to cause 2 million deaths per year worldwide (Sussman & Ames, 2001). Nicotine is highly addictive and tobacco use is the single largest preventable cause of death in the world (Sussman & Ames, 2001). Tobacco use is associated with approximately 30% of all cancer deaths annually in the United States.

Second, the distinction between hard and soft drugs and corresponding legislation are not internationally established. In the Netherlands, legislation for hard drugs (defined as drugs of an unacceptable risk) differs from that of soft drugs (e.g., hemp products). The Dutch employ a policy of tolerance with respect to soft drugs. In some municipalities, soft drugs may be sold in so-called coffee shops, with a maximum supply of 500 g. Strictly speaking, possession of either hard or soft drugs is illegal, but one will not be prosecuted for possessing half a gram of hard drugs or 30 g of soft drugs for personal use. Arguably, the terms *hard* and *soft drugs* are useful as a means of grouping specific drugs into categories, and the highest prevalence drugs are the ones that tend to get labeled as soft drugs, but this terminology is not well descriptive of the effects or consequences of the drugs.

Illicit Drugs

The term *illicit drugs* is typically used to set illegal drugs apart from legal drugs or pharmaceuticals. It is apparent from the above discussion on hard and soft drugs that the

legality (or the quality of the illegality) of a specific set of drug categories is not universal. As another example, in political and medical arenas in the United States, there is debate about legalizing cannabis for medicinal purposes. Cannabis can relieve side effects of chemotherapy and help control seizures in patients suffering from epilepsy. Furthermore, it can be beneficial for patients with glaucoma, migraine headaches, acquired immunodeficiency syndrome (AIDS) wasting syndrome, multiple sclerosis, spinal cord injuries, arthritis, and chronic pain (Gurley, Aranow, & Katz, 1998; Smith, 1998). Currently, medical marijuana use is legal in some states (e.g., California), whereas it is illegal on a federal level (http://www.drugpolicy.org/statebystate/).

In addition to the debate about legalizing cannabis, in the light of the previously mentioned deteriorating and addictive effects of alcohol and nicotine, one can argue that it is regrettable that alcohol and nicotine are licit drugs. This term is appropriate and precise as a label for what legislation entails within a specific geopolitical and historical context.

Designer Drugs

Designer drugs are synthetic drugs that are equivalent to an existing drug in chemical structure but for a minor modification (Sussman & Ames, 2001). Scientists refer to designer drugs as *substance analogs*. The new drug (child) will have the same or very similar pharmacological effects as the original drug (parent). For example, ecstasy is one of the most widely used designer drugs, with a chemical structure similar to that of methamphetamine (Christophersen, 2000). It has been put forward that designer drugs were created to bypass legislation of the U.S. Drug Enforcement Administration (Jerrard, 1990). In the past, drugs were not illegal until they were classified as controlled substances by law. In 1986, the Controlled Substances Act was modified to ban all variations of controlled substances, hence banning all designer drugs. This term seems fairly precise, although because of the continuing production of designer drugs, it is impossible to comprehensively list drugs under this label.

Club Drugs

The term *club drugs* is a generic term for drugs used in clubs or bars or at trance parties or raves, mostly by adolescents or emerging adults. Often, youth will dance or gather together all night at these venues. Arguably, such dances permit youth to be involved in a social recreational activity, be involved in a shared youth ritual, and experience a symbolic transition to adulthood. However, drug use often is inextricably associated with these situations. Club drugs, also referred to as *party drugs*, are most commonly taken orally in tablet form and include ecstasy, Rohypnol (the "date rape" drug), γ-hydroxybutyric acid (GHB), ketamine, and lysergic acid diethylamide (LSD), among others (http://www.clubdrugs.org/). There is no comprehensive list of what drugs are considered club drugs, although their location of use is suggested as being in group clublike situations. Certainly, many club drugs are used outside of party situations, such as in youths' bedrooms (Sussman & Ames, 2001). This term appears to have the same difficulties in clarity as does the term *street drugs* (see Table 1.2).

Search for Clarification of Words Used to Describe Drugs That Can Be Misused

Terms described by Sussman and Huver (2006) included *street drugs* (and several variants), *hard* or *soft drugs*, *illicit drugs*, *designer drugs*, and *club drugs*. Although *illicit drugs* are defined