

# CHAPTER 11. SUBSTANCE-RELATED DISORDERS

## 11.1 INTRODUCTION AND OVERVIEW

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Whether a society views substance use primarily as a moral or a legal problem, when it creates difficulties for the user or ceases to be entirely volitional it becomes the concern of all the helping professions, including psychiatry. This chapter on substance-related disorders is made up of separate sections organized around the syndromes engendered by the use of each of the major groups of pharmacological agents that are commonly misused (abused). This section deals with issues that are common across categories of drugs—the nomenclature and diagnostic schemes of the fourth edition of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) and the 10th revision of *International Classification of Diseases and Related Health Problems* (ICD-10), the history of substance use and dependence, epidemiology, and the etiological factors and treatment principles that appear to be common to these syndromes.

**General Organization of DSM-IV and ICD-10** DSM-IV includes two broad categories of substance-related disorders: substance use disorders (substance dependence and substance abuse), and a diverse grouping of substance-induced disorders (such as intoxication, withdrawal, psychotic disorder, and mood disorders). Thus, in DSM-IV the topic of substance-related disorders goes beyond substance dependence and abuse and closely related problems to include a wide variety of adverse reactions not only to substances of abuse, but also to medications and toxins. The medications associated with substance-induced disorders range from anesthetics to over-the-counter medications and include such diverse drug categories as anticholinergics, antidepressants, anticonvulsants, antimicrobial drugs, antihypertensive agents, corticosteroids, antiparkinson agents, chemotherapeutic agents, nonsteroidal anti-inflammatory drugs, and disulfiram (Antabuse). In addition, several categories of substance-induced disorders can be associated with a wide range of nonmedicinal toxic materials, ranging from heavy metals and industrial solvents to insecticides and household cleaning agents. DSM-IV groups the

diagnostic criteria for substance dependence, abuse, intoxication, hallucinogen persisting perception disorder, and withdrawal syndromes in a section titled “Substance-Related Disorders,” whereas the other substance-related disorders (e.g., substance-induced mood disorders and substance-induced delusional disorders) are described in the sections covering the disorders that they most closely resemble phenomenologically ([Table 11.1-1](#)).

Substance-induced disorders cause a variety of symptoms that are characteristic of other mental disorders. To facilitate differential diagnosis, the text and criteria for these other substance-induced disorders are included in the sections of DSM-IV and this textbook with disorders with which they share phenomenology.

Substance-induced delirium (see Chapter 10) is included in the “Delirium, Dementia, and Amnesic and Other Cognitive Disorders” section.

Substance-induced persisting dementia (see Chapter 10) is included in the “Delirium, Dementia, and Amnesic and Other Cognitive Disorders” section.

Substance-induced persisting amnesic disorder (see Chapter 10) is included in the “Delirium, Dementia, and Amnesic and Other Cognitive Disorders” section.

Substance-induced psychotic disorder (see Section 13.3) is included in the “Schizophrenia and Other Psychotic Disorders” section. (In DSM-III-R, these disorders were classified as organic hallucinosis and organic delusional disorder.)

Substance-induced mood disorder (see Section 14.6) is included in the “Mood Disorders” section.

Substance-induced anxiety disorder (see Section 15.6) is included in the “Anxiety Disorders” section.

Substance-induced sexual dysfunction (see Section 19.1a) is included in the “Sexual and Gender Identity Disorders” section.

Substance-induced sleep disorder (see Chapter 21) is included in the “Sleep Disorders” section.

In addition, hallucinogen persisting perception disorder (flashbacks) (see Section 11.7) is included under hallucinogen-related disorder.

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**Table 11.1-1** Substance-Induced Mental Disorders Included Elsewhere in the Textbook

The DSM-IV section dealing with substance dependence and substance abuse presents descriptions of the clinical phenomena associated with the use of 11 designated classes of pharmacological agents: alcohol, amphetamines or similarly acting agents; caffeine; cannabis; cocaine; hallucinogens; inhalants; nicotine; opioids; phencyclidine (PCP) or similar agents; and sedatives, hypnotics, and anxiolytics. A residual twelfth category includes a variety of agents, such as anabolic steroids and nitrous oxide, that are not in the 11 designated classes.

ICD-10 considers the disorders due to psychoactive substance use within the confines of an alphanumeric system that allows only nine categories of pharmacological agents, with one residual category to cover both multiple drug use and use of psychoactive substances not included in the nine designated categories. DSM-IV and ICD-10 categorize substances comparably, with the following exceptions. Caffeine and PCP are considered distinct categories in DSM-IV; whereas in ICD-10, problems related to caffeine are included in the category of other stimulants such as amphetamine, and phencyclidine must be included with hallucinogens or in the residual category. Also, ICD-10 has a special category for abuse of non-dependence-producing substances ([Table 11.1-2](#)). Specifically mentioned are antidepressants, analgesics, antacids, vitamins, and steroids or hormones.

**Table 11.1-2** ICD-10 Diagnostic Criteria for Abuse of Non-Dependence-Producing Substances

In certain cases, the use of psychoactive drugs may be associated with the development of dependence, which is a state of physical and psychological dependence on the drug. This state is characterized by a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state.

# DEFINITIONS AND DIAGNOSIS

**Substance Dependence** The revised third edition of DSM (DSM-III-R), DSM-IV, and ICD-10 formulations for substance abuse and dependence closely follow the concepts and terminology developed in 1980 by an International Working Group sponsored by the World Health Organization (WHO) and the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) of the United States, which defined substance dependence as follows:

A syndrome manifested by a behavioral pattern in which the use of a given psychoactive drug, or class of drugs, is given a much higher priority than other behaviors that once had higher value. The term “syndrome” is taken to mean no more than a clustering of phenomena so that not all the components need always be present or not always present with the same intensity. . . . The dependence syndrome is not absolute, but is a quantitative phenomenon that exists in different degrees. The intensity of the syndrome is measured by the behaviors that are elicited in relation to using the drug and by the other behaviors that are secondary to drug use. . . . No sharp cut-off point can be identified for distinguishing drug dependence from non-dependent but recurrent drug use. At the extreme, the dependence syndrome is associated with “compulsive drug-using behavior.”

That central notion is continued in DSM-IV, which states:

The essential feature of dependence is a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues substance use despite significant substance-related problems.

The central notion in ICD-10 is virtually the same:

a cluster of behavioural, cognitive, and physiological phenomena that develop after repeated substance use and typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state.

The DSM-IV and ICD-10 criteria for substance dependence are presented in [Table 11.1-3](#) and [Table 11.1-4](#). DSM-IV uses seven criteria to describe a generic concept of dependence that applies across 11 classes of pharmacological agents. ICD-10 requires that three of six criteria be met and also applies across classes of drugs.

**Table 11.1-3 DSM-IV Diagnostic Criteria for Substance Dependence**

A polythetic syndrome consisting of substance use, resulting in a clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the 12-month period:

1. Tolerance, as evidenced by one of the following:
  - (a) a need for markedly increased amounts of the substance to achieve the desired effect, or
  - (b) persistently diminished effects with continued use of the same amount of the substance.
2. Withdrawal, as manifested by one of the following:
  - (a) a characteristic withdrawal syndrome, or
  - (b) the use of a substance to relieve or avoid withdrawal symptoms.
3. The substance is taken in larger amounts or over a longer period than was intended.
4. There is a persistent desire or unsuccessful effort to cut down or stop substance use.
5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
6. Important social, occupational, or recreational activities are given up or reduced because of substance use.
7. The substance use continues despite knowledge of having a persistent or recurrent physical or psychological problem that is clearly or likely to be caused or exacerbated by the substance.

**Note:** 1. A 12-month period is required for criteria 1 and 2 in general. Withdrawal is not required if criterion 1 or 2 is present.

**Substances:** Alcohol, amphetamine, barbiturate, benzodiazepine, cocaine, heroin, marijuana, opiates, phencyclidine, sedative-hypnotic, stimulant, and tobacco.

**Source:** American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition*. Washington, DC: Author.

**Table 11.1-3 DSM-IV Diagnostic Criteria for Substance Dependence**

**Table 11.1-4 ICD-10 Diagnostic Criteria for Mental and Behavioral Disorders Due to Psychoactive Substance Use**

A polythetic syndrome consisting of substance use, resulting in a clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the 12-month period:

1. Tolerance, as evidenced by one of the following:
  - (a) a need for markedly increased amounts of the substance to achieve the desired effect, or
  - (b) persistently diminished effects with continued use of the same amount of the substance.
2. Withdrawal, as manifested by one of the following:
  - (a) a characteristic withdrawal syndrome, or
  - (b) the use of a substance to relieve or avoid withdrawal symptoms.
3. The substance is taken in larger amounts or over a longer period than was intended.
4. There is a persistent desire or unsuccessful effort to cut down or stop substance use.
5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
6. Important social, occupational, or recreational activities are given up or reduced because of substance use.

**Note:** 1. A 12-month period is required for criteria 1 and 2 in general. Withdrawal is not required if criterion 1 or 2 is present.

**Substances:** Alcohol, amphetamine, barbiturate, benzodiazepine, cocaine, heroin, marijuana, opiates, phencyclidine, sedative-hypnotic, stimulant, and tobacco.

**Source:** World Health Organization. (1989). *International Classification of Diseases, 10th Edition*. Geneva: Author.

**Table 11.1-4 ICD-10 Diagnostic Criteria for Mental and Behavioral Disorders Due to Psychoactive Substance Use**

DSM-IV and ICD-10 use a polythetic syndrome definition, in which no one specific criterion is required so long as three or more are present. However, DSM-IV asks the clinician to specify whether physiological dependence (evidence of criterion 1, tolerance, or criterion 2, withdrawal) is present or absent. Evidence indicates that physiological dependence is associated with a more severe form of the disorder.

In addition to requiring the clustering of three criteria in a 12-month period, DSM-IV includes a few other qualifications. It states specifically that the diagnosis of dependence can be applied to every class of substances except caffeine. That point is admittedly controversial, and some researchers believe, on the basis of the same DSM-IV generic criteria, that caffeine produces a distinct form of dependence, although it is relatively benign for most persons.

Some persons use several categories of drugs and are clearly drug dependent, according to the generic criteria, but it may not be possible to ascertain whether they are dependent on any one specific class of drugs. When at least three groups of substances are involved, DSM-IV calls the condition polysubstance

dependence ([Table 11.1-5](#)). DSM-IV also makes provision for classifying substance-related disorders that cannot be classified in any of the previous categories (e.g., nitrous oxide, anticholinergics, anabolic-androgenic steroids) or for an initial diagnosis of dependence or abuse when the specific substance is not known. A similar residual category is included in ICD-10, but steroids are given a distinct code. The DSM-IV diagnostic criteria for other (or unknown) substance-related disorders are listed in [Table 11.1-6](#).

This diagnosis is reserved for behavior during the same 12-month period in which the person was repeatedly using at least three groups of substances (not including caffeine and nicotine), but no single substance predominated. Further, during this period, the dependence criteria were met for substances as a group but not for any specific substance.

**Table 11.1-5** DSM-IV Diagnostic Criteria for Polysubstance Dependence

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**Table 11.1-6** DSM-IV Diagnostic Criteria for Other (or Unknown) Substance-Related Disorders

**Patterns of Remission and Course Specifiers** DSM-IV and ICD-10 deal with remission by providing distinct modifying terms that can be appended to a diagnosis of substance dependence. DSM-IV terms are more varied than those of ICD-10 ([Table 11.1-7](#)). The DSM-IV course specifiers require a period of at least 1 month, after a period of active dependence, during which no criteria of dependence are present. If a patient has not met any criteria for dependence for at least 1 month but for less than 12 months, the course specifier to use is early full remission. If the period during which no criteria of dependence are met exceeds 12 months, the specifier of sustained full remission can be used. If the full criteria for dependence or abuse have not been met for less than a year, but one or more criteria have been present, early partial remission may be used. If the period exceeds 12 months, sustained partial remission may be used. Two additional remission specifiers should be used when appropriate: “on agonist therapy (includes partial agonists)” and “in a controlled environment.” Several factors, such as duration of remission and duration of period of dependence, must be considered in deciding that a person has fully recovered and no longer warrants a diagnosis of dependence. The modifiers that describe the course of dependence in ICD-10 are similar, but specific criteria for selecting them are not provided.



**Substance Withdrawal** *Substance withdrawal*, as used in DSM-IV, is a diagnostic term rather than a technical term. Thus minor symptoms that technically are due to cessation of substance use (e.g., the coffee drinker's early morning precoffee lethargy or minor headache) would not by themselves fulfill the criteria for substance withdrawal, unless they are accompanied by a maladaptive behavior change and cause some clinically significant distress or impairment in social, occupational, or other important area of functioning. DSM-IV does not recognize withdrawal from caffeine, cannabis, or PCP, although some observers believe that specific signs and symptoms can be observed when those agents are abruptly discontinued after a period of heavy use. ICD-10 does describe a cannabinoid withdrawal state.

Withdrawal is commonly, but not invariably, associated with substance dependence. The signs and symptoms of withdrawal vary with the specific class of drug. In general, the severity of withdrawal is related to the amount of substance used and the duration and patterns of use. Withdrawal is seen not only when substance use is stopped but also when reduced use of a substance or a change in metabolism results in lower tissue levels. The DSM-IV generic criteria for substance withdrawal are shown in [Table 11.1-9](#); the ICD-10 general criteria are shown in [Table 11.1-4](#). Specific diagnostic criteria for withdrawal from each category of drugs, to be used when the general criteria have been met, are also provided.

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- A. The development of a substance-specific syndrome due to the cessation of (or reduction in) substance use that has been heavy and prolonged.
  - B. The substance-specific syndrome causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
  - C. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.
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**Table 11.1-9** DSM-IV Diagnostic Criteria for Substance Withdrawal

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**Substance Intoxication** Substance intoxication is defined more narrowly in DSM-IV than it might be in a pharmacology text. A variety of substances may produce unwanted physiological or psychological effects that could be construed as substance intoxication effects (e.g., excessive sleepiness following use of an antihistamine), but unless the symptoms are associated with maladaptive behavior, the effects would not constitute substance-induced intoxication as defined in DSM-IV. Furthermore, whether a behavioral effect is maladaptive depends on the social and environmental context in which it occurs. If alcohol makes a person unusually sociable, a bit garrulous, and a little uncoordinated at a family celebration this is probably not maladaptive drinking behavior, the same behavior at a formal business meeting probably is. Similarly, ICD-10 specifies that intoxication must produce disturbances in the level of consciousness, cognition, perception, affect, or behavior that are of clinical importance. However, it requests clinicians to further specify which of several common complications of intoxication (e.g., trauma, delirium, convulsions) are also present. The DSM-IV general criteria for substance intoxication are shown in [Table 11.1-10](#). In addition, ICD-10 provides specific sets of diagnostic criteria for each of the drug categories and for multiple drugs, to be used once the generic criteria for intoxication have been

met. Also shown are the additional specifiers for complications of intoxication ([Table 11.1-4](#)).

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- A. The development of a reversible substance-specific syndrome due to recent ingestion of (or exposure to) a substance. **Note:** Different substances may produce similar or identical syndromes.
  - B. Clinically significant maladaptive behavioral or psychological changes that are due to the effect of the substance on the central nervous system (e.g., belligerence, mood lability, cognitive impairment, impaired judgment, impaired social or occupational functioning) and develop during or shortly after use of the substance.
  - C. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.
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**Table 11.1-10** DSM-IV Diagnostic Criteria for Substance Intoxication

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**Substance-Induced Disorders** In addition to dependence, abuse, intoxication, and withdrawal, the use of certain psychoactive drugs can induce syndromes that used to be called organic mental disorders. To avoid implying that other psychiatric disorders do not have an organic basis, DSM-IV designates these syndromes substance-induced disorders and recognizes the following categories: substance intoxication, substance withdrawal, substance-induced withdrawal delirium, substance-induced intoxication delirium, substance-induced persisting dementia, substance-induced persisting amnesic disorder, substance-induced mood disorder, substance-induced anxiety disorder, substance-induced psychotic disorder, substance-induced sexual dysfunction, and substance-induced sleep disorder.

In recording a diagnosis of a substance-related disorder, the clinician should indicate the specific agent causing the disorder, if known, rather than the broad drug category; that is, substance-induced intoxication, pentobarbital (Nembutal) rather than substance-induced intoxication, sedative-hypnotics. However, the diagnostic code should be selected from the list of classes of substances provided in sets of criteria for the substance-induced disorder being recorded. For each of the substance-induced disorders (other than intoxication and withdrawal), the clinician is asked to specify whether the onset was during intoxication or during withdrawal. Thus, a specific substance-induced disorder would have a three-part name delineating (1) the specific substance, (2) the context (whether the disorder occurred during intoxication or during withdrawal or occurs or persists beyond those stages), and (3) the phenomenological presentation (e.g., diazepam [Valium]-induced anxiety disorder with onset during withdrawal).

[Table 11.1-11](#) shows the various disorders induced by the major categories of substances recognized by DSM-IV and indicates which disorders are seen during intoxication and during withdrawal. Although they are not included specifically in the table, anabolic-adrenergic steroids can also induce psychotic mood, anxiety, and sleep and sexual disorders, and their withdrawal can also be associated with mood and sleep disorders. ICD-10 has a distinctly different approach to recording these drug-related disorders. With the first and second digits after the letter committed to designating the drug category, additional psychiatric syndromes are indicated by the use of the third and fourth digits. For example, persistent mood disorder associated with hallucinogens is designated F16.72. For the diagnosis to be made, the mood disorder would need to meet the criteria listed for mood (affective) disorders.



	Depen- dence	Abuse	With- out depen- dence	With depen- dence	With depen- dence	With depen- dence	With depen- dence	With depen- dence	With depen- dence	With depen- dence	With depen- dence	With depen- dence	With depen- dence	With depen- dence
Alcohol	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Dephensives	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Cocaine	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Cannabis	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Ecstasy	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Heroin	1	1	1	1	1	1	1	1	1	1	1	1	1	1
MDA	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PCP	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Stimulants	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Other	1	1	1	1	1	1	1	1	1	1	1	1	1	1

**Table 11.1-11 DSM-IV Diagnoses Associated With Class of Substances**

**Evolving Terminology** The terminology used to describe the substance-related disorders has been repeatedly revised as concepts about the nature of drug-using behavior have evolved. In the 1980 third edition of the DSM (DSM-III) drug use disorders were divided into two major categories, drug abuse and drug dependence, and specific criteria for diagnosis were given. In DSM-III-R, adopted in 1987, the two categories were retained, but the diagnostic criteria were modified. Further revisions were made for DSM-IV, which adopted the terms “substance abuse” and “substance dependence,” probably to eliminate the use of the more cumbersome term “alcohol and drug dependence including tobacco.” For similar reasons, ICD-10 adopted the term “psychoactive substance dependence.”

In much of the world literature on drug dependence, the term “dependence” is used to convey two distinct ideas: (1) a behavioral syndrome and (2) physical or physiological dependence. *Physiological dependence* can be defined as an alteration in neural systems that is manifested by tolerance and the appearance of withdrawal phenomena when a chronically administered drug is discontinued or displaced from its receptor. Because the dual use of the word causes confusion, the 1980 ADAMHA-WHO working group recommended restricting use of the term “dependence” to describe the behavioral syndrome and substituting the term “neuroadaptation” for physical dependence. Such a substitution would have emphasized several points. First, the continued use of many drugs, including tricyclic antidepressants and  $\beta$ -adrenergic receptor antagonists, causes neuroadaptive changes followed by withdrawal phenomena, but not by drug-seeking behavior, on their discontinuation. Second, neuroadaptive changes begin with the first dose of an opioid or sedative drug, and therefore, such changes in and of themselves are not a sufficient cause (or definition) of drug dependence as a behavioral syndrome.

**Why Use “Addiction”?** The words “addict” and “addiction” often have pejorative connotations; they are also frequently trivialized and used to refer to ordinary activities, such as exercising and solving crossword puzzles. However, the term “addiction” continues to have the core connotation of decreased control, and some chapters in this book have retained such terms as “opioid addict” because they are less awkward to use than terms such as “severely opioid-dependent person” when referring to persons who are dependent on drugs to a severe degree. Here the word “dependent,” unmodified, is used to mean behaviorally dependent. The term “physiological dependence” or “physical dependence” is used to refer to the physiological changes that result in withdrawal symptoms when drugs are discontinued.

## COMPARATIVE NOSOLOGY

**DSM-IV and ICD-10** The generic concept of dependence is virtually identical in DSM-IV and ICD-10. By requiring the clinician to specify whether tolerance and withdrawal are present, DSM-IV appears to recognize a special significance for tolerance and physiological dependence. Some data indicate that among alcoholics the presence of physical dependence and, to a lesser degree, tolerance is associated with a more severe variety of the syndrome. In practice, however, requiring evidence of these criteria would not substantially reduce the number of cases meeting the criteria for dependence in most drug categories, with the exception of hallucinogens, a class of drugs for which DSM-IV does not list physiological dependence as a criterion. There is generally a high level of agreement between DSM-IV and ICD-10 for making a diagnosis of dependence, although the descriptions of the criteria for determining the presence and severity of the syndrome differ. They both require that three elements of the syndrome have been present in a 12-month period. The DSM-IV categorization of drug classes differs somewhat from the one used by ICD-10, which, constrained by a new alphanumeric system, uses only nine drug categories by including caffeine with amphetamine-like stimulants and PCP with other psychoactive agents.

The word “abuse” is also commonly used in ways that differ significantly from the definitions developed for use in DSM-IV. In popular and legislative contexts *drug abuse* means any use of an illicit substance or any nonprescribed use of a drug intended as a medicine, as well as the harmful or excessive use of legally available substances, such as alcohol and tobacco.

Despite the reliability of DSM-IV and ICD-10 criteria for dependence in many European and Anglo-American cultures, several criteria (e.g., narrowing of drinking repertoire, time spent obtaining the drug, and even tolerance for the drug) have posed difficulties in other cultures, especially when dealing with alcohol. Tolerance is often understood when applied to drugs, but not to alcohol; in some cultures, holding one's liquor is a sign of manhood. Clinicians are more likely to make a diagnosis of drug dependence than alcohol dependence even when behavioral signs are comparable. In several cultures, little or no distinction is recognized between use, abuse, and harmful use of illicit drugs.

**Other Perspectives** The criteria for diagnosis in DSM-IV and ICD-10 were developed from what is essentially a biopsychosocial model of substance dependence. In such a model multiple factors—genetic, psychological, sociological, and pharmacological—contribute to the observed clinical syndromes. Such apparent unanimity about drug dependence should not obscure the existence of dissenting perspectives, which take several forms. In one the biopsychosocial model is accused of giving too much weight to biological factors and too little recognition to the notion of human will and responsibility, of medicalizing deviant behavior for the benefit of treatment professionals, and of creating universal exculpation for all those who fail to live up to reasonable societal expectations. But some professionals have implicitly criticized the same biopsychosocial model for not giving sufficient weight to the ideas that substance dependence is a specific primary disease (i.e., not a symptom of other psychiatric difficulties), that those who develop the disease have no control over their intake of certain

substances, and that denial of the presence of a problem is a major characteristic of the disease.

Concepts about substance dependence can be arrayed along several dimensions that are not entirely independent or orthogonal: broad versus narrow, disease versus learned behavior, and social versus medical. The narrow concept of substance dependence accepts as disorders those maladaptive behaviors associated primarily, if not exclusively, with the ingestion of substances generally accepted as pharmacological agents. Compulsive eating, gambling, running, hair pulling, and repetitive excessive sexual activities are not included among the dependence disorders, although those problems may share certain features that resemble a decreased ability to choose and are sometimes ameliorated by participation in support groups founded on principles similar to those of Alcoholics Anonymous (AA). A broad approach would create a superclass of disorders that would include a number of such behaviors not involving pharmacological agents.

At the disease end of the disease-versus-behavioral syndrome dimension is a belief that dependence is not a learned behavior that can be modified or ameliorated with relearning but is a primary disorder caused by an interaction between a substance and a person with some genetic vulnerability and that only total abstinence can arrest the progression of the disease. The medical-versus-social dimension typically describes a range of views on how best to respond to problems with substances, rather than differences about the essential nature of the problems. The medical model stresses issues of assessment—treatment, planning, and record keeping—and sometimes treatment that can be rendered only by those with professional training (not necessarily physicians). The social model emphasizes the importance of social supports and integrating the person with a problem into a network of recovering persons who can offer continuing support. The assessment and recording of progress and outcome as generally practiced by credentialed professionals is minimized.

## **HISTORY**

The most commonly abused drugs have been in use for hundreds, if not thousands, of years. For example, opium has been used for medicinal purposes for at least 3500 years, references to cannabis (marijuana) as medicinal can be found in ancient Chinese herbals, and wine is mentioned frequently in the Bible. The indigenous people of the Western Hemisphere were smoking tobacco and chewing coca leaves generations before the arrival of the Spaniards. Some of the problems caused by alcohol and other drugs, such as drunkenness, are described in the Bible and in the writings of the ancient Greeks and Romans. As new and more concentrated forms of drugs were discovered or invented or new routes of administering them were developed, new problems related to their use emerged. For instance, when cheap gin was introduced into England in the eighteenth century, the alcohol-related problems that emerged were considered more serious than those associated with beer and wine. Although opium smoking was a major problem in Asia in the eighteenth and nineteenth centuries, new problems were seen after morphine, the most active opium alkaloid, was isolated in 1806. Morphine was subject to misuse by injection from the late nineteenth century on, and intravenous morphine and heroin use began to spread in the early part of the twentieth century. Tobacco use and its associated problems did not become widespread until the nineteenth century, when new methods of curing the leaves produced a

mild smoking tobacco and cigarettes were introduced, which made common the practice of inhaling tobacco smoke deeply into the lungs. By the early twentieth century, cigarette smoking was a popular practice.

**Medicalizing Excessive Drug Use** In 1810 Benjamin Rush, who is often credited as the first American physician to suggest that excessive use of alcohol was a disease rather than exclusively a moral defect, proposed the establishment of a sober house; in 1835 Samuel Woodward, a pioneer in the establishment of asylums for the insane, advocated similar asylums for inebriates. Contemporaneous with those early moves to involve medicine in dealing with excessive alcohol use was the emergence of the temperance movement and the Washingtonians—groups of reformed drunkards concerned with helping others to adopt and maintain sobriety. In the process the Washingtonians developed many of the principles of self-help that were rediscovered by AA almost a century later. When the ideas of voluntarism and self-help as exemplified by Washingtonian societies failed to eliminate the problem of drunkenness, physicians began to debate more seriously the idea of coerced treatment in inebriate asylums supported by public funds. In 1870 advocates of the approach established the American Association for the Cure of Inebriates (AACI), dedicated to setting up hospitals for such persons, conducting research, and teaching medical students and physicians how to treat inebriety. At first those physicians who believed in a more spiritual, voluntary approach to the problem (neo-Washingtonians) were part of the AACI, but gradually the more somatically oriented factions, which advocated medically supervised asylums (and compulsory treatment when needed), gained ascendancy. Furthermore, the focus of concern was no longer limited to those who abused alcohol. Thomas Crothers, the secretary of AACI, saw inebriate asylums as places to treat all those who used any variety of intoxicant or narcotic to excess. However, very few publicly supported inebriate asylums ever opened.

**Early Attitudes** The closing years of the nineteenth century saw growing concern about the excessive and inappropriate use of drugs, including alcohol and tobacco as well as opiates and cocaine. First isolated from the coca leaf in 1860, cocaine came into widespread use in 1885 when pharmaceutical companies began selling it in the United States and Europe. In 1884 Sigmund Freud had published a review of the potential therapeutic uses of cocaine. Some medical authorities in the United States shared his enthusiasm, and cocaine was recommended by the Hay Fever Association as a remedy for that malady. Within a few years, however, it was recognized that cocaine had the capacity to induce toxic psychosis as well as gain control over behavior. It was also recognized that long-term opiate use had dependence-inducing effects. Nevertheless, in the United States, until the beginning of the twentieth century, both the opium alkaloids and cocaine were still found in patent medicines that were sold over the counter for a wide variety of indications, and their labeling often did not reveal their contents.

Although achieving long-term cure of morphinism was reported to be exceedingly difficult, until the turn of the twentieth century neither the public nor the medical profession saw the habitual user of opium or morphine as invariably suffering from a moral deficit. Those who had developed the morphine habit represented the entire socioeconomic spectrum, with women outnumbering men by about two to one. Various political and literary figures were known to use opiates but to lead otherwise productive and exemplary lives. However, cocaine use and the morphine habit were also common among gamblers, petty thieves, prostitutes, and other disreputable members of society. Persons with emotional problems

and those who had formerly used alcohol to excess were probably also overrepresented among opium users, since it was not unusual at the time for physicians to prescribe opiates to control emotional problems and alcoholism.

The problem of using the same institution for treatment of drug users who had antisocial tendencies and those who led more conventional lives was as vexing to early advocates of medical treatment as it is to present-day practitioners. Many proponents of inebriate asylums did not want to take responsibility for persons who had frequent or serious encounters with the police because it was thought that such persons would make it impossible to create an atmosphere conducive to recovery. Partly to cope with the problem, even some of the proponents of a disease model of inebriety maintained the distinction between “inebriety the disease” and “intemperance the vice.”

**Early Control Efforts: Evolution of the Criminal Model** By the late 1890s the public and the medical community were no longer indifferent to drug use and habituation. In 1893 the Anti-Saloon League was founded, reinvigorating a temperance movement that advocated the total prohibition of alcohol. Medical texts in England, Europe, and the United States contained descriptions of morphinism, theories of its causation, and recommendations for withdrawal and postwithdrawal treatment. Some texts also described problems of cocaineism. Medical authorities in the United States cautioned against overly liberal prescribing of cocaine and opiates by physicians and expressed great concern about the presence of those drugs in unlabeled proprietary over-the-counter medicines. State laws were passed aimed at controlling the sale of opiates and cocaine, especially in patent medicines. In 1900 the cocaine in Coca-Cola was replaced by caffeine.

Partly to support the efforts of the Chinese government to control opium use in China, representatives of the United States government led the movement to negotiate an international treaty to control traffic in opium, cocaine, and related drugs. The first such treaty was signed in The Hague in 1912. Negotiators from the United States were also interested in the international control of cannabis but could not get other nations to view the substance as sufficiently problematic to warrant it. (Such control was achieved in 1925 at the Second Geneva Convention.) The Hague Convention required the signatories to pass domestic legislation controlling opiates and cocaine. The Harrison Act of 1914, the first federal legislation to regulate opiates and cocaine, was designed to restrict access to opiates and cocaine to doctors, dentists, pharmacists, and legitimate importers and manufacturers and brought the United States into compliance with the convention.

State regulations concerning the sale of opiates and cocaine, the introduction of aspirin and the barbiturates, and the Pure Food and Drug Act of 1906, which required labeling of patent medicines, were already having an impact on the use of opiates in medicine when the Harrison Act was passed in 1914. Although many medical and political leaders in the United States believed that much of the problem of drug dependence resulted from careless prescribing by physicians, the Harrison Act was not originally intended to interfere with the legitimate practice of medicine or to cause special hardship for those already dependent on opiates. For several years after the Harrison Act was passed, a few cities operated clinics that prescribed morphine to persons with established morphine habits. Most of those dependent on opiates before the Harrison Act became abstinent within a few years after it was passed,

although generally not as a result of treatment at the clinics.

**Fluctuating Attitudes** Major changes had taken place in American attitudes and practices by the 1920s. The Eighteenth Amendment to the U.S. Constitution, which prohibited the sale of alcohol, became law in 1920 and radically changed drinking behavior in the United States. Within a year after alcohol prohibition was enacted, 14 states also passed cigarette prohibition laws. Even less popular than alcohol prohibition, those laws were all repealed by 1927, and by the mid-1920s Americans were smoking 80 billion cigarettes a year. However, cocaine use, so prevalent at the turn of the century, was no longer widespread.

Disillusioned by the reluctance of morphine addicts at clinics to detoxify and by repeated relapses among those who did, doctors began to recommend (not for the first time) compulsory treatment with confinement until cure. As the new laws curtailed legitimate supplies of opiates, an illicit traffic developed to provide them to morphine addicts who could not or would not use the clinics. Increasingly, the drug sold was heroin, which had been introduced for medical use in 1898 but was quickly found by drug users to have effects quite similar to those of morphine. Many who patronized the illicit traffickers and used the clinics had histories of delinquency and criminal activity, and eventually that subgroup came to predominate. Reformers, moralists, and the popular press found in the opiate habit, and in the reputation of those who continued to use morphine, proof of the evils inherent in those drugs.

Negative publicity, lurid stories, medical disillusionment, and pressure from law enforcement agents combined to label the morphine clinics as medical folly and brought about their closing, the last in 1923. At the same time a series of United States Supreme Court decisions implied that prescribing even small amounts of opiates or cocaine to an addict for treatment of addiction was not proper medical practice and was thus an illegal sale of narcotic drugs. Several physicians were imprisoned, and numerous others were tried, reprimanded, or otherwise harassed. By the early 1920s persons addicted to opiates were not welcome in doctor's offices, and they were often refused treatment at hospitals. *Dope addict* and *dope fiend* had become common terms, and the average layperson, as well as some otherwise well-informed members of the medical profession, appeared to believe that the opiate molecule was inherently evil. In the late 1930s cannabis acquired a similar reputation, and in 1937 the United States Congress passed legislation prescribing criminal penalties for its use, sale, or possession. Alcohol prohibition had been repealed in 1933.

**New Drug Problems** The first of the barbiturate sedatives, barbital, was introduced into clinical medicine in 1903, followed over the next 30 years by scores of congeners that differed primarily in their duration of action. Within a few years after the introduction of each new compound, the first case reports of abuse, dependence, and withdrawal appeared in the medical journals, a pattern that was repeated with the nonbarbiturate sedatives, such as glutethimide (Doriden), ethchlorvynol (Placidyl), and meprobamate (Miltown) in the 1950s.

Amphetamine, first synthesized in 1887, was put into clinical use in 1932 as a drug to shrink mucous membranes. By 1935 its central stimulant effects had been recognized and found useful for treating

narcolepsy, and dozens of other suggested uses soon followed. Reports that amphetamine was being used as a euphoriant began to appear in the late 1930s, but the full significance of its abuse potential was not appreciated until the post-World War II epidemic of intravenous methamphetamine addiction in Japan. That epidemic, precipitated by the sale of surplus methamphetamine tablets intended for combat troops, involved millions of people. Other amphetamine-like drugs, which have also been subject to abuse, were introduced during the 1950s and early 1960s.

The psychological effects of mescaline were already known and written about at the end of the 19th century. However, public concern about hallucinogens did not reach a high level until the 1960s, when the use of a newly discovered and exceedingly potent compound, lysergic acid diethylamide (LSD), evolved from experimentation by a few college students to more widespread use by even younger people. Phencyclidine, a general anesthetic developed in the 1950s, also became a drug of abuse in the 1970s.

Despite repeated reports of abuse and dependence associated with barbiturates, barbiturate-like sedatives, and amphetamines and related stimulants, and in spite of concerns about experimentation with LSD and related hallucinogens, there were no federal criminal sanctions related to these drugs until 1964, when authority for their control was assigned to the Food and Drug Administration (FDA). In contrast, in the 1950s, concern about heroin addiction had led to ever harsher criminal penalties for its sale or possession. Although law enforcement efforts aimed at controlling heroin use were increased, both the number of new heroin addicts and the crime rates continued to rise throughout the late 1960s. At about that time there was also a sharp increase in the nonmedical use of other substances, such as cannabis and LSD, and a major epidemic of amphetamine abuse and dependence. In addition to amphetamines diverted from medical channels, supplies came from clandestine laboratories. Drug use, especially cannabis, became linked to antiestablishment attitudes, politics, and lifestyles.

**Evolving Treatment Approaches** Treatment for substance-related problems underwent several dramatic changes during the twentieth century. The large specialized asylums that were advocated in the nineteenth century never materialized. Toward the end of the nineteenth century physicians were primarily concerned about how to manage withdrawal syndromes and whether or not longer compulsory treatment was needed. With the advent of prohibition, the impetus to develop treatments for alcoholism declined sharply. Interest in treating opioid-dependent patients also declined as physicians became discouraged by their tendency to relapse after being detoxified and as opioid use and dependence came to be seen more as criminal behaviors than as medical disorders. A few private sanitoriums continued to provide treatment for opioid dependence. By 1930, as drug-addicted prisoners began to fill the penitentiaries, the federal government saw the need to establish two hospitals, at Lexington, Kentucky, and Fort Worth, Texas, to provide treatment for that population and also to conduct research on the problem of opiate addiction. Treatment of barbiturate and amphetamine dependence took place largely in the mainstream of medical practice and in state hospitals, but there was no consensus on what constituted effective posthospital care.

In the mid-1930s two recovering alcoholics rediscovered the principles of the Washingtonians, added some new principles, and initiated the self-help movement now known as AA. By the 1950s, this

movement had begun to inspire analogous self-help efforts among other types of substance abusers.

The situation changed again in the early 1960s. With new outbreaks of heroin use by young people and increasing crime, the federal government and individual states attempted to respond to the problem. California initiated a civil commitment program for addicts under the administrative control of the Department of Corrections; New York City reopened Riverside Hospital to treat juvenile heroin addicts. The first follow-up studies of patients treated at the federal hospital at Lexington revealed exceedingly high rates of relapse after treatment. Both the medical community and the general public demanded new ideas and solutions, including a reconsideration of providing addicts with legitimate opioids through medical channels.

From 1958 to 1967 several major new approaches to treating opioid dependence were developed. Synanon, the prototype therapeutic community, was started in California in 1958 and was soon replicated in New York with the establishment of Daytop Village and Phoenix House. Vincent Dole and Marie Nyswander showed that maintaining selected long-term heroin addicts on large daily doses of methadone (Dolophine) was effective in reducing crime and heroin use. Several research groups demonstrated that heroin addicts would voluntarily try treatment with narcotic antagonists. In the mid-1960s, New York State and the federal government legislated civil commitment programs modeled after the program in California, with an initial period of prolonged institutional care as a key element. Although many treatment programs initiated in the early 1960s continued to focus on the treatment of opioid dependence, others, especially the therapeutic communities, viewed all nonmedical drug use as stemming from similar defects in character structure and offered a generic approach to treating drug dependence.

**Alcohol and Nicotine** In the 1950s clinicians at Wilmar State Hospital in Minnesota developed a treatment program for alcoholism built on a synthesis of the medical model and the experiences of recovering alcohol abusers using the 12-step principles of AA. That treatment approach was refined and expanded at the Johnson Institute and Hazelden Foundation, also in Minnesota. The modified programs, widely adopted by others, are often referred to as 28-day programs, 12-step programs, or the Minnesota model. In the early 1970s the effort to recognize alcoholism as a disease gained momentum, and the decision of medical insurance carriers to provide coverage for detoxification and inpatient treatment fueled an unprecedented growth of private-sector facilities offering treatment for alcoholism. Almost without exception, they were residential programs using the Minnesota model. The decriminalization of public intoxication spurred a parallel increase in alcohol treatment programs supported by the public sector.

The Surgeon General's Report of 1964 linked cigarette smoking to lung cancer and concluded that tobacco smoking was a form of dependence, although not an addiction. By the 1970s, tobacco dependence was more widely accepted as a valid clinical entity, and various treatments for it were developed. By the late 1980s, as smoking was becoming socially unacceptable, many buildings were declared smoke free, smoking was banned on most airplane flights and in many hospitals, and pharmaceutical companies began to market new products for delivering nicotine (e.g., nicotine chewing gum and transdermal patches) as aids for smoking cessation. By the late 1990s the tobacco companies



were negotiating settlements in multiple civil law suits by states and by individuals who had been injured by their tobacco use, and Congress had unsuccessfully debated major tax increases on tobacco and regulation by the FDA.

**Two-Tiered System** When the cocaine epidemic of the early 1980s struck the middle class, much of the large, private-sector system for treating alcoholism evolved into chemical dependency units offering similar treatments to persons with alcohol problems and those with other varieties of substance dependence. By 1990 it was estimated that more than 8000 recognized programs existed that deal with alcoholism and other substance dependence. The treatment methods used varied widely in terms of settings, costs, philosophical underpinnings, and populations served. New categories of substance-abuse professionals had emerged, and psychiatrists who once had considered the problems to be a low-status area successfully lobbied for the creation of a recognized subspecialty in addiction psychiatry. Treatment capacity was described as a two-tiered system with private and public sectors, in which the private sector served 40 percent of the population but received 60 percent of the total expenditures for treatment. One response to the escalating cost of substance abuse services among those with private medical insurance was the rise of a managed care industry created to control costs on behalf of employers who pay for health insurance, generally by severely limiting the length of stay in hospital settings. Managed care, by refusing to recognize (and pay for) the medical necessity of inpatient treatment for most cases of substance dependence, largely dismantled the rest of the “28-day” inpatient alcohol and drug treatment programs that had serviced patients with insurance. By the mid-1990s managed care principles were routine in the public sector as well, and little remained of the two-tiered system.

**Legislation and National Strategies** In 1969 Congress recognized the need to give greater attention to the problem of alcoholism and established the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in the National Institute of Mental Health (NIMH). In 1970 legislation was passed, reorganizing the jumble of drug regulatory statutes that had evolved since the passage of the Harrison Act, increasing the resources for controlling the availability of illicit drugs, and assigning the task of enforcement to a new agency, the Drug Enforcement Agency (DEA), which incorporated elements of the FDA and the Bureau of Narcotic and Dangerous Drugs. All drugs subject to special controls were included in one of several categories of the Controlled Substances Act.

In 1971 when United States troops in Vietnam were reported to be using heroin heavily, the Special Action Office for Drug Abuse Prevention (SAODAP) was established in the Executive Office of the President to coordinate government activities and policies relating to drug abuse and to develop and publish an overall national drug strategy. The creation of that office and the associated legislation marked a turning point in United States policy. The notion that opioid dependence was an incurable disorder, which justified the harshest of penalties in the name of prevention, was superseded by a policy that recognized that a substantial proportion of opioid addicts (as well as those with other varieties of drug dependence) could eventually reenter the mainstream of society. New commitments were made to basic research, epidemiology, development of new treatment methods, and evaluation of existing treatment approaches. Methadone maintenance was moved, by executive fiat, from the legal limbo of experimental status to a category that recognized its legitimacy. Regulations intended to prevent

inappropriate prescribing of opioids were developed. Federal support for the expansion of community treatment programs was also greatly increased. By 1973 about 200,000 substance users, most of them opioid users, were in treatment in community programs. Those programs were repeatedly and intensively evaluated over the subsequent decade. The legislation that established SAODAP also provided the legislative framework for the National Institute on Drug Abuse (NIDA) in the Department of Health, Education and Welfare (HEW). When it was established in 1974 NIDA became the lead agency for implementing federal policy on treatment, research, and prevention.

By the early 1980s treatment for opioid dependence was generally accepted to have demonstrable impact. However, for most patients in treatment programs, the primary drugs of abuse were no longer opioids but more typically, cannabis, stimulants, or sedatives. During the early and mid-1970s some groups had argued for the decriminalization or legalization of cannabis. The arguments lost much of their force when it was found that in 1979 almost 10 percent of high school students were using cannabis on a daily basis. In response to what they perceived as tolerance toward cannabis use, a number of parents' organizations were formed that were committed to making all drug use unacceptable. Those groups forced NIDA to review and remove from all its publications any statements that could be interpreted as tolerating drug use. This decreased tolerance for drug use grew in parallel with a more general conservative shift in public attitudes. For example, in the 1970s the public and the courts had rejected the use of urine testing as a means of detecting drug use in an effort to interrupt the heroin epidemic; but starting in 1986, federal employees were required by presidential order to undergo such tests. Similar drug testing was encouraged in private industry, giving rise to new industries for detecting the presence of drugs, interpreting test results, and placing drug users in treatment.

By the 1970s it was obvious that the major drug abuse problems in the United States in terms of social and economic impact and health costs were alcoholism and tobacco dependence. Although the Surgeon General's Report of 1964 linking cigarettes to cancer had not produced any dramatic decrease in smoking, the rate of increase in cigarette consumption among men had begun to level out. In 1988 the *Surgeon General's report on the Health Consequences of Smoking* officially defined tobacco dependence as analogous to other varieties of drug dependence. In 1994 the FDA held hearings on the appropriateness of regulating the nicotine in tobacco as an addictive drug. Shortly thereafter, with backing from the president, the FDA assumed authority to regulate advertising of tobacco products; the White House lobbied Congress to pass legislation that would limit advertising and raise federal taxes on tobacco.

In the early 1980s rising demand for the treatment of cocaine dependence, the sudden cocaine-induced deaths of several prominent athletes, and concern about the spread of the human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) among intravenous drug users led to the Anti-Drug Abuse Act of 1986, which authorized the government to spend nearly \$4 billion to intensify efforts against drugs and drug abuse. Although most of that money was allocated to law enforcement activities, federal resources for the treatment of drug dependence and research were also substantially increased. Recognizing the need to do more to prevent drug dependence and provide more treatment, the federal government created a series of offices that by 1992 evolved into the Substance Abuse and Mental Health Services Administration (SAMHSA), with several constituent centers, including the

Center for Substance Abuse Treatment (CSAT) and the Center for Substance Abuse Prevention (CSAP). The 1988 Anti-Drug Abuse Act and the 1989 Emergency Supplemental Appropriation created the Office of National Drug Control Policy (ONDCP) in the White House. While still devoting more than two thirds of federal resources available for drug problems to controlling drug supply, this legislation also increased funding for treatment and prevention.

Critics of the emphasis on supply-control gained public attention when they were supported by several prominent conservative writers and economists and garnered the financial support of several well-endowed foundations. While the more thoughtful of these critics have stopped calling for outright legalization of drugs, they have called for greater emphasis on reducing the harm related to drug use by medically prescribing heroin and other psychoactive drugs and more support for needle-exchange programs. Despite some evidence suggesting that availability of sterile needles can reduce HIV transmission, the federal government continues to ban the use of federal money for such programs.

## **EPIDEMIOLOGY**

A number of distinct methods have been developed to gauge the extent and medical consequences of substance use, abuse, and dependence in the United States. The major recurring surveillance instrument are the National Household Survey on Drug Abuse (Household Survey), the Drug Abuse Warning Network (DAWN), Arrestee Drug Abuse Monitoring System (ADAM—formerly known as the Drug Use Forecasting [DUF] program), and the Monitoring the Future Study (better known as the High School Survey). In addition, data on street availability and purity of illicit drugs, drug seizures, and arrests for drug offenses are collected nationally from the DEA and the Federal Bureau of Investigation (FBI) and locally from municipal police departments. Each of these data sources has strengths and limitations. For example, the Household Survey annually interviews a representative sample of individuals age 12 and older living in households, college dormitories, homeless shelters, and rooming houses. It oversamples minority populations and certain large urban areas, and focuses in detail on drug-using behaviors. It does not interview military personnel or individuals who are living on the street or in institutions (jails or hospitals). It does not attempt to determine whether respondents need treatment or meet formal criteria for drug dependence. In addition, some respondents may be reluctant to admit to certain types of drug use.

The ADAM system interviews, and obtains anonymous urine specimens from, a sample of arrestees in moderate-size cities in the United States. By design, persons charged with sale or possession of drugs cannot make up more than 25 percent of the sample. Although it does not depend on self-reports to measure use, the ADAM results cannot be easily extrapolated to a national population, and the information that can be derived from a single urine test is limited.

In 1989 the DAWN system, which obtains data on drug-related episodes from medical examiners and hospital emergency rooms, was modified so that the reporting emergency rooms constitute a representative sample of such facilities in the continental United States. The DAWN data provide useful information on trends in the morbidity associated with various illicit drugs; but these data need to be

interpreted with caution because the DAWN system reports only episodes in which a drug is part of the presenting clinical picture. For example, a rising number of emergency room episodes associated with heroin could mean that more heroin users with AIDS-related problems are seeking primary medical care, rather than that more individuals are using heroin. Similarly, reports by medical examiners of more violent deaths associated with cocaine may signal an escalation of competition among drug dealers, rather than more people using cocaine. The analytical methods do not reveal the nature of the linkage between drug use and the presenting problem, which drugs (if any) played a causal role in the episode, or whether the user was a novice or a chronic user.

The High School Survey has obtained information each year since 1975 from forms returned anonymously by high school seniors. It now includes former seniors now in college and students in the eighth and tenth grades. Although the survey depends on self-report, the trend information it provides is exceedingly useful.

In addition to the recurring data-gathering efforts, important epidemiological information is available from two national studies that systematically interviewed representative samples of the population and used DSM-III or DSM-III-R criteria to develop estimates of current and lifetime prevalence of psychiatric disorders, including substance abuse and substance dependence. These studies are the NIMH Epidemiological Catchment Area (ECA) Study, conducted in the early 1980s, and the National Comorbidity Survey (NCS), conducted between 1990 and 1992. The ECA interviews in five areas of the United States included individuals in institutions (mental hospitals, jails, nursing homes, etc.) and used DSM-III criteria to develop estimates of prevalence. The NCS interviews of a nationally representative sample of noninstitutionalized people used DSM-III-R criteria. Although the ECA was conducted before the cocaine epidemic of the 1980s crested and criteria for diagnosis used were altered somewhat in DSM-III-R, it nevertheless remains a landmark study of the extent of drug abuse and dependence and co-occurring psychiatric disorders.

The ECA study found that 16.7 percent of the U.S. population ages 18 and older met the DSM-III criteria for a lifetime diagnosis of either abuse or dependence on some substance, with 13.8 percent meeting the criteria for an alcohol-related disorder, and 6.2 percent meeting the criteria for abuse or dependence of a drug other than alcohol or tobacco. The NCS found a 26.6 percent lifetime prevalence of substance abuse and dependence, substantially higher than the 16.7 percent found in the ECA. Some of this is probably due to questions in the NCS about prescription drugs that were posed when a patient reported symptoms of dependence, and on differences in criteria (DSM-III versus DSM-III-R). However, there may also have been real increases in prevalence. For illegal drugs and the nonmedical use of prescription drugs, the lifetime rate for dependence in the NCS was 7.9 percent, a figure much closer to the 6.2 percent found for such drugs in the ECA study. The NCS found a 12-month prevalence estimate for any addictive disorder (including dependence and abuse) of 8.2 percent; 4.5 percent alcohol dependence, and 1.8 percent drug dependence. Except for tobacco, men are far more likely than women to use drugs and alcohol and are correspondingly more likely to develop dependence. For example, lifetime and 12-month prevalence rates of alcohol dependence are 20.1 percent and 6.6 percent for men, but only 8.2 percent and 2.2 percent for women.

Among the major achievements of the NCS analyses were the findings on the proportions of people who had used drugs at any time in their lives (*lifetime users*) who became dependent (overall and for each drug category); the demographic factors that predicted use, dependence, and persistence of dependence; and the prevalence and significance of multiple psychiatric diagnoses. Dependence cannot develop if a drug is never used; thus, presenting data on the prevalence of dependence in the population as whole, including those who never used, can obscure the likelihood of dependence developing among those who do use a particular drug. In the NCS, prevalence of lifetime dependence on the broad range of illicit and nonprescribed medications was 14.7 percent, with male users only slightly more likely (16.4 percent) than female users (12.6 percent) to develop dependence. In a similar analysis of the 12-month prevalence of dependence on these drugs, the rate for the population as a whole was 1.8 percent. However, the 12-month prevalence was 3.5 percent for those who had used any of these drugs at any time in their lives; 10.3 percent for those who had used them in the past 12 months, and 23.8 percent among those who had a lifetime history of dependence. The likelihood of being drug dependent within the past 12 months, given a lifetime history of dependence, was similar for men (24.9 percent) and women (22.2 percent). Lower educational and lower income levels predicted a lifetime history of dependence (odds ratios greater than 2), but race, ethnicity, or living in an urban environment did not. There were also differences in the likelihood that users of a particular drug would become dependent on it. For example, for heroin, the lifetime opioid dependence rate was 23 percent; for tobacco, 32 percent; for cocaine, 16.7 percent; for alcohol, 15.4 percent but only 4.9 percent for psychedelics. Men who used alcohol were more likely to become dependent (21.4 percent) than women (9.2 percent), possibly because they drink more than women but genetics may also play a role.

[Table 11.1-12](#) shows data from the 1996 Household Survey on percentage of respondents who reported using various drugs. The data are shown for four age groups. Persons aged 18 to 25 years reported the highest level of use of illicit drugs during the 30 days preceding the interview; those ages 26 to 34 had the next highest rate and reported a higher lifetime experience with cocaine. Illicit drug use during the 30 days preceding the interview is far more prevalent among young adults (ages 18 to 34, and particularly those 18 to 25 years old) than among those above age 35 or below age 18. Also, whereas recent use is more common in large metropolitan areas than in rural areas, regional, racial, and ethnic differences vary with the age group considered. With the exception of tobacco dependence, all forms of substance abuse or dependence are more common among men than among women. However, recent data indicate that when adjustment is made for differences in rates of use and experimentation with illicit drugs, women are about as likely as men to become dependent. Current illicit drug use (past 30 days) was more common among male (8.1 percent) than female (4.2 percent) respondents, and among the unemployed. Among other demographic subgroups, it was slightly more common among blacks and in the western states.

**Table 11.1-12** Use of Illicit Drugs, Alcohol, and Tobacco in the U.S. Population by Age Groups

Drug	Adolescent Use (%)				Peak Year Use (%)				Peak Month Use (%)				
	1977	1978	1979	1980	1977	1978	1979	1980	1992	1993	1994	1995	1996
Any illicit drug*	23.7	49.0	33.1	29.0	36.7	36.9	44.6	37.7	10.0	10.6	10.6	10.4	11.9
Marijuana and hashish	16.8	40.0	28.0	24.0	32.0	32.0	39.0	32.0	3.8	4.1	4.1	4.1	4.8
Cocaine	1.9	18.2	28.0	18.9	1.8	4.7	3.1	0.9	2.0	2.0	2.3	2.3	2.3
Crack	0.7	3.0	4.4	1.6	0.4	1.1	1.1	0.4	0.7	0.6	0.9	0.9	0.9
Heroin	0.8	10.0	8.0	3.8	0.0	1.0	0.0	0.0	1.7	1.7	1.7	1.7	1.7
Amphetamines	0.8	16.0	13.0	7.0	0.3	0.0	0.0	1.0	2.0	2.0	2.3	2.3	2.3
MDA	1.2	2.0	4.0	1.0	0.7	0.0	0.0	0.0	0.7	0.7	0.7	0.7	0.7
Other	0.1	0.9	0.7	1.0	0.8	0.6	0.6	0.8	0.0	0.0	0.0	0.1	0.1
Heroin	0.1	1.1	1.1	1.2	0.1	0.0	0.2	0.0	0.2	0.4	0.4	0.4	0.0
Heroin (any use)	0.8	12.7	10.4	6.0	0.7	0.7	0.2	1.0	1.0	1.0	1.0	1.0	1.0
Heroin (heavy use)	0.2	4.2	3.5	1.7	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Heroin (light use)	0.6	8.5	6.9	4.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Heroin (any use)	0.8	12.7	10.4	6.0	0.7	0.7	0.2	1.0	1.0	1.0	1.0	1.0	1.0
Heroin (heavy use)	0.2	4.2	3.5	1.7	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Heroin (light use)	0.6	8.5	6.9	4.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Heroin (any use)	0.8	12.7	10.4	6.0	0.7	0.7	0.2	1.0	1.0	1.0	1.0	1.0	1.0
Heroin (heavy use)	0.2	4.2	3.5	1.7	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Heroin (light use)	0.6	8.5	6.9	4.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

The High School Survey found that self-reported use of cannabis and illicit drugs in general (mostly cannabis) in the past 30 days declined sharply from the high levels (38 to 40 percent) reported in 1977 through 1979 to much lower levels (16 percent) in 1991. The decline in cocaine use began in 1987. However, 30-day prevalence rates for cannabis increased from 1992 through 1997. Cocaine and crack cocaine 30-day prevalence rates also increased slightly from a low of 1.3 percent in 1993 to 2.3 percent in 1997. Other substance use increased also, but levels were still below the peaks observed a decade earlier. In 1997 the annual prevalence rate among high school seniors for use of any illicit drug was 42.4 percent, and for an illicit drug other than cannabis, it was 20.7 percent.

The ADAM system obtains data from a population in which illicit drug use is high and thus provides trend data not readily available from other sources. In general, current drug use among arrestees is several times higher than that among those sampled by national surveys, even though urine tests detect drug use for only a few days, whereas surveys typically ask about drug use over the preceding 30 days. For example, in 1988, the peak of the cocaine epidemic, more than 60 percent of arrestees tested positive for cocaine (80 percent among male arrestees in Manhattan). More-recent data (1995) show a decline in cocaine use and low levels of heroin use.

**Epidemics** Several major overlapping drug abuse epidemics have occurred over the past 30 years, affecting somewhat different populations. Cannabis use, which had been endemic among certain minority groups and jazz musicians, began to increase in the 1960s, especially among young people, and then spread to other segments of the population. At its peak, in 1978 to 1979, 10 percent of high school seniors were using marijuana on a daily basis. Daily use declined to 5 percent by 1984, to 2 percent by 1991, and then reversed direction and again rose. Similar changes in use rates were reflected in the Household Survey.

An epidemic of heroin use also began in the early 1960s, and incidence peaked between 1969 and 1971. The population of active heroin users reached its highest levels in the early 1970s, but periodic upsurges have occurred as supplies became more available, law enforcement activity waxed and waned, and relapse rates increased among former users. In 1977 the United States government estimated that there were 500,000 opioid abusers and dependent users, and more recently, it revised the estimate to 320,000 occasional users and 810,000 chronic users. In general, the heroin-using population is an aging one, with a high and still growing prevalence of HIV in some areas. The 1996 Household Survey estimated that about 2.3 million people had tried heroin at least once and that 245 thousand had used it in the past year.

However, it is believed that a large percentage of heroin users are outside the population interviewed by the survey.

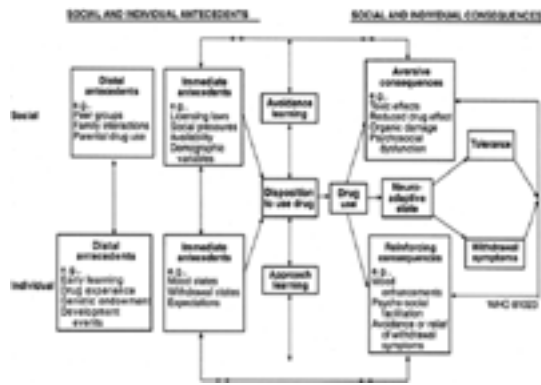
The cocaine epidemic began in the 1970s and reached its peak around 1985, when it was estimated that 5.8 million people in the United States (2.9 percent of the population) had used cocaine in the month prior to survey. The epidemic seems to have passed its peak in most segments of society, with current (past 30 days) use rates in 1996 at about 1.5 to 2 percent among those 18 to 34 (0.8 percent for ages 17 and older). Cocaine use among the heaviest users (weekly or almost weekly) did not decline significantly, but rates decreased among arrestees in 1995.

In the early 1990s, fueled by abundant supplies of cheap illicit methamphetamine produced in many small laboratories, methamphetamine use began to increase in a number of cities in western, southwestern and northwestern parts of the United States. By 1996, gauged by drug tests on arrestees, that epidemic had passed its peak in those areas.

## **ETIOLOGY**

The model of drug dependence from which the DSM-IV and ICD-10 criteria were derived conceptualizes dependence as a result of a process in which multiple interacting factors influence drug-using behavior and the loss of flexibility with respect to decisions about using a given drug. Although the actions of a given drug are critical in the process, it is not assumed that all persons who become dependent on the same drug experience its effects in the same way or are motivated by the same set of factors. Furthermore, it is postulated that different factors may be more or less important at different stages of the process. Thus, drug availability, social acceptability, and peer pressures may be the major determinants of initial experimentation with a drug, but other factors such as personality and individual biology probably are more important in how the effects of a given drug are perceived. Still other factors, including the particular actions of the drug, may be primary determinants of whether drug use will progress to drug dependence, whereas still others may be important influences on the likelihood that drug use will lead to adverse effects or the likelihood of successful recovery from dependence.

[Figure 11.1-1](#) illustrates how various factors might interact in the development of drug dependence. The central element is the drug-using behavior itself. The decision to use a drug is influenced by immediate social and psychological situations, as well as by the person's more remote history. Use of the drug initiates a sequence of consequences that can be rewarding or aversive, and which, through a process of learning, can result in a greater or lesser likelihood that the drug-using behavior will be repeated. For some drugs, use also initiates the biological processes associated with tolerance, physical dependence, and (not shown in the figure) sensitization. In turn, tolerance can reduce some of the adverse effects of the drug, permitting or requiring the use of larger doses, which then can accelerate or intensify the development of physical dependence. Above a certain threshold, physical dependence is generally a distinct recurrent motive for further drug use. Sensitization of motivational systems may increase the salience of drug-related stimuli.



**FIGURE 11.1-1** WHO schematic model of drug use and dependence. (Reprinted with permission from Edwards G, Arif A, Hodgson R: Nomenclature and classification of drug- and alcohol-related problems. A WHO memorandum. Bull WHO 99:225, 1981.)

For simplicity [Figure 11.1-1](#) shows drug use alone as initiating that chain of consequences, but the choices a person makes over and over again are more complex. The decision is whether to use one drug or another or to engage in some behavior that does not involve drug use. Each of those decisions can initiate positive and negative consequences. Changes in the availability, costs, and consequences of alternative behaviors can also influence what appears to be compulsive use of a pharmacological agent. For example, patients in a methadone maintenance program who were using cocaine despite negative consequences (no take-home methadone) reduced their cocaine use when vouchers for goods and services were awarded for clean (negative for cocaine) urine specimens.

**Social and Environmental Factors** Cultural factors, social attitudes, peer behaviors, laws, and drug cost and availability all influence initial experimentation with substances, including alcohol and tobacco. These factors also influence initial use of more socially disapproved drugs such as cocaine and opioids, but personality factors assume a more important role. Social and environmental factors also influence continued use, although individual vulnerability and psychopathology are probably more important determinants of the development of dependence. In general, the use of the less socially disapproved substances (alcohol, tobacco, and cannabis) precedes the use of opioids and cocaine, and those antecedent substances are sometimes referred to as gateway drugs.

Substantial evidence indicates that consumption of alcohol and tobacco in a population can be altered by changes in their price and availability. When alcohol availability is increased by increasing the number of sales outlets or extending sale hours, consumption tends to rise. When the cost of either alcohol or tobacco is increased in relation to disposable income (e.g., by increased taxes), consumption falls. These factors even influence the behavior of dependent persons, although perhaps not to the same degree as for those who are not dependent. Availability can be altered independently of cost, and alterations can be limited to selected populations (e.g., prohibiting sale of alcohol and tobacco to those under a specific age).

Social, cultural, and economic factors do not always operate synergistically but may sometimes influence consumption in opposite directions. For example, in the late 1980s increased public awareness of how alcohol use adversely affects health resulted in a decline in its consumption. That decline occurred even though alcohol was more freely available, its cost relative to income remained constant or actually decreased, and social pressures against women drinking (unless pregnant) also decreased.



**Illicit Drugs** Social and cultural factors, including beliefs about the effects of a drug, frequently exert more influence on drug-use patterns than the laws that supposedly reflect such factors. For example, cannabis use increased among high school students from the early 1970s to 1979 and then fell steadily over the next decade, although use and possession were illegal throughout the entire 18-year period, and nothing indicates that it became more expensive or less available during the 1980s. An upward trend in use was noted from 1993 to 1997, although it never reached the peak levels of 1979. Some experts believe the decline in use seen during the 1980s was linked to changing perceptions about the toxic effects of cannabis on health. The rise beginning in the 1990s was correlated with a decline in the perception of the risk of harm from regular use. Similarly, cocaine use increased in the late 1970s, despite high prices for the drug and high risk of criminal penalties; but following several well-publicized deaths from cocaine in the mid-1980s, its use declined among high school seniors and in the general population, even as the price of the drug declined.

Social and cultural factors profoundly influence the availability of illicit drugs, which in turn influences which groups in a society are most likely to become users. Currently, illicit opioids and cocaine are more available in the inner cities of large urban areas than in other parts of the country. Such availability not only influences initial and continued use but also affects relapse rates among those who seek treatment but must live in high-availability areas. When a significant number of users of illicit drugs live in one area, a subculture evolves that supports experimentation and continued use. Many of the areas in which illicit drugs are readily available are also characterized by a high crime rate, high unemployment, and demoralized school systems—all of which serve to reduce the sense of hope and sense of self-esteem associated with resistance to use and good prognosis once dependence develops. Social and educational factors also affect the likelihood for successful recovery from drug dependence; those who find satisfying alternatives are more likely to abstain from drug use.

**VIETNAM** The experience of United States service personnel who used heroin in Vietnam provided a unique natural experiment in which the influences of availability, vulnerability, and social norms could be observed. From 1970 to 1972 high-grade heroin at very low cost was readily available to young persons separated from their families and usual social norms. Among Army enlisted personnel, about half of those who tried heroin became dependent (at least they developed withdrawal symptoms when they attempted to stop using heroin). Of those who used heroin at least five times, 73 percent became dependent. The background factors that predicted heroin use in the general civilian population—early deviant behavior, such as fighting, drunkenness, arrest, and school expulsion—also predicted drug use in Vietnam, but they were not the best predictors of relapse after the soldiers returned to the United States. Relapse was related to being white, being older, and having parents who had criminal histories or were alcoholic.

**Availability and Health Professionals** The important role of availability is also illustrated by the repeated observation that physicians, dentists, and nurses have far higher rates of dependence on DEA-controlled substances, such as opioids, stimulants, and sedatives, than other professionals of comparable educational achievement (e.g., accountants or lawyers) who do not have such easy access to the drugs. Compared with controls, physicians appear to be four to five times as likely to take sedatives and minor

tranquilizers without supervision by a professional other than themselves. Yet even in that situation other factors play a role. Physicians who had unhappy childhoods are more likely to self-prescribe than those who are healthier psychologically.

**Drugs as Reinforcers** The belief that persons take drugs because of the subjective effects the drugs produce can be traced to antiquity. Different drugs produce distinctive subjective states, and extensive laboratory evidence shows that persons with experience can distinguish one drug class from another and can even rank different classes and doses on the basis of how much they like the effects. Yet the hold that drugs can eventually exert on a user's behavior is not entirely a function of its initial likeable or euphorogenic actions. For example, the effects of cocaine are typically described as powerfully euphorogenic, producing increased self-esteem, alertness, energy, and well-being; the effects of nicotine are more subtle, producing some mixture of alerting and relaxing; and the subjective effects of alcohol are more likely to be described as relaxing, are more variable, and appear to be more dependent on personality. Despite those differences, dependence (or addiction) can occur with each, and they appear to have shared or overlapping neural substrates for their reinforcing properties.

Almost all of the drugs that are used for their subjective effects and are associated with the development of dependence induce some degree of tolerance. In some cases the tolerance to the toxic and aversive effects is more pronounced than the tolerance to the reinforcing and mood-elevating effects. For example, most opioid users quickly develop tolerance to opioid-induced nausea and vomiting. This may allow users to increase the dose and thus experience greater euphoric effects. Conversely, those who continue to experience aversive drug effects (such as severe flushing with alcohol) may be less likely to persist in using the drug and are at lower risk for developing dependence. Tolerant opioid users do not continue to self-administer opioids solely to prevent the highly aversive withdrawal phenomena. Interviews with heroin users have indicated that despite some tolerance to many of the drug's effects, they continue to experience a brief euphoric effect immediately after an intravenous injection. Among nonalcoholic sons of alcoholic fathers, intrinsic tolerance may be a marker of biological vulnerability to developing alcohol dependence. Sons of alcoholic fathers who were more tolerant to a test dose of alcohol were far more likely to have developed alcohol dependence at 8-year follow-up than those who were less tolerant.

With a few notable exceptions, animals in experimental situations will self-administer most of the drugs that humans tend to use and abuse. Included among the drugs are  $\mu$  and  $\delta$  opioid agonists, cocaine, amphetamine and amphetamine-like agents, alcohol, barbiturates, many benzodiazepines, a number of volatile gases and vapors (e.g., nitrous oxide and ether), and PCP. Nicotine is also self-administered, although under more specialized conditions; cannabinoid self-administration has been difficult to demonstrate; and LSD-like drugs are not generally found to be reinforcing.

**Biological Substrates** Knowledge about the neurobiology of drug reinforcement and the mechanisms underlying tolerance and dependence has increased substantially. For opioids (and probably for other drugs as well) the neural systems involved in drug reinforcement and self-administration are distinct from those responsible for some of the other actions (e.g., opioid-induced analgesia) as well as from

those that mediate the more visible signs of the withdrawal syndrome characteristic for that drug class. The pathways critical for the reinforcing actions of a number of dependence-producing drugs, such as opioids, amphetamine, cocaine, and to some degree nicotine and alcohol, have their origins in dopaminergic neurons with cell bodies in the ventral tegmental area and projections to the nucleus accumbens and the related structures that make up the “extended amygdala.” This comprises several neural structures receiving input from the limbic cortex, hippocampus, lateral amygdala and midbrain, and projecting axons to the ventral pallidum, the medial ventral tegmental area and the lateral hypothalamus. The medial part of the nucleus accumbens is a particularly important site; dopamine release here is critical for the reinforcing effects of cocaine and amphetamines. It is also important for the reinforcing effects of opioids, but there are opioid receptors on neurons in the nucleus accumbens, and opioids can exert reinforcing effects at that site even when the dopaminergic terminals are destroyed. Evidence suggests that such drugs as nicotine, cannabinoids, and alcohol also activate dopaminergic pathways linked to the nucleus accumbens. Some researchers have proposed that all positive reinforcement, including the reinforcement associated with food reward and sex, critically depends on this dopaminergic circuit.

Dopamine release from mesolimbic dopaminergic neurons may play more than one role in the genesis of drug seeking and drug dependence. Dopamine release has been postulated to facilitate learning which events and behaviors lead to important consequences for the organism and to alert the organism to pay greater attention to such events. In this way, drug-induced dopamine release leads to a greater salience of drug-using opportunities and is linked to wanting and craving.

However, the diverse categories of drugs that activate the mesolimbic dopaminergic system do so by distinct mechanisms, and most have actions on many other neural systems. Reinforcing mechanisms are briefly described in the chapters devoted to specific drugs; however, only a few examples are given. The ventral tegmental area dopaminergic neurons have both nicotinic and  $\gamma$ -aminobutyric acid (GABA) receptors. These neurons normally are inhibited by GABAergic activity. The GABAergic neurons acting on the ventral tegmental area express  $\mu$ - and  $\delta$ -opioid receptors. When these receptors are activated by  $\mu$  opioids, GABAergic transmission is inhibited and the dopaminergic ventral tegmental area neurons become more active and release dopamine in the nucleus accumbens. However, opioids can also act directly on neurons in the nucleus accumbens, independent of dopamine action.

As a reinforcing drug, cocaine acts primarily at the nerve endings of the serotonergic, dopaminergic, and noradrenergic neurons. When transmitters are released from these neuron into the synapse, they are transported back into the nerve endings by transporter proteins. By occupying these transporter sites, cocaine prevents the reuptake of the transmitters, thus increasing their concentration in the synapse. Cocaine's binding to the dopamine transporter is primarily responsible for its reinforcing effects, but the actions on other neurotransmitters also influence its subjective effects. Amphetamine too, increases dopamine levels at the synapse and binds to the dopamine transporter to some degree. But amphetamine actions at the transporter are not as important as its major action, which is to displace dopamine and norepinephrine from their storage sites in the neuron and thereby lead to their release.

Alcohol is no longer believed to act like a general anesthetic, altering neuronal membranes. Instead, at clinically relevant concentrations its actions may be exerted more selectively on specific receptors and neurotransmitter systems. At clinically relevant concentrations these actions include enhancing the inhibitory action of GABAergic neurotransmitters (by increasing the sensitivity of the GABA receptor) and reducing the excitatory actions of glutamatergic neurotransmitters (by altering the response of the *N*-methyl D-aspartate [NMDA] receptors). By its blocking actions at the NMDA receptor, ethanol can indirectly alter the release of other neurotransmitters (e.g., serotonin, dopamine, norepinephrine, glutamate, aspartate, and GABA). Low doses of alcohol increase dopamine levels in the nucleus accumbens and elevate brain serotonin concentration. Various regions of the brain differ in their sensitivity to these actions of ethanol. The endogenous opioid system may be involved in some aspects of the mood-elevating effects of alcohol, since the opioid antagonist naloxone reduces alcohol self-administration in animals and the antagonist naltrexone reduces relapse rates in treated alcoholics.

Mesolimbic dopaminergic neurons have multiple nicotinic cholinergic receptors on their cell bodies and terminals in the nucleus accumbens. When activated, these receptors increase dopamine release. Interestingly, regular exposure to tobacco smoke containing nicotine may be more reinforcing than nicotine itself because other chemical entities in tobacco inhibit brain monoamine oxidase type A (MAO<sub>A</sub>) and MAO<sub>B</sub>, which are involved in the regulation of intraneuronal stores of dopamine. This inhibition increases the amount of dopamine available for release when the dopaminergic neurons are activated.

Drugs can also be reinforcers by terminating aversive states; some of these actions involve dopaminergic systems, but others do not. Some researchers argue that compulsive drug use can be explained on the basis of the positive reinforcing effects of drugs without any need to invoke alleviation of withdrawal distress or any obvious source of antecedent pain or dysphoria. Furthermore, they argue, craving is primarily associated not with cues that evoke withdrawal but with those that evoke memories of positive reinforcement (euphoria). However, evidence now indicates that even when there are no obvious and dramatic withdrawal symptoms (e.g., cocaine, nicotine), adaptive changes in the reward system result in a relative dopaminergic deficiency state (measurable as decreased dopamine levels in the nucleus accumbens) when drug use is stopped or its action ceases. This deficiency state is experienced as dysphoria or anhedonia. Quite often the same drug-using behavior that terminates this dysphoria moves the system to a hyperdopaminergic state associated with euphoria. In short, the behaviors associated with chronic drug use are typically driven by both the avoidance of dysphoria (negative reinforcement) and the pursuit of euphoria (positive reinforcement).

The sensitivity of neural systems to reinforcing drugs such as cocaine and opioids is enhanced by corticosteroids. In animal models, a variety of stresses acting through release of corticotropin-releasing factor (CRF) and the hypothalamic pituitary-adrenal axis can sensitize neural systems and trigger reinitiation of drug taking. There is ample clinical evidence that such stresses can act similarly in drug-dependent individuals immediately following withdrawal and for long periods thereafter. In addition, some drugs may sensitize neural systems to the reinforcing effects of the drug.

**Learning and Conditioning** Drug use, whether occasional or compulsive, can be viewed as behavior maintained by its consequences. Any event that strengthens an antecedent behavior pattern can be considered a reinforcer of that behavior. In that sense certain drugs reinforce drug-taking behavior. Drugs can also reinforce antecedent behaviors by terminating some noxious or aversive state, such as pain, anxiety, or depression. In some social situations the use of the drug, quite apart from its pharmacological effects, can be reinforcing if it results in special status or the approval of friends. Social reinforcement can maintain drug use until the effects of primary reinforcement or reinforcement by alleviation of withdrawal symptoms come into play. Each use of the drug evokes rapid positive reinforcement, either as a result of the *rush* (the drug-induced euphoria), alleviation of disturbed affects, alleviation of withdrawal symptoms, or any combination of these effects. In addition, some drugs may sensitize neural systems to the reinforcing effects of the drug. With short-acting substances, such as heroin, cocaine, nicotine, and alcohol, such reinforcement occurs several times a day, day in and day out, creating powerfully reinforced habit patterns. Eventually, the paraphernalia (needles, bottles, cigarette packs) and behaviors associated with substance use can become secondary reinforcers as well as cues signaling availability of the substance, and in their presence, craving or a desire to experience the effects increases. With socially acceptable substances, such as tobacco, use becomes so woven into the matrix of daily functioning that some users are reminded of the substances when performing ordinary tasks. Stresses can also act as cues that induce drug taking, particularly in the postwithdrawal period.

**Classical Conditioning** In addition to the operant reinforcement of drug-using and drug-seeking behaviors, other learning mechanisms probably play a role in dependence and relapse. Opioid and alcohol withdrawal phenomena can be conditioned (in the Pavlovian or classic sense) to environmental or interoceptive stimuli. Such conditioning has been demonstrated in both laboratory animals and abstinent and methadone-dependent human volunteers. For a long time following withdrawal (from opioids, nicotine, or alcohol), the addict exposed to environmental stimuli previously linked with substance use or withdrawal may experience conditioned withdrawal, conditioned craving, or both. The increased feelings of craving are not necessarily accompanied by symptoms of withdrawal. The most intense craving is elicited by conditions associated with the availability or use of the substance, such as watching someone else use heroin or light a cigarette or being offered some drug by a friend. Some workers now believe that the cues that induce memories of drug-induced euphoria are more important for stimulating craving and in predisposing to relapse than either protracted or conditioned withdrawal. Those learning and conditioning phenomena can be superimposed on any preexisting psychopathology, but preexisting difficulties are not required for the development of powerfully reinforced substance-seeking behavior.

**Withdrawal Syndromes and Negative Reinforcement** Although positive reinforcement is a powerful etiological factor in the genesis of cocaine, amphetamine, and (in some cases) opioid dependence, aversive withdrawal phenomena and negative reinforcement may be equally important influences for a number of other drugs and dominant influences for others. One example of this is seen in most persons who become dependent on benzodiazepines taken in the course of treatment for anxiety syndromes. When drug use is interrupted, some seem to experience a reappearance of the original symptoms; others have new distressing symptoms indicating withdrawal. The use of benzodiazepines alleviates both kinds of aversive states. In either case the drug is acting as a negative reinforcer in perpetuating drug use.

Benzodiazepines can induce euphoria in alcoholic patients or in persons with histories of sedative abuse, but they are not reliably euphorogenic in normal, nonalcoholic persons. Benzodiazepine anxiolytic agents may induce euphoria in nondependent, nonanxious persons, but such instances are rare relative to the number of those who experience only relief of anxiety.

In most clinical situations, even among users of highly euphoric illicit drugs, the distinction between positive and negative reinforcing effects does not exist. The alcoholic, the heavy smoker, and the heroin user may experience, simultaneously or sequentially, relief of withdrawal, a sense of ease, and perhaps alleviation of dysphoria and depression. With intravenous drugs there may also be a sudden rush of intense pleasure.

**Long-Lasting Changes Associated With Chronic Drug Use** After long-term use, most drugs of abuse produce adaptive changes in the brain that are manifested as acute and chronic withdrawal syndromes when drug use ceases. How these changes are produced, how long they persist after cessation of drug use, and how they contribute to relapse are still being explored. But much progress has occurred, as is illustrated by several examples of recent developments.

Tolerance and dependence on opioids involves several mechanisms. Opioid agonist binding to the opioid receptors results in an inhibition of adenylyl cyclase and lower intracellular cyclic adenosine monophosphate (cAMP) concentrations. Long-term exposure elicits compensatory upregulation of the cAMP pathway, internalization of  $\mu$ - and  $\delta$ -receptors, and a decrease in the number of G proteins, which couple the receptors to the second messengers and ion channels. Upregulation of adenylyl cyclase is mediated by the transcription factor cAMP response element-binding protein (CREB), which also plays a role in the generation of distinct and persistent Fos-like proteins, which are also thought to be involved in tolerance. As a result of upregulation of cAMP, GABAergic neurons innervating the ventral tegmental area become hyperactive when opioids are withdrawn, thus inhibiting dopaminergic neurons. Such a mechanism may account, in part, for the dysphoria and anhedonia of opioid withdrawal. In addition, chronic opioid use reduces the size of dopamine neurons in the ventral tegmental area; increased production of dynorphin may also serve to inhibit dopaminergic activity at the ventral tegmental area and nucleus accumbens. The glutamatergic system is also involved in opioid adaptation, since NMDA receptor sensitivity is altered by opioids and NMDA antagonists can alter the development of opioid tolerance and physical dependence.

With chronic alcohol use, affected neurons develop adaptive changes that include, among a number of others, supersensitivity or increased numbers of NMDA receptors. When the alcohol is withdrawn the actions of excitatory neurotransmitters at supersensitive NMDA receptors are postulated to produce the hyperexcitability of alcohol withdrawal, including hyperactivity in noradrenergic systems and glutamate-induced neuronal excitotoxicity. Alcohol-dependent patients tested 1 week and 1 month after cessation of alcohol use had cerebrospinal fluid with substantially lower concentrations of GABA and substantially higher concentrations of the excitatory transmitters glycine aspartate, glutamate, and *N*-acetylaspartylglutamate (NAAG) than that of healthy controls. Although these changes may be trait markers rather than consequences of long-term alcohol use, they are what might be expected to result from withdrawal of alcohol after adaptive changes have occurred. Most agents currently used to treat

alcohol withdrawal act directly or indirectly at GABA receptors, and perhaps those that act at NMDA sites may provide alternative or even superior therapeutic agents.

Nicotine tolerance may involve desensitization of nicotinic receptors. However, chronic nicotine use increases the number of nicotinic cholinergic receptors, and the mechanisms underlying the nicotine withdrawal syndrome remain unclear. From the symptoms, which include craving, inability to concentrate, irritability, increased appetite, dysphoria, and (sometimes) depression, some hypoactivity in dopaminergic systems is likely. Given the many other actions of nicotine on learning, attention, arousal, and appetite, changes in systems in addition to the mesolimbic are probably also involved.

Cocaine and amphetamines can induce tolerance, dependence, and sensitization, depending in part on whether exposure is continuous or intermittent.

One way to determine the contribution of negative reinforcement to the motivation to continue using a substance or to relapse after withdrawal is to introduce agents that can modify withdrawal syndromes or aversive states. Abundant evidence shows that when psychological interventions are held constant, noninhaled nicotine (delivered by transdermal patches [Nicoderm] or nicotine gum [Nicorette]) significantly increases the probability that smokers trying to quit will be successful. Neither nicotine gum nor transdermal patches produce positive reinforcing effects, but they do alleviate aspects of the nicotine withdrawal syndrome. Thus, it is reasonable to infer that although the symptoms may not be life threatening, the avoidance of nicotine withdrawal plays a significant role in continued smoking and relapse. However, evidence suggests that for some, nicotine (or some other component of tobacco) controls negative effects other than those usually associated with withdrawal. Persons with histories of major mood disorder are more likely to become regular smokers if they try cigarettes and may experience symptoms of depression when they try to stop smoking; those symptoms are suppressed by returning to smoking. Heroin addicts treated with oral methadone or sublingual buprenorphine (Subutex) experience a reduction in opioid withdrawal symptoms but little or no euphoric effects from those agents. Yet, such treatment dramatically reduces self-administration of heroin. Such findings support the view that acute and protracted opioid withdrawal (or opioid suppression of aversive affects) is an important factor in the perpetuation of heroin use and relapse after withdrawal. Similarly, acamprosate, a structural analogue of glutamate is postulated to reduce relapse in alcoholics following alcohol withdrawal by dampening the hyperexcitability in the glutamatergic system.

**Conditioned Withdrawal and Stress Sensitivity** In addition to the direct contribution of withdrawal phenomena to the perpetuation of drug use are the indirect effects exerted through learning mechanisms. The regular recurrence of withdrawal-induced aversive states provides ample opportunity for those states to become linked through learning to environmental cues and other mood states, and the rapid relief of withdrawal by drug use results in repeated reinforcement of drug-taking behavior. Long after there are measurable manifestations of acute withdrawal, certain moods or environmental cues can evoke components of the original withdrawal state along with urges to use the drug again. Considerable evidence shows that in former opioid addicts, stress can trigger both craving and relapse, and dysregulation of the hypothalamic-pituitary-adrenal axis persists for long periods after drug cessation.

How long withdrawal phenomena, stress sensitivity, or both continue to contribute to risk of relapse is not clear. Substantial evidence supports a withdrawal syndrome period for alcohol, opioids, and certain sedatives with subtle disturbances of mood, sleep, and cognition that persists for many weeks or months after the acute syndrome subsides. Whether the dysregulation of the hypothalamic-pituitary-adrenal axis is causally related to protracted withdrawal or has a similar time course is still uncertain.

**Biological Factors—Vulnerability** The children of alcoholic parents are at higher risk for developing alcoholism and drug dependence than are children of nonalcoholic parents. Dependence on other drugs also shows a familial pattern. The increased risk is partly due to environmental factors (parental modeling, neglect, early child abuse), but genetic factors are also important. Numerous studies of laboratory animals have revealed genetically transmitted differences in the reinforcing effects of alcohol and various drugs such as cocaine and opioids and show that genetic factors powerfully influence sensitivity to toxic effects. The evidence for genetic factors in human vulnerability to alcoholism and other drug dependence is derived most convincingly from twin and adoption studies, but family studies are also revealing. Several studies of twins have found a higher concordance rate for alcoholism among identical twins than among fraternal twins. Although identical twins are generally believed to have more social contact than fraternal twins, when the effects of environmental factors are adjusted statistically, genetic factors are still found to have a major influence on the likelihood of becoming dependent. Indeed, in one population-based twin study 48 to 58 percent of the variation in liability to dependence was attributable to genetic factors; the remainder was due to general environmental influences not shared by family members.

In studies of 3372 Vietnam-era veteran twin pairs, the concordance rates for dependence on at least one illicit drug were higher for monozygotic twins (26.3 percent) than for dizygotic (16.5 percent) twins. Generally, overall rates of dependence did not differ among these veterans and contemporary civilians. Biometric modeling identified both common (shared) and drug-specific genetic vulnerability factors as well as general and drug-specific effects of family and nonfamily environment. In the common vulnerability models, 31 percent of the variance for common (shared) vulnerability was due to additive genetic factors, 25 percent to family environmental effects, and 44 percent to nonfamily environmental effects. The importance of common (shared) genetic factors versus drug-specific genetic factors varies considerably for different categories of drugs. For marijuana, stimulant, and sedative abuse, common genetic vulnerability factors accounted for most of the genetic variance, with unique specific genetic factors accounting little. For psychedelics, no specific genetic influence was found. For heroin, 54 percent of the total variance was due to genetic factors, with 38 percent (70 percent of total genetic variance) contributed by unique genetic factors and only 16 percent by common (shared) ones. Another analysis of data from this group of veterans showed that both genetic and environmental factors influenced the initiation of cigarette smoking, but genetic effects accounted for 70 percent of the variance in the persistence of smoking for those who became regular smokers. This study, which is consistent with other genetic studies of smoking, found the genetic contribution to the persistence of smoking to be as great as or greater than the genetic contribution in the genesis of other psychiatric disorders, including alcoholism.



Twin studies in women have revealed strong genetic contributions to the use of caffeine and development of caffeine tolerance, dependence, and withdrawal.

Family studies also point towards general and drug-specific vulnerability factors. In a study of alcoholic probands and their siblings, about 50 percent of the brothers and 25 percent of the sisters met lifetime criteria for alcohol dependence. Compared with controls, these siblings also showed higher rates of tobacco, cocaine, and marijuana use, but the siblings of subjects who were dependent on alcohol and another drug, (presumably a more severe form of dependence), were not more likely to develop alcoholism than siblings of subjects who were dependent only on alcohol. However, siblings of probands who were dependent on both alcohol and marijuana had an elevated risk for marijuana dependence; siblings of probands dependent on alcohol and cocaine were more likely to become cocaine dependent. Statistical analysis that controlled for access to the drugs still showed specific family clustering.

Studies of boys adopted soon after birth have shown higher rates of alcoholism among those whose biological fathers were alcoholics than among those whose biological fathers were not. Some adoption studies pointed toward subtypes of alcoholism among men: one is a later-onset disorder that is less severe and far more sensitive to environmental factors (type I) and the other is associated with early onset, antisocial behavior and criminality in the biological fathers, and a stronger genetic basis for the increased vulnerability (type II). The hypothesis that two genetically distinct types of alcoholism (type I and type II) exist has been criticized on the grounds that it is essentially a relabeling of the older primary-secondary categorization. In the latter, alcohol-dependent persons who do not have antisocial personality disorder are designated as having primary alcoholism; those who first exhibit antisocial personality disorder and later develop alcoholism are designated antisocial personality disorder with secondary alcoholism. Also, several groups have been unable to use the type I and type II criteria to categorize patients with alcohol dependence accurately in clinical studies. However, arguments about the validity of the type I–type II categorization do not diminish the importance of genetic factors in vulnerability to developing alcohol dependence. The results of a large-scale efforts to identify the genes that contribute to vulnerability to alcoholism are now emerging.

As many as one third of alcohol-dependent persons have no family history of the disorder. Men are more likely to develop alcoholism than are women (fourfold to fivefold in the United States). This is true across every culture studied, probably reflecting, in part, social sanctions on drug use and deviant behavior by women. But it is also postulated that women are less likely to drink heavily because they are less tolerant to alcohol. Women who do drink heavily run the same risk of developing alcoholism as men who drink heavily, and women who use illicit drugs are about as likely to develop dependence as men who use such drugs.

In some, but not all studies alcohol-dependent persons are at far higher risk for developing other varieties of drug dependence. A more consistent finding is that drug-dependent persons also are at high risk for alcoholism and often have a family history of alcoholism. Such findings are consistent with data from the twin studies that have found general as well as drug-specific vulnerability factors.

Most researchers believe that no single gene will be found to account for the complexities of inherited risk for drug and alcohol dependence. Some genetic factors may not increase vulnerability to alcoholism but decrease it. A genetically determined variation in the activity of enzymes that metabolize alcohol (alcohol dehydrogenase and aldehyde dehydrogenase [ALDH]), common among some Asian groups, results in high levels of acetaldehyde in response to alcohol ingestion. The effect is to cause alcohol flush reaction and to exert some deterrent effect on alcohol ingestion. Alcoholism is lower among many Asian groups than among whites. Further, Asians with alcoholism are much less likely to have the inactive form of the ALDH enzyme.

**Biological and Behavioral Differences** Studies exploring how persons with and without family histories of alcoholism might differ have involved measures of personality, drug-use and alcohol-use patterns, psychomotor and cognitive performance, electrical activity of the brain, endocrine responses to challenges with alcohol and other substances, as well as measures of receptor numbers and affinities and enzyme activities (e.g., MAO) in peripheral tissues (e.g., blood platelets and lymphocytes). One finding that has been replicated is that under some conditions, the electrical response of the brain that occurs about 300 ms after a sensory stimulus (the P300 wave) has a smaller amplitude in nondrinking sons and daughters of alcoholic fathers than in control subjects without family histories of alcoholism. The decreased amplitude is believed to reflect a decreased capacity to recognize and interpret complex environmental stimuli. Most studies have found no differences in intelligence among subjects with and without family histories of alcoholism. However, the results of personality studies are conflicting; some find no differences and others find greater impulsivity, adventurousness, and sensation seeking among those with a positive family history. Studies of the drinking patterns of adolescent and young adult sons of alcoholic persons also have not yielded consistent results; some (but not all) studies show that sons of alcoholic parents are heavier drinkers. Other studies have compared the subjective, motoric, and endocrine responses of young men with and without family histories of alcoholism following challenge exposures to alcohol and other potentially euphoriant drugs (such as benzodiazepines). Sons of alcoholic fathers seem to be more tolerant to the intoxicating effects of modest doses of alcohol, and in some (but not all) studies, higher doses of alcohol produced smaller changes in their prolactin and cortisol concentrations. Furthermore, one study found that sons who had smaller responses to test doses of alcohol at age 20 (i.e., were more tolerant) were fourfold more likely to have developed alcoholism 8 years later. Another study of sons of alcoholic parents found that those who had exhibited smaller electroencephalographic (EEG) alpha frequency responses to alcohol were more likely to be alcohol dependent at 10-year follow-up.

The results of studies using benzodiazepine challenges are also not consistent; one showed a greater euphoric response to alprazolam (Xanax) in sons of alcoholic parents, and another showed no difference between positive and negative family-history groups after a dose of diazepam.

A number of studies have shown that conduct disorder and early childhood aggression are associated with a substantial increase in the likelihood of early involvement with illicit drug use and development of dependence on alcohol and illicit drugs. Considerable evidence supports a role for both genetics and environmental factors in the development of conduct disorder. Antisocial personality disorder represents an independent additional risk factor for addictive disorders. The effects of antisocial personality

disorder and family history of an substance-related disorder appear to be additive rather than synergistic. It seems possible that in some of the studies of children and young people at high risk for later drug dependence, the electrophysiological differences, cognitive deficits, and personality differences reflected the presence of conduct disorder or antisocial personality disorder rather than a family history of alcoholism per se.

**Psychodynamic Factors and Psychopathology** Early psychoanalytic formulations postulated that drug users, in general, suffered from either a special form of affective dysregulation (tense depression) that was alleviated by drug use or from a disorder of impulse control in which the search for pleasure was dominant. More-recent formulations postulate ego defects, which are evinced by the addict's inability to manage painful affects (guilt, anger, anxiety) and to avoid preventable medical, legal, and financial problems. The newer formulations postulating ego defects are to some degree the older formulations with a modest change in terminology that gives greater weight to the inability to cope with painful affects than to the intensity or abnormality of the affects per se. It is postulated that some substances pharmacologically and symbolically aid the ego in controlling those affects and that their use can be viewed as a form of self-medication. For example, it has been suggested that opioids help users control painful anger, that alcohol helps alcoholics control panic, and that nicotine may help some cigarette smokers control symptoms of depression. Although it is conceded that some of those observations may reflect problems produced by long-term use, the psychodynamic perspective is that the psychopathology is the underlying motivation for initial use, dependent use, and relapse after a period of abstinence. However, traditions of passivity and uncovering techniques derived from the psychoanalysis of neurosis are poorly suited to the treatment of most drug addicts. Further, some addicts have great difficulty differentiating and describing what they feel, a difficulty that has been called alexithymia (i.e., no words for feelings).

**Family Dynamics** One family member's substance abuse is often influenced by substance-using behaviors of others in the family, and these complex interrelationships can profoundly affect their lives. An understanding of the relationships among substance-using patients and their families is relevant for understanding the etiology of substance dependence and its treatment and for helping other family members to cope with problems associated with the substance-using behavior.

More has been written about the families of alcohol-dependent persons and heroin users than about families affected by users of other drugs. Similarities between the family dynamics in these two prototypical dependencies have led researchers and clinicians to assume that certain general principles apply to all varieties of substance dependence. The observation that alcoholism is commonly found in the families of those seeking treatment for other types of dependence, that alcohol-dependent persons are often dependent on other substances as well, and that those addicted to illicit drugs are often alcoholic suggests that there are common features among families with an addicted member. However, there are few data to suggest that the families of those dependent on tobacco or benzodiazepines are as dysfunctional as those affected by alcohol, opioids, or cocaine.

It is not always clear to what degree one family member's behavior causes the substance-using behavior

of another or is primarily a response to that behavior. Some writers emphasize that the addiction is a symptom that provides a displaced focus for conflict among other family members and that the user (the designated patient) may be playing a role in maintaining the homeostasis of a dysfunctional family. At the same time, addiction often arises in families in which one or both parents (and sometimes grandparents) have drug or alcohol problems and other psychopathology. Some characteristics commonly observed both in families of persons who are alcohol dependent and of those addicted to illicit drugs are multigenerational drug dependence; a high incidence of parental loss through divorce, death, abandonment, or incarceration; overprotection or overcontrol by one parent (usually the mother), whose life is inordinately dependent on the behavior of the addicted offspring (symbiotic relationships); distant, cold, disengaged, or absent father (when the father is alive); defiant drug-using child, who appears to be engaged with peers but remains unusually dependent on the family well into adult life (pseudo-independence). The actual family dynamics are difficult to characterize because the family members' self-reports about their relationships do not reliably correspond to what outsiders observe. Such families typically do not describe themselves in the way that family therapists see them. Some workers have proposed that unresolved family grief plays a role in the genesis of drug addiction in a family member and that such families cannot deal effectively with separation because of previous losses. Despite the pathological interdependence between the addict and other family members, the addict is often described as passive, dependent, withdrawn, and unable to form close relationships.

Despite all the apparent pathology found in families, in many instances the family brings the substance user into treatment, and the patient often believes that it is the family that is most likely to be helpful in recovery. Furthermore, clinicians now generally believe that involving families in treatment is important, if not essential, to effective intervention. One aspect of treating families is dealing with the tendency of some members to shield the patients from the consequences of their substance use, a behavior usually labeled by clinicians as “enabling” but usually experienced by the family member as loving, supporting, accepting, and protecting. A variation on family therapy, sometimes called network therapy, involves enlisting family members and close friends as allies of the therapist to provide social support and reinforcement of drug-abstaining behaviors. The persons selected to fulfill this role function as part of a treatment team rather than as patients.

**CODEPENDENCE** The terms “coaddiction,” “coalcoholism,” or more commonly “codependency” or “codependence” have recently come into vogue to designate the behavioral patterns of family members who have been significantly affected by another family member's substance use or addiction. The terms have been used in various ways, and there are no established criteria for codependence, a concept that some writers have expanded far beyond its origins to encompass any personality disorder that involves difficulty in expressing emotions. However, many have criticized the expanded concept of codependence as a largely invalid notion based solely on anecdote. The following summary of some characteristics frequently described as aspects of codependence is not meant to imply the validity of a unitary syndrome.

*Enabling* Enabling was one of the first and more agreed upon characteristics of codependence or coaddiction. Sometimes family members feel that they have little or no control over the enabling acts. Either because of the social pressures for protecting and supporting family members or because of

pathological interdependencies, or both, enabling behavior often resists modification. Other characteristics of codependence include an unwillingness to accept the notion of addiction as a disease. The family members continue to behave as if the substance-using behavior were voluntary and willful (if not actually spiteful) and the user cares more for alcohol and drugs than for the members of the family. This results in feelings of anger, rejection, and failure. In addition to those feelings, the family members may feel guilty and depressed because the addict, in an effort to deny loss of control over drugs and to shift the focus of concern away from their use, often tries to place the responsibility for such use on the other family members, who often seem willing to accept some or all of it.

*Denial* Family members, like the substance users themselves, often behave as if the substance use that is causing obvious problems were not really a problem; that is, they engage in denial. The reasons for the unwillingness to accept the obvious vary. Sometimes denial is self-protecting, in that the family members believe that if there is a drug or alcohol problem, then they are responsible.

Like the addicts themselves, codependent family members seem unwilling to accept the notion that outside intervention is needed and, despite repeated failures, continue to believe that greater will power and greater efforts at control can restore tranquility. When additional efforts at control fail, they often attribute the failure to themselves rather than to the addict or the disease process, and along with failure come feelings of anger, lowered self-esteem, and depression.

*Other Problems* Some clinicians have reported high levels of somatic disorders, such as ulcers, colitis, and migraine, among family members of alcoholic persons and addicts and have attributed those illnesses to stress or a somatic expression of the feelings engendered by trying to cope with the family member's addiction. However, in light of the findings that there may be a genetic basis for somatization disorders among the daughters of certain subtypes of alcoholic persons, it is not clear that all of the illnesses seen among the family members of substance users are responses to the stresses of living with an addict.

**Other Factors** There are other factors that influence the pattern of use and cessation of any given substance. For example, the decision not to use a substance also has consequences that can be aversive or reinforcing, and evidence indicates that when the rewards of not using the substance are high, the likelihood of use is reduced. In addition, many of the substances associated with dependence act directly on systems that subserve both motivation and decision making, raising questions about whether use is always influenced solely by its consequences (learning processes). The cognitive processes and skills that would ordinarily subserve decision-making appear to be impaired by alcohol, barbiturates, cannabis, and several other categories of self-administered agents. Thus, whereas substance use is influenced by learning, the substances also alter the brain itself. This suggests additional problems and possibilities for intervention. Evidence is accumulating that limited cognitive skills reduce the likelihood of successful recovery from substance use and that coping skills can help a person avoid or deal with aversive affective states, environmental stresses, and situations that are associated with a high risk for substance use.

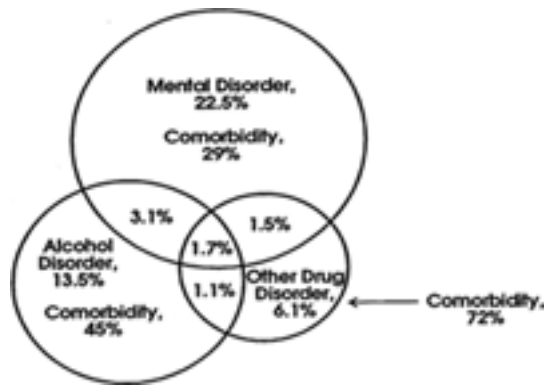
Other factors that influence the course of substance use and dependence are difficult to operationalize or teach or prescribe, but they deserve mention. Studies of the natural history of substance use indicate that recovery is powerfully influenced by the support of family and friends. Many persons report that hope, faith, formal religious affiliation, or the sustaining love of some significant person was more important to their recovery than any specific treatment.

**Multiple Factors** The biopsychosocial general model of substance dependence presented here does not attempt to assign a weight or special significance to any one factor or interaction. The implication is that for different categories of drugs, different factors may play more or less powerful causal roles in perpetuating substance use or facilitating relapse. For example, positive reinforcing effects may be more important for the development of cocaine dependence, whereas acute and protracted withdrawal phenomena may be more important in the return to opioid use following withdrawal. Even with the same substance, different factors may be more or less important for different persons. Thus, the emergence of depressive symptoms may make it difficult for some cigarette smokers to quit, particularly those with a history of major depressive disorder, and those persons may be helped by antidepressants. Such a multifactorial model implies that certain treatments or interventions may be more effective for one substance category than another and that even among persons using the same substances, different treatments may be indicated.

[Figure 11.1-1](#) also implies that the notion of dependence is not a property of any one element but an abstraction inferred from the relations among the elements of the system. While it is convenient (and required by DSM-IV) to see dependence as a disorder located within a person, any interpretation that overemphasizes one part of the system, whether the biology of the person, social influences, or behavior, is missing part of the nature of dependence.

**Comorbidity** *Comorbidity* is the co-occurrence of two or more psychiatric disorders in a single patient. A high prevalence of additional psychiatric disorders is found among persons seeking treatment for alcohol, cocaine, or opioid dependence. Although opioid, cocaine, and alcohol abusers with current psychiatric problems are more likely to seek treatment, it should not be assumed that those who do not seek treatment are free of comorbid psychiatric problems; such persons may have social supports that enable them to deny the impact that drug use is having on their lives. Two large epidemiological studies have shown that even among representative samples of the population, those who meet the criteria for alcohol or drug abuse and dependence (excluding tobacco dependence) are far more likely to meet the criteria for other psychiatric disorders also. In the NCS, 51 percent of those who met the criteria for a lifetime addictive disorder received at least one additional mental disorder diagnosis; in the earlier ECA study, the comparable figure was 38 percent. In the ECA study, among those diagnosed with drug dependence the most common additional diagnosis was alcohol abuse-dependence, followed in frequency by antisocial personality disorder, phobic disorders, and major depression for men and phobic disorders, major depression, and dysthymia for women. Almost every psychiatric diagnosis was more common among those who met the criteria for drug dependence, with notable increases in odds ratios for alcoholism, antisocial personality disorder, and mania among women, and for mania, antisocial personality disorder, and dysthymia among men. Both men and women with drug abuse-dependence are at a substantially higher risk for schizophrenia. The extent of comorbidity among individuals in the ECA

study is illustrated in [Figure 11.1-2](#).



**FIGURE 11.1-2** Lifetime prevalence of comorbid mental and addictive disorders in the United States, combined community and institutional five-site Epidemiologic Catchment Area data, standardized to the U.S. population. (Reprinted with permission from Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK: Comorbidity of mental disorders with alcohol and other drug abuse. *JAMA* 264:2511, 1990.)

In general, the probability of comorbidity is higher for those with a lifetime diagnosis of an opioid or cocaine disorder than for those with a diagnosis of cannabis abuse. Among people in prison the comorbidity rates were even higher than in the general population; addictive disorders were found in 92 percent of prisoners with schizophrenia, 90 percent of those with antisocial personality disorder, and 89 percent of those with bipolar disorders. Among persons with mental disorders seeking treatment in psychiatric specialty settings, 20 percent have a current substance abuse disorder diagnosis.

The findings from the NCS largely confirm the observations of the ECA study that those with substance use disorders are substantially more likely to experience other mental disorders and that those with other mental disorders are far more likely to develop substance use disorders. The NCS also underscored the finding that although 52 percent of respondents had never experienced any DSM-III-R disorder and 21 percent had one such disorder, 13 percent had two disorders and 14 percent had three or more disorders. Furthermore, the 12-month prevalence of a disorder was more likely among those with more than one disorder: 59 percent of all of 12-month disorders occurred in the 14 percent with a lifetime history of three or more disorders, and 89 percent of severe 12-month disorders occurred in the same group.

These findings describe rather than explain comorbidity. They do not shed much light on the question of whether, or in which cases, drug use is at least initially an adaptive effort at self-medication, or whether those with a variety of psychiatric disorders are less able to cope with the effects of substance use and so are more likely to become dependent. It is also not clear whether psychiatric disorders increase the vulnerability to drug abuse and drug dependence or whether some common factor contributes to both. In some cases, however, there does appear to be a causal link between drug use and some psychiatric disorders. For example, evidence indicates that substance abuse (especially alcohol) can cause or increase the risk for depressive disorder; cocaine can increase the frequency of panic disorder; and cannabis, cocaine, and amphetamine use can aggravate or precipitate schizophrenic symptomatology. Some of these are drug-induced disorders (particularly some of the depressive symptoms seen in alcoholics) and clear with cessation of alcohol use. However, some psychiatric disorders (e.g., mood disorder and antisocial personality disorder) often antedate substance use and can be viewed as risk

factors or predictors for substance abuse and dependence. This is particularly true of conduct disorder adult antisocial behavior, in which the symptoms often begin before the onset of problematic drug use. The NCS found that the odds of developing alcohol or drug dependence increased fivefold in the presence of conduct disorder without adult antisocial behavior and 10- to 14-fold if only adult antisocial behavior or both conduct disorder and antisocial behavior were present. Of the Axis I disorders, bipolar I disorder is more strongly related to dependence on alcohol or drugs than any other mood or anxiety disorder. In general, about 24.5 percent of those with a 12-month addictive disorder had a mood disorder as well, and 35.6 percent had an anxiety disorder. Overall, 42.7 percent of those with a 12-month addictive disorder had at least one 12-month Axis I mental disorder. In terms of lifetime disorders, 41 to 65.5 percent of those with a lifetime addictive disorder have a lifetime history of at least one Axis I mental disorder, while 51 percent of those with one or more lifetime mental disorders (Axis I or II) have a history of one or more addictive disorders. For lifetime conduct disorder or adult antisocial behavior, the rate of lifetime substance use disorder rises to 82 percent.

Although the possibility of recall bias exists, those with both an affective and an addictive disorder usually report that depression began earlier than substance use. However, temporal relationship between two disorders does not prove causality, even when the development of the first disorder is a predictor of both the likelihood and course of the subsequent disorder. There is the possibility, as has been suggested for smoking and depression, that both disorders are linked to some third common factor. In the NCS, a more chronic course of an addictive disorder was found for those who reported earlier development of primary anxiety disorder, conduct disorder, or adult antisocial behavior but was not found with earlier onset of other mental disorders.

In the NCS, co-occurring mental disorders also influenced the likelihood of seeking treatment and the treatment sector from which service would be sought. As mentioned, those who had a substance dependence problem were far more likely to seek and receive treatment if they also had a co-occurring mental disorder. About one-third of people with a 12-month history of affective disorder received some treatment; but those who also had an addictive disorder were more likely to have received it in a specialty addiction treatment program.

A collaborative study of the genetics of alcoholism used extensive structured interviews to separate independent mood and anxiety disorders from those that occurred only within the context of active drinking or withdrawal. This study found that over a lifetime, independent mood disorder was less common in alcoholics (14 percent) than in controls (17.1 percent), although more than twice as many alcoholics (2.3 percent) as controls (1.0 percent) met criteria for bipolar disorder. Panic disorder and social phobia were also substantially more common as independent disorders among alcoholics. In general, in this study the large majority of alcohol-dependent men and women did not have independent mood or anxiety disorders. This suggests that the higher rates of co-occurrence of most anxiety and affective disorders found in epidemiological studies or clinical populations probably reflect substance (alcohol)-induced anxiety and mood disorders that will resolve without special intervention once drug use ceases.



# TREATMENT

Many people who develop substance-related problems recover without formal treatment. For those who do seek help or advice, particularly those patients with less severe disorders, relatively brief interventions are often as effective as more intensive treatments. Since these brief interventions do not change the environment, alter drug-induced brain changes, or provide new skills, a change in the patient's motivation (cognitive change) probably best explains their impact on the drug-using behavior. For those individuals who do not respond or whose dependence is more severe, a variety of interventions appear to be effective. Although each section in this chapter discusses treatment relevant to the particular substance use disorder, the clinician sees few drug-dependent people who use only one drug. (Nicotine dependence may be an exception.) For example, among patients using an illicit drug, the most common additional diagnosis is alcohol dependence.

It is useful to distinguish among specific procedures or techniques (e.g., individual therapy, family therapy, group therapy, relapse prevention, and pharmacotherapy) and treatment programs. Most programs use a number of specific procedures and involve several professional disciplines as well as nonprofessionals who have special skills or personal experience with the substance problem being treated. The best treatment programs combine specific procedures and disciplines to meet the needs of the individual patient after a careful assessment. However, there is no generally accepted classification either for the specific procedures used in treatment or for programs making use of various combinations of procedures. This lack of standardized terminology for categorizing procedures and programs presents a problem, even when the field of interest is narrowed from substance problems in general to treatment for a single substance, such as alcohol, tobacco, or cocaine. Except in carefully monitored research projects, even the definitions of specific procedures (e.g., individual counseling, group therapy, and methadone maintenance) tend to be so imprecise that one usually cannot infer just what transactions are supposed to occur. Nevertheless, for descriptive purposes, programs are often broadly grouped on the basis of one or more of their salient characteristics: whether the program is aimed at merely controlling acute withdrawal and consequences of recent drug use (detoxification) or is focused on longer-term behavioral change; whether the program makes extensive use of pharmacological interventions; and the degree to which the program is based on individual psychotherapy, AA or other 12-step principles, or therapeutic community principles. For example, government agencies recently categorized publicly funded treatment programs for drug dependence as either methadone maintenance (mostly outpatient), outpatient drug-free programs, therapeutic communities, or short-term inpatient programs. However, these broad descriptions mask as much as they reveal, tend to confuse the setting with the procedures, and obscure differences in the etiological models underlying the treatments used in different programs.

**Selecting a Treatment** Not all interventions are applicable to all varieties of substance use or dependence, and some of the more coercive interventions used for illicit drugs are not applicable to substances that are legally available, such as tobacco. Changes in addictive behaviors do not occur abruptly, but rather through a series of stages. Five stages in this gradual process has been proposed: precontemplation, contemplation, preparation, action, and maintenance. For some types of addiction the therapeutic alliance is enhanced when the treatment approach is tailored to the patient's stage or readiness to change. For some drug use disorders, a specific pharmacological agent may be an important

component of an intervention; for example, disulfiram, naltrexone (ReVia) or acamprostate for alcoholism; methadone, levomethadyl acetate (ORLAAM) (also called L- $\alpha$ -acetylmethadol [LAAM]) or buprenorphine (Buprenex) for heroin addiction; nicotine delivery devices or bupropion (Zyban) for tobacco dependence. Not all interventions are likely to be useful to health care professionals. For example, many youthful offenders with histories of drug use or dependence are now remanded to special facilities (boot camps), other programs for offenders (and sometimes for employees) rely almost exclusively on the deterrent effect of frequent urine testing, and a third group are built around religious conversion or rededication in a specific religious sect or denomination. In contrast to the numerous studies suggesting some value for brief interventions for smoking and for problem drinking, there are few controlled studies of brief interventions for those seeking treatment for dependence on illicit drugs.

In general, for those persons who are severely dependent on illicit opioids, brief interventions (such as a few weeks of detoxification, whether in or out of a hospital) have limited effect on outcome measured a few months later. Among patients dependent on cocaine or heroin, substantial reductions in illicit drug use, antisocial behaviors, and psychiatric distress are much more likely following treatment lasting at least 3 months. Such a time-in-treatment effect is seen across very different modalities, from residential therapeutic communities to ambulatory methadone maintenance programs. Although some patients appear to benefit from a few days or weeks of treatment, a substantial percentage of users of illicit drugs drop out (or are dropped) from treatment before they have achieved significant benefits. Some of the variance in outcome of treatment can be attributed to differences in the characteristics of patients entering treatment and by events and conditions following treatment. However, programs based on similar philosophical principles and using what seem to be similar therapeutic procedures vary greatly in effectiveness. Some of the differences among programs that seem to be similar reflect the range and intensity of services offered. Programs with professionally trained staffs that provide more-comprehensive services to patients with more severe psychiatric difficulties are more likely to be able to retain those patients in treatment and to help them to make positive changes. Differences in the skills of individual counselors and professionals can powerfully affect outcomes. Such generalizations concerning programs serving illicit drug users may not hold for programs dealing with those seeking treatment for alcohol or tobacco or even cannabis problems uncomplicated by heavy use of illicit drugs. In such cases, relatively brief periods of individual or group counseling can produce long-lasting reductions in drug use. The outcomes usually considered in programs dealing with illicit drugs have typically included measures of social functioning, employment, and criminal activity, as well as decreases in drug-using behavior. Treatment for alcoholism and other mental health problems generally has more limited expectations (e.g., reduction in alcohol use and symptoms of psychiatric disorders), although changes in the use of health care resources subsequent to treatment is sometimes an additional measure of treatment efficacy.

**Measuring Treatment Outcome** The latest published large multisite study of treatment, the Drug Abuse Treatment Outcome Study (DATOS, carried out from 1991 to 1993), interviewed patients at intake and 1, 3, and 12 months after treatment. As in previous multisite studies, sites selected were stable representatives of four major program types: drug-free outpatient, methadone maintenance, short-term residential (chemical dependency), and long-term residential (therapeutic community). Except at the methadone programs, which used group and individual counseling about equally, group counseling was

the common element of the other treatments. Some antidepressants and antipsychotic agents were used in the nonmethadone programs, but they were incidental.

This study found a lower level of services available to patients seeking treatment than were available a decade earlier. Also, the patients were older and more likely to have a variety of special medical problems (e.g., HIV positive, concurrent psychiatric disorders) and social needs (homelessness). Treatment outcomes were generally consistent with those of previous studies of drug treatment in the public sector. One year after treatment there were substantial decreases in drug use. Levels of weekly or daily cocaine use at 1 year were about 50 percent of pretreatment levels, with greater reduction for those who participated in treatment for 3 months or more. Daily heroin use was lower among patients who remained in methadone maintenance treatment than among those who left. Although cocaine use among patients treated with methadone was somewhat lower, the reduction could not be attributed to treatment. Alcohol and marijuana use did not decline significantly. There was also no apparent decrease in suicidal thoughts or increase in employment, and in contrast to a number of previous multisite studies, multivariate analysis in this study did not confirm the widely reported reduction in predatory and or high-risk sexual behaviors for those in methadone programs. Those who stayed in long-term residential treatment for 6 months or longer showed a major decrease in drug use from preadmission levels for all categories of drugs—66.4 to 22 percent for cocaine; 17.2 to 5.8 percent for heroin; alcohol and marijuana use reduced by more than half. These individuals also reported a 50 percent decrease in illegal activities and about a 10 percent increase in full-time employment.

In DATOS, outpatient drug-free and short-term inpatient programs had very few admissions in which the major drug problem was heroin; the most common presenting drug problem for both was cocaine, followed by alcohol and marijuana. Participation in the outpatient drug-free programs for 3 months or more was associated with a greater decrease in cocaine use at 1 year, (about 50 percent compared with those who stayed 3 months or less). But even 58 percent of those who stayed less than 3 months reported some decrease in cocaine use over preadmission levels. Patients who entered short-term inpatient programs also reported major decreases in drug use at 1 year, but there was no difference between those who stayed more than 2 weeks and those who stayed less than 2 weeks. Since the decision to enter any of the programs studied in DATOS was made by the patient, the study does not give much guidance to a clinician weighing a recommendation for a specific patient.

More guidance comes from a large-scale, random-assignment study of the treatment of alcoholics, which found that three distinct methods of delivering individual therapy over a 12-week period—12-step facilitation, cognitive-behavioral coping skills, and motivational enhancement (four sessions only)—produced comparable and generally quite favorable outcomes. Patient characteristics interacted significantly with the treatment in only one area, alcoholics with low-level psychiatric problems had better outcomes in terms of days of abstinence if assigned to 12-step facilitation rather than cognitive behavioral therapy. Patients who received individual therapy after a brief period of inpatient and intensive day-care treatment (aftercare) had better 1-year outcomes than those who began individual treatment as outpatients.

Currently, entry into treatment rarely reflects a truly informed choice aimed at matching the

characteristics and needs of the patient with the capacities and skills of a provider. Findings from studies of public-sector programs serving drug users with relatively few social supports show that more-intensive services, such as vocational, health, and mental health services, increase retention and produce better outcomes at follow-up.

**Influence of Philosophical Orientation** The kinds of therapeutic procedures deemed valuable or essential by treatment professionals are profoundly affected by their philosophical orientation. For example, one study found that many professionals who adhere to a disease model of substance dependence view reduction of denial, acceptance of disease, need for lifelong abstinence, commitment to recovery, and affiliation with AA as the most important elements of intervention. In contrast, dealing with responsibility, instilling motivation and confidence, teaching relapse prevention, and avoiding high-risk situations were rated highest by psychologists espousing a behavioral model of dependence. Until quite recently, even physicians were unlikely to view pharmacological interventions as having significant value in treating alcoholism or most other forms of drug dependence, although some physicians did prescribe various forms of nicotine for tobacco dependence.

Many controlled studies over many years have shown that the use of illicit opioids (heroin) can be markedly reduced by supervised administration of oral methadone or LAAM. Because of government regulations, the use of these agents is currently limited to practitioners and programs who have obtained special licenses; such programs and practices are rigidly regulated. Buprenorphine, a partial opioid agonist, is also effective. Data also show that naltrexone can reduce relapse rates for alcoholics following withdrawal. Controlled studies conducted in Europe show that acamprosate, a drug believed to act via actions on the glutamatergic system, can also reduce alcoholism relapse rates. However, to date, the pharmacological agents available to treat substance-related disorders have not been widely used, even when there are few regulatory barriers. The relatively indifferent or negative attitudes of physicians toward the use of pharmacological agents in the treatment of alcoholism and drug dependence may change if new and more effective medications become available at reasonable cost and unencumbered by burdensome government regulations. However, at present there seems to be only a modest correlation between the evidence showing that a given intervention or procedure is effective and the likelihood that it will be widely used.

**Treatment of Comorbidity—Integrated Versus Concurrent** The treatment of the severely mentally ill (primarily those with schizophrenia and schizoaffective disorders) who are also drug dependent continues to pose problems for clinicians. Although some special facilities have been developed that use both antipsychotic drugs and therapeutic community principles, for the most part specialized addiction agencies have difficulty treating these patients. Generally, integrated treatment in which the same staff can treat both the psychiatric disorder and the addiction is more effective than either parallel treatment (a mental health and a specialty addiction program providing care concurrently) or sequential treatment (treating either the addiction or the psychiatric disorder first and then dealing with the comorbid condition.)

**Services and Outcome** The extension of managed care into the public sector has produced a major reduction in the use of hospital-based detoxification and virtual disappearance of residential

rehabilitation programs for alcoholics. Unfortunately, managed-care organizations tend to assume that the relatively brief courses of outpatient counseling that are effective with private-sector alcoholic patients are also effective with patients who are dependent on illicit drugs and who have minimal social supports. For the present, the trend is to provide the care that costs least over the short term and to ignore studies showing that more services can produce better long-term outcomes.

Treatment is often a worthwhile social expenditure. For example, treatment of antisocial illicit drug users in outpatient settings can produce decreases in antisocial behavior and reductions in rates of HIV seroconversion that more than offset the treatment cost. Treatment in a prison setting can produce favorable decreases in postrelease costs associated with drug use and rearrests. Despite such evidence there are problems maintaining public support for treatment of substance dependence, both in the public and private sectors. This lack of support suggests that these problems continue to be viewed, at least in part, as moral failings rather than as medical disorders.

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**Table 11.1-1** Substance-Induced Mental Disorders Included Elsewhere in the Textbook

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Substance-induced disorders cause a variety of symptoms that are characteristic of other mental disorders. To facilitate differential diagnosis, the text and criteria for these other substance-induced disorders are included in the sections of DSM-IV and this textbook with disorders with which they share phenomenology:

Substance-induced delirium (see Chapter 10) is included in the "Delirium, Dementia, and Amnesic and Other Cognitive Disorders" section.

Substance-induced persisting dementia (see Chapter 10) is included in the "Delirium, Dementia, and Amnesic and Other Cognitive Disorders" section.

Substance-induced persisting amnesic disorder (see Chapter 10) is included in the "Delirium, Dementia, and Amnesic and Other Cognitive Disorders" section.

Substance-induced psychotic disorder (see Section 13.3) is included in the "Schizophrenia and Other Psychotic Disorders" section. (In DSM-III-R these disorders were classified as organic hallucinosis and organic delusional disorder.)

Substance-induced mood disorder (see Section 14.6) is included in the "Mood Disorders" section.

Substance-induced anxiety disorder (see Section 15.6) is included in the "Anxiety Disorders" section.

Substance-induced sexual dysfunction (see Section 19.1a) is included in the "Sexual and Gender Identity Disorders" section.

Substance-induced sleep disorder (see Chapter 21) is included in the "Sleep Disorders" section.

In addition, hallucinogen persisting perception disorder (flashbacks) (see Section 11.7) is included under hallucinogen-related disorder.

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**Table 11.1-2** ICD-10 Diagnostic Criteria for Abuse of Non-Dependence-Producing Substances

---

A wide variety of medicaments and folk remedies may be involved, but the particularly important groups are: psychotropic drugs that do not produce dependence, such as antidepressants; laxatives, and analgesics that may be purchased without medical prescription, such as aspirin and paracetamol. Although the medication may have been medically prescribed or recommended in the first instance, prolonged, unnecessary, and often excessive dosage develops, which is facilitated by the availability of the substances without medical prescription.

Persistent and unjustified use of these substances is usually associated with unnecessary expense, often involves unnecessary contacts with medical professionals or supporting staff, and is sometimes marked by the harmful physical effects of the substances. Attempts to discourage or forbid the use of the substance are often met with resistance; for laxatives and analgesics this may be in spite of warnings about (or even the development of) physical harm such as renal dysfunction or electrolyte disturbances. Although it is usually clear that the patient has a strong motivation to take the substance, no dependence or withdrawal symptoms develop as in the case of the psychoactive substances specified in mental and behavioral disorders due to psychoactive substance use.

Identify the type of substance involved:

**Antidepressants**

(such as tricyclic and tetracyclic antidepressants and monoamine oxidase inhibitors)

**Laxatives**

**Analgesics**

(such as aspirin, paracetamol, phenacetin, not specified as psychoactive mental and behavioral disorders due to psychoactive substance use)

**Antacids**

**Vitamins**

**Steroids or hormones**

**Specific herbal or folk remedies**

**Other substances that do not produce dependence**

(such as diuretics)

**Unspecified**

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**Table 11.1-3** DSM-IV Diagnostic Criteria for Substance Dependence

---

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

- (1) tolerance, as defined by either of the following:
  - (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect
  - (b) markedly diminished effect with continued use of the same amount of the substance
- (2) withdrawal, as manifested by either of the following:
  - (a) the characteristic withdrawal syndrome for the substance (refer to criteria A and B of the criteria sets for withdrawal from the specific substances)
  - (b) the same (or closely related) substance is taken to relieve or avoid withdrawal symptoms
- (3) the substance is often taken in larger amounts or over a longer period than was intended
- (4) there is a persistent desire or unsuccessful effort to cut down or control substance use
- (5) a great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects
- (6) important social, occupational, or recreational activities are given up or reduced because of substance use
- (7) the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption)

*Specify if:*

**With physiological dependence:** evidence of tolerance or withdrawal (i.e., either item 1 or 2 is present)

**Without physiological dependence:** no evidence of tolerance or withdrawal (i.e., neither item 1 nor 2 is present)

*Course specifiers:*

**Early full remission**

**Early partial remission**

**Sustained full remission**

**Sustained partial remission**

**On agonist therapy**

**In a controlled environment**

**Sustained partial remission  
On agonist therapy  
In a controlled environment**

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**Mental and behavioral disorders due to use of alcohol**  
**Mental and behavioral disorders due to use of opioids**  
**Mental and behavioral disorders due to use of cannabinoids**  
**Mental and behavioral disorders due to use of sedatives or hypnotics**  
**Mental and behavioral disorders due to use of cocaine**  
**Mental and behavioral disorders due to use of other stimulants, including caffeine**  
**Mental and behavioral disorders due to use of hallucinogens**  
**Mental and behavioral disorders due to use of tobacco**  
**Mental and behavioral disorders due to use of volatile solvents**  
**Mental and behavioral disorders due to multiple drug use and use of other psychoactive substances**

**Acute intoxication**

- G1. There must be clear evidence of recent use of a psychoactive substance (or substances) at sufficiently high dose levels to be consistent with intoxication.
- G2. There must be symptoms or signs of intoxication compatible with the known actions of the particular substance (or substances), as specified below, and of sufficient severity to produce disturbances in the level of consciousness, cognition, perception, affect, or behavior that are of clinical importance.
- G3. The symptoms or signs present cannot be accounted for by a medical disorder unrelated to substance use, and are not better accounted for by another mental or behavioral disorder.

Acute intoxication frequently occurs in persons who have more persistent alcohol- or drug-related problems in addition. Where there are such problems, e.g., harmful use, dependence syndrome, or psychotic disorder, they should also be recorded.

The following may be used to indicate whether the acute intoxication was associated with any complications:

**Uncomplicated**

Symptoms are of varying severity, usually dose dependent.

With trauma or other bodily injury

With other medical complications

Examples are hematemesis, inhalation of vomit.

With delirium

With perceptual distortions

With coma

With convulsions

**Pathological intoxication**

Applies only to alcohol

**Acute intoxication due to use of alcohol**

- A. The general criteria for acute intoxication must be met.
- B. There must be dysfunctional behavior as evidenced by at least one of the following:
  - (1) disinhibition
  - (2) argumentativeness
  - (3) aggression
  - (4) lability of mood
  - (5) impaired attention
  - (6) impaired judgment
  - (7) interference with personal functioning
- C. At least one of the following signs must be present:
  - (1) unsteady gait
  - (2) difficulty in standing
  - (3) slurred speech
  - (4) nystagmus
  - (5) decreased level of consciousness (e.g., stupor, coma)
  - (6) flushed face
  - (7) conjunctival injection

**Comment**

When severe, acute alcohol intoxication may be accompanied by hypotension, hypothermia, and depression of the gag reflex. If desired, the blood alcohol level may be specified.

**Pathological alcohol intoxication**

*Note.* The status of this condition is being examined. These research criteria must be regarded as tentative.

- A. The general criteria for acute intoxication must be met, with the exception that pathological intoxication occurs after drinking amounts of alcohol insufficient to cause intoxication in most people.
- B. There is verbally aggressive or physically violent behavior that is not typical of the person when sober.
- C. The intoxication occurs very soon (usually a few minutes) after consumption of alcohol.
- D. There is no evidence of organic cerebral disorder or other mental disorders.

**Comment**

This is an uncommon condition. The blood alcohol levels found in this disorder are lower than those that would cause acute intoxication in most people, e.g., below 40 mg/100 mL.

**Acute intoxication due to use of opioids**

- A. The general criteria for acute intoxication must be met.
- B. There must be dysfunctional behavior, as evidenced by at least one of the following:
  - (1) apathy and sedation
  - (2) disinhibition
  - (3) psychomotor retardation
  - (4) impaired attention
  - (5) impaired judgment
  - (6) interference with personal functioning
- C. At least one of the following signs must be present:
  - (1) drowsiness
  - (2) slurred speech
  - (3) pupillary constriction (except in anoxia from severe overdose, when pupillary dilatation occurs)
  - (4) decreased level of consciousness (e.g., stupor, coma)

**Comment**

When severe, acute opioid intoxication may be accompanied by respiratory depression (and hypoxia), hypotension, and hypothermia.

**Acute intoxication due to use of cannabinoids**

- A. The general criteria for acute intoxication must be met.
- B. There must be dysfunctional behavior or perceptual abnormalities, including at least one of the following:
  - (1) euphoria and disinhibition
  - (2) anxiety or agitation
  - (3) suspiciousness or paranoid ideation
  - (4) temporal slowing (a sense that time is passing very slowly, and/or the person is experiencing a rapid flow of ideas)
  - (5) impaired judgment
  - (6) impaired attention
  - (7) impaired reaction time
  - (8) auditory, visual, or tactile illusions
  - (9) hallucinations with preserved orientation
  - (10) depersonalization
  - (11) derealization
  - (12) interference with personal functioning
- C. At least one of the following signs must be present:
  - (1) increased appetite
  - (2) dry mouth
  - (3) conjunctival injection
  - (4) tachycardia

### Acute intoxication due to use of sedatives or hypnotics

- A. The general criteria for acute intoxication must be met.
- B. There is dysfunctional behavior, as evidenced by at least one of the following:
- (1) euphoria and disinhibition
  - (2) apathy and sedation
  - (3) abusiveness or aggression
  - (4) lability of mood
  - (5) impaired attention
  - (6) anterograde amnesia
  - (7) impaired psychomotor performance
  - (8) interference with personal functioning
- C. At least one of the following signs must be present:
- (1) unsteady gait
  - (2) difficulty in standing
  - (3) slurred speech
  - (4) nystagmus
  - (5) decreased level of consciousness (e.g., stupor, coma)
  - (6) erythematous skin lesions or blisters

#### Comment

When severe, acute intoxication from sedative or hypnotic drugs may be accompanied by hypotension, hypothermia, and depression of the gag reflex.

### Acute intoxication due to use of cocaine

- A. The general criteria for acute intoxication must be met.
- B. There must be dysfunctional behavior or perceptual abnormalities, as evidenced by at least one of the following:
- (1) euphoria and sensation of increased energy
  - (2) hypervigilance
  - (3) grandiose beliefs or actions
  - (4) abusiveness or aggression
  - (5) argumentativeness
  - (6) lability of mood
  - (7) repetitive stereotyped behaviors
  - (8) auditory, visual, or tactile illusions
  - (9) hallucinations, usually with intact orientation
  - (10) paranoid ideation
  - (11) interference with personal functioning
- C. At least two of the following signs must be present:
- (1) tachycardia (sometimes bradycardia)
  - (2) cardiac arrhythmias
  - (3) hypertension (sometimes hypotension)
  - (4) sweating and chills
  - (5) nausea or vomiting
  - (6) evidence of weight loss
  - (7) pupillary dilatation
  - (8) psychomotor agitation (sometimes retardation)
  - (9) muscular weakness
  - (10) chest pain
  - (11) convulsions

#### Comment

Interference with personal functioning is most readily apparent from the social interactions of cocaine users, which range from extreme gregariousness to social withdrawal.

### Acute intoxication due to use of other stimulants, including caffeine

- A. The general criteria for acute intoxication must be met.
- B. There must be dysfunctional behavior or perceptual abnormalities, as evidenced by at least one of the following:
- (1) euphoria and sensation of increased energy
  - (2) hypervigilance
  - (3) grandiose beliefs or actions

- (4) abusiveness or aggression
  - (5) argumentativeness
  - (6) lability of mood
  - (7) repetitive stereotyped behaviors
  - (8) auditory, visual, or tactile illusions
  - (9) hallucinations, usually with intact orientation
  - (10) paranoid ideation
  - (11) interference with personal functioning
- C. At least two of the following signs must be present:
- (1) tachycardia (sometimes bradycardia)
  - (2) cardiac arrhythmias
  - (3) hypertension (sometimes hypotension)
  - (4) sweating and chills
  - (5) nausea or vomiting
  - (6) evidence of weight loss
  - (7) pupillary dilatation
  - (8) psychomotor agitation (sometimes retardation)
  - (9) muscular weakness
  - (10) chest pain
  - (11) convulsions

#### Comment

Interference with personal functioning is most readily apparent from the social interactions of the substance users, which range from extreme gregariousness to social withdrawal.

### Acute intoxication due to use of hallucinogens

- A. The general criteria for acute intoxication must be met.
- B. There must be dysfunctional behavior or perceptual abnormalities, as evidenced by at least one of the following:
- (1) anxiety and fearfulness
  - (2) auditory, visual, or tactile illusions or hallucinations occurring in a state of full wakefulness and alertness
  - (3) depersonalization
  - (4) derealization
  - (5) paranoid ideation
  - (6) ideas of reference
  - (7) lability of mood
  - (8) hyperactivity
  - (9) impulsive acts
  - (10) impaired attention
  - (11) interference with personal functioning
- C. At least two of the following signs must be present:
- (1) tachycardia
  - (2) palpitations
  - (3) sweating and chills
  - (4) tremor
  - (5) blurring of vision
  - (6) pupillary dilatation
  - (7) incoordination

### Acute intoxication due to use of tobacco [acute nicotine intoxication]

- A. The general criteria for acute intoxication must be met.
- B. There must be dysfunctional behavior or perceptual abnormalities, as evidenced by at least one of the following:
- (1) insomnia
  - (2) bizarre dreams
  - (3) lability of mood
  - (4) derealization
  - (5) interference with personal functioning
- C. At least one of the following signs must be present:
- (1) nausea or vomiting
  - (2) sweating
  - (3) tachycardia
  - (4) cardiac arrhythmias

### Acute intoxication due to use of volatile solvents

- A. The general criteria for acute intoxication must be met.
- B. There must be dysfunctional behavior, evidenced by at least one of the following:
  - (1) apathy and lethargy
  - (2) argumentativeness
  - (3) abusiveness or aggression
  - (4) lability of mood
  - (5) impaired judgment
  - (6) impaired attention and memory
  - (7) psychomotor retardation
  - (8) interference with personal functioning
- C. At least one of the following signs must be present:
  - (1) unsteady gait
  - (2) difficulty in standing
  - (3) slurred speech
  - (4) nystagmus
  - (5) decreased level of consciousness (e.g., stupor, coma)
  - (6) muscle weakness
  - (7) blurred vision or diplopia

#### Comment

Acute intoxication from inhalation of substances other than solvents should also be coded here.

When severe, acute intoxication from volatile solvents may be accompanied by hypotension, hypothermia, and depression of the gag reflex.

### Acute intoxication due to multiple drug use and use of other psychoactive substances

This category should be used when there is evidence of intoxication caused by recent use of other psychoactive substances (e.g., phencyclidine) or of multiple psychoactive substances where it is uncertain which substance has predominated.

#### Harmful use

- A. There must be clear evidence that the substance use was responsible for (or substantially contributed to) physical or psychological harm, including impaired judgment or dysfunctional behavior, which may lead to disability or have adverse consequences for interpersonal relationships.
- B. The nature of the harm should be clearly identifiable (and specified).
- C. The pattern of use has persisted for at least 1 month or has occurred repeatedly within a 12-month period.
- D. The disorder does not meet the criteria for any other mental or behavioral disorder related to the same drug in the same time period (except for acute intoxication).

#### Dependence syndrome

- A. Three or more of the following manifestations should have occurred together for at least 1 month or, if persisting for periods of less than 1 month, should have occurred together repeatedly within a 12-month period:
  - (1) a strong desire or sense of compulsion to take the substance
  - (2) impaired capacity to control substance-taking behavior in terms of its onset, termination, or levels of use, as evidenced by: the substance being often taken in larger amounts or over a longer period than intended; or by a persistent desire or unsuccessful efforts to reduce or control substance use
  - (3) a physiological withdrawal state when substance use is reduced or ceased, as evidenced by the characteristic withdrawal syndrome for the substance, or by use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms
  - (4) evidence of tolerance to the effects of the substance, such that there is a need for significantly increased amounts of the substance to achieve intoxication or the desired effect, or a marked diminished effect with continued use of the same amount of the substance;

- (5) preoccupation with substance use, as manifested by important alternative pleasures or interests being given up or reduced because of substance use; or a great deal of time being spent in activities necessary to obtain, take, or recover from the effects of the substance
- (6) persistent substance use despite clear evidence of harmful consequences, as evidenced by continued use when the individual is actually aware, or may be expected to be aware, of the nature and extent of harm

Diagnosis of the dependence syndrome may be further specified by the following:

Currently abstinent

Early remission

Partial remission

Full remission

Currently abstinent but in a protected environment (e.g., in hospital, in a therapeutic community, in prison, etc.)

Currently on a clinically supervised maintenance or replacement regime (controlled dependence) (e.g., with methadone; nicotine gum or nicotine patch)

Currently abstinent, but receiving treatment with aversive or blocking drugs (e.g., naltrexone or disulfiram)

Currently using the substance (active dependence)

Without physical features

With physical features

The course of the dependence may be further specified, if desired, as follows:

Continuous use

Episodic use (dipsomania)

#### Withdrawal state

- G1. There must be clear evidence of recent cessation or reduction of substance use after repeated, and usually prolonged and/or high-dose, use of that substance.
- G2. Symptoms and signs are compatible with the known features of a withdrawal state from the particular substance or substances (see below).
- G3. Symptoms and signs are not accounted for by a medical disorder unrelated to substance use, and not better accounted for by another mental or behavioral disorder.

The diagnosis of withdrawal state may be further specified by using the following:

Uncomplicated

With convulsions

#### Alcohol withdrawal state

A. The general criteria for withdrawal state must be met.

B. Any three of the following signs must be present:

- (1) tremor of the tongue, eyelids, or outstretched hands
- (2) sweating
- (3) nausea, retching, or vomiting
- (4) tachycardia or hypertension
- (5) psychomotor agitation
- (6) headache
- (7) insomnia
- (8) malaise or weakness
- (9) transient visual, tactile, or auditory hallucinations or illusions
- (10) grand mal convulsions

#### Comment

If delirium is present, the diagnosis should be alcohol withdrawal state with delirium (delirium tremens).



### Opioid withdrawal state

- A. The general criteria for withdrawal state must be met. (Note that an opioid withdrawal state may also be induced by administration of an opioid antagonist after a brief period of opioid use.)
- B. Any three of the following signs must be present:
- (1) craving for an opioid drug
  - (2) rhinorrhea or sneezing
  - (3) lacrimation
  - (4) muscle aches or cramps
  - (5) abdominal cramps
  - (6) nausea or vomiting
  - (7) diarrhea
  - (8) pupillary dilatation
  - (9) piloerection, or recurrent chills
  - (10) tachycardia or hypertension
  - (11) yawning
  - (12) restless sleep

### Cannabinoid withdrawal state

*Note.* This is an ill-defined syndrome for which definitive diagnostic criteria cannot be established at the present time. It occurs following cessation of prolonged high-dose use of cannabis. It has been reported variously as lasting from several hours to up to 7 days.

Symptoms and signs include anxiety, irritability, tremor of the outstretched hands, sweating, and muscle aches.

### Sedative or hypnotic withdrawal state

- A. The general criteria for withdrawal state must be met.
- B. Any three of the following signs must be present:
- (1) tremor of the tongue, eyelids, or outstretched hands
  - (2) nausea or vomiting
  - (3) tachycardia
  - (4) postural hypotension
  - (5) psychomotor agitation
  - (6) headache
  - (7) insomnia
  - (8) malaise or weakness
  - (9) transient visual, tactile, or auditory hallucinations or illustrations
  - (10) paranoid ideation
  - (11) grand mal convulsions

### Comment

If delirium is present, the diagnosis should be sedative or hypnotic withdrawal state with delirium.

### Cocaine withdrawal state

- A. The general criteria for withdrawal state must be met.
- B. There is dysphoric mood (for instance, sadness or anhedonia).
- C. Any two of the following signs must be present:
- (1) lethargy and fatigue
  - (2) psychomotor retardation or agitation
  - (3) craving for cocaine
  - (4) increased appetite
  - (5) insomnia or hypersomnia
  - (6) bizarre or unpleasant dreams

### Withdrawal state from other stimulants, including caffeine

- A. The general criteria for withdrawal state must be met.
- B. There is dysphoric mood (for instance, sadness or anhedonia).
- C. Any two of the following signs must be present:
- (1) lethargy and fatigue
  - (2) psychomotor retardation or agitation
  - (3) craving for stimulant drugs
  - (4) increased appetite
  - (5) insomnia or hypersomnia
  - (6) bizarre or unpleasant dreams

### Hallucinogen withdrawal state

*Note:* There is no recognized hallucinogen withdrawal state.

### Tobacco withdrawal state

- A. The general criteria for withdrawal state must be met.
- B. Any two of the following signs must be present:
- (1) craving for tobacco (or other nicotine-containing products)
  - (2) malaise or weakness
  - (3) anxiety
  - (4) dysphoric mood
  - (5) irritability or restlessness
  - (6) insomnia
  - (7) increased appetite
  - (8) increased cough
  - (9) mouth ulceration
  - (10) difficulty in concentrating

### Volatile solvents withdrawal state

*Note:* There is inadequate information on withdrawal states from volatile solvents for research to be formulated.

### Multiple drugs withdrawal state

#### Withdrawal state with delirium

A. The general criteria for withdrawal state must be met.

B. The criteria for delirium must be met.

The diagnosis of withdrawal state with delirium may be further specified by using the following:

Without convulsions

With convulsions

#### Psychotic disorder

- A. Onset of psychotic symptoms must occur during or within 2 weeks of substance use.
- B. The psychotic symptoms must persist for more than 48 hours.
- C. Duration of the disorder must not exceed 6 months.

The diagnosis of psychotic disorder may be further specified by using the following:

Schizophrenia-like

Predominantly delusional

Predominantly hallucinatory

Predominantly polymorphic

Predominantly depressive symptoms

Predominantly manic symptoms

Mixed

For research purposes it is recommended that change of the disorder from a nonpsychotic to a clearly psychotic state further specified as either abrupt (onset within 48 hours) acute (onset in more than 48 hours but less than 2 weeks).

#### Amnesic syndrome

- A. Memory impairment is manifest in both:
- (1) a defect of recent memory (impaired learning of new material) to a degree sufficient to interfere with daily living
  - (2) a reduced ability to recall past experiences
- B. All of the following are absent (or relatively absent):
- (1) defect in immediate recall (as tested, for example, by the digit span)
  - (2) clouding of consciousness and disturbance of attention, as defined in delirium, not induced by alcohol and other psychoactive substances, criterion A
  - (3) global intellectual decline (dementia).
- C. There is no objective evidence from physical and neurological examination, laboratory tests, or history of a disorder or disease of the brain (especially involving bilaterally the diencephalic and medial temporal structures), other than that related to substance use, that can reasonably be presumed to be responsible for the clinical manifestations described under criterion A.

**Residual and late-onset psychotic disorder**

- A. Conditions and disorders meeting the criteria for the individual syndromes listed below should be clearly related to substance use. Where onset of the condition or disorder occurs subsequent to use of psychoactive substances, strong evidence should be provided to demonstrate a link.

**Comments**

In view of the considerable variation in this category, the characteristics of such residual states or conditions should be clearly documented in terms of their type, severity, and duration. For research purposes full descriptive details should be specified.

If required, use as follows:

Flashbacks

Personality or behavior disorder

- B. The general criteria for personality and behavioral disorder due to brain disease, damage and dysfunction must be met.

Residual affective disorder

- B. The criteria for organic mood (affective) disorder must be met.

Dementia

- B. The general criteria for dementia must be met.

Other persisting cognitive impairment

- B. The criteria for mild cognitive disorder must be met, except for the exclusion of psychoactive substance use in criterion D.

Late-onset psychotic disorder

- B. The general criteria for psychotic disorder must be met, except with regard to the onset of the disorder, which is more than 2 weeks but not more than 6 weeks after substance use.

**Other mental and behavioral disorders****Unspecified mental and behavioral disorder**

**Table 11.1-5** DSM-IV Diagnostic Criteria for Polysubstance Dependence

---

This diagnosis is reserved for behavior during the same 12-month period in which the person was repeatedly using at least three groups of substances (not including caffeine and nicotine), but no single substance predominated. Further, during this period, the dependence criteria were met for substances as a group but not for any specific substance.

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**Table 11.1-6** DSM-IV Diagnostic Criteria for Other (or Unknown) Substance-Related Disorders

The other (or unknown) substance-related disorders category is for classifying substance-related disorders associated with substances not listed above. Examples of these substances, which are described in more detail below, include anabolic steroids, nitrite inhalants (“poppers”), nitrous oxide, over-the-counter and prescription medications not otherwise covered by the 11 categories (e.g., cortisol, antihistamines, benzotropine), and other substances that have psychoactive effects. In addition, this category may be used when the specific substance is unknown (e.g., an intoxication after taking a bottle of unlabeled pills).

**Anabolic steroids** sometimes produce an initial sense of enhanced well-being (or even euphoria), which is replaced after repeated use by lack of energy, irritability, and other forms of dysphoria. Continued use of these substances may lead to more severe symptoms (e.g., depressive symptomatology) and general medical conditions (liver disease).

**Nitrite inhalants** (“poppers”—forms of amyl, butyl, and isobutyl nitrite) produce an intoxication that is characterized by a feeling of fullness in the head, mild euphoria, a change in the perception of time, relaxation of smooth muscles, and a possible increase in sexual feelings. In addition to possible compulsive use, these substances carry dangers of potential impairment of immune functioning, irritation of the respiratory system, a decrease in the oxygen-carrying capacity of the blood, and a toxic reaction that can include vomiting, severe headache, hypotension, and dizziness.

**Nitrous oxide** (“laughing gas”) causes rapid onset of an intoxication that is characterized by lightheadedness and a floating sensation that clears in a matter of minutes after administration is stopped. There are reports of temporary but clinically relevant confusion and reversible paranoid states when nitrous oxide is used regularly.

Other substances that are capable of producing mild intoxication include **catnip**, which can produce states similar to those observed with marijuana and which in high doses is reported to result in LSD-type perceptions; **betel nut**, which is chewed in many cultures to produce a mild euphoria and floating sensation; and **kava** (a substance derived from the South Pacific pepper plant), which produces sedation, incoordination, weight loss, mild forms of hepatitis, and lung abnormalities. In addition, individuals can develop dependence and impairment through repeated self-administration of **over-the-counter** and **prescription drugs**, including **cortisol**, **antiparkinsonian agents** that have anticholinergic properties, and **antihistamines**.

Texts and criteria sets have already been provided to define the generic aspects of substance dependence, substance abuse, substance intoxication, and substance withdrawal that are applicable across classes of substances. The other (or unknown) substance-induced disorders are described in the sections of the manual with disorders with

which they share phenomenology (e.g., other (or unknown) substance-induced mood disorder is included in the mood disorders section). Listed below are the other (or unknown) substance use disorders and the other (or unknown) substance-induced disorders.

**Other (or unknown) substance use disorders**

**Other (or unknown) substance dependence**

**Other (or unknown) substance abuse**

**Other (or unknown) substance-induced disorders**

**Other (or unknown) substance intoxication**

*Specify if:*

With perceptual disturbances

**Other (or unknown) substance withdrawal**

*Specify if:*

With perceptual disturbances

**Other (or unknown) substance-induced delirium**

**Other (or unknown) substance-induced persisting dementia**

**Other (or unknown) substance-induced persisting amnestic disorder**

**Other (or unknown) substance psychotic disorder, with delusions**

*Specify if:*

With onset during intoxication

With onset during withdrawal

**Other (or unknown) substance-induced psychotic disorder, with hallucinations**

*Specify if:*

With onset during intoxication

With onset during withdrawal

**Other (or unknown) substance-induced mood disorder**

*Specify if:*

With onset during intoxication

With onset during withdrawal

**Other (or unknown) substance-induced anxiety disorder**

*Specify if:*

With onset during intoxication

With onset during withdrawal

**Other (or unknown) substance-induced sexual dysfunction**

*Specify if:*

With onset during intoxication

**Other (or unknown) substance-induced sleep disorder**

*Specify if:*

With onset during intoxication

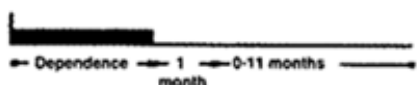
**Other (or unknown) substance-related disorder not otherwise specified**

**Table 11.1-7 DSM-IV Course Modifiers for Substance Dependence**

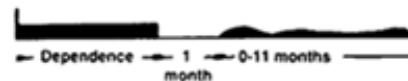
Six course specifiers are available for substance dependence. The four remission specifiers can be applied only after none of the criteria for substance dependence or substance abuse have been present for at least 1 month. The definition of these four types of remission is based on the interval of time that has elapsed since the cessation of dependence (early versus sustained remission) and whether there is continued presence of one or more of the items included in the criteria sets for dependence or abuse (partial versus full remission). Because the first 12 months following dependence is a time of particularly high risk for relapse, this period is designated early remission. After 12 months of early remission have passed without relapse to dependence, the person enters into sustained remission. For both early remission and sustained remission, a further designation of full is given if no criteria for dependence or abuse have been met during the period of remission; a designation of partial is given if at least one of the criteria for dependence or abuse has been met, intermittently or continuously, during the period of remission. The differentiation of sustained full remission from recovered (no current substance use disorder) requires consideration of the length of time since the last period of disturbance, the total duration of the disturbance, and the need for continued evaluation. If, after a period of remission or recovery, the individual again becomes dependent, the application of the early remission specifier requires that there again be at least 1 month in which no criteria for dependence or abuse are met. Two additional specifiers have been provided: on agonist therapy and in a controlled environment. For an individual to qualify for early remission after cessation of agonist therapy or release from a controlled environment, there must be a 1-month period in which none of the criteria for dependence or abuse are met.

The following remission specifiers can be applied only after no criteria for dependence or abuse have been met for at least 1 month. Note that these specifiers do not apply if the individual is on agonist therapy or in a controlled environment (see below).

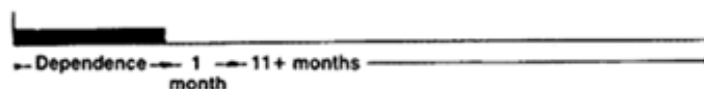
**Early full remission.** This specifier is used if, for at least 1 month, but for less than 12 months, no criteria for dependence or abuse have been met.



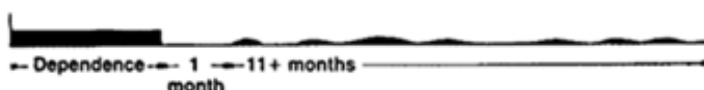
**Early partial remission.** This specifier is used if, for at least 1 month, but less than 12 months, one or more criteria for dependence or abuse have been met (but the full criteria for dependence have not been met).



**Sustained full remission.** This specifier is used if none of the criteria for dependence or abuse have been met at any time during a period of 12 months or longer.



**Sustained partial remission.** This specifier is used if full criteria for dependence have not been met for a period of 12 months or longer; however, one or more criteria for dependence or abuse have been met.



The following specifiers apply if the individual is on agonist therapy or in a controlled environment:

**On agonist therapy.** This specifier is used if the individual is on a prescribed agonist medication, and no criteria for dependence or abuse have been met for the class of medication for at least the past month (except tolerance to, or withdrawal from, the agonist). This category also applies to those being treated for dependence using a partial agonist or an agonist/antagonist.

**In a controlled environment.** This specifier is used if the individual is in an environment where access to alcohol and controlled substances is restricted, and no criteria for dependence or abuse have been met for at least the past month. Examples of these environments are closely supervised and substance-free jails, therapeutic communities, or locked hospital units.

**Table 11.1-8** DSM-IV Diagnostic Criteria for Substance Abuse

- 
- A. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:
- (1) recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)
  - (2) recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)
  - (3) recurrent substance-related legal problems (e.g., arrests for substance-related disorderly conduct)
  - (4) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of intoxication, physical fights)
- B. The symptoms above never met the criteria for substance dependence for this class of substance.
- 

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**Table 11.1-9** DSM-IV Diagnostic Criteria for Substance Withdrawal

- 
- A. The development of a substance-specific syndrome due to the cessation of (or reduction in) substance use that has been heavy and prolonged.
  - B. The substance-specific syndrome causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
  - C. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.
- 

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**Table 11.1-10** DSM-IV Diagnostic Criteria for Substance Intoxication

- 
- A. The development of a reversible substance-specific syndrome due to recent ingestion of (or exposure to) a substance. **Note:** Different substances may produce similar or identical syndromes.
  - B. Clinically significant maladaptive behavioral or psychological changes that are due to the effect of the substance on the central nervous system (e.g., belligerence, mood lability, cognitive impairment, impaired judgment, impaired social or occupational functioning) and develop during or shortly after use of the substance.
  - C. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.
- 

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**Table 11.1-11 DSM-IV Diagnoses Associated With Class of Substances**

	Depen- dence	Abuse	Intoxi- cation	With- drawal	Intoxi- cation Delirium	With- drawal Delirium	Dementia	Amnesic Disorders	Psychotic Disorders	Mood Dis- orders	Anxiety Disorders	Sexual Dys- functions	Sleep Dis- orders
Alcohol	X	X	X	X	I	W	P	P	I/W	I/W	I/W	I	I/W
Amphetamines	X	X	X	X	I				I	I/W	I	I	I/W
Caffeine			X								I		I
Cannabis	X	X	X		I				I		I		
Cocaine	X	X	X	X	I				I	I/W	I/W	I	I/W
Hallucinogens	X	X	X		I				I*	I	I		
Inhalants	X	X	X		I		P		I	I	I		
Nicotine	X			X									
Opioids	X	X	X	X	I				I	I		I	I/W
Phencyclidine	X	X	X		I				I	I	I		
Sedatives, hypnotics, or anxiolytics	X	X	X	X	I	W	P	P	I/W	I/W	W	I	I/W
Polysubstance	X												
Other	X	X	X	X	I	W	P	P	I/W	I/W	I/W	I	I/W

\* Also hallucinogen persisting perception disorder (flashbacks).

Note: X, I, W, I/W, or P indicates that the category is recognized in DSM-IV. In addition, I indicates that the specifier "with onset during intoxication" may be noted for the category (except for intoxication delirium); W indicates that the specifier "with onset during withdrawal" may be noted for the category (except for withdrawal delirium); and I/W indicates that either "with onset during intoxication" or "with onset during withdrawal" may be noted for the category. P indicates that the disorder is "persisting."

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Table 11.1-12 Use of Illicit Drugs, Alcohol, and Tobacco in the U.S. Population by Age Groups

Drug	Lifetime Use (%)				Past-Year Use (%)				Past-Month Use (%)			
	12 to 17	18 to 25	26 to 34	>35	12 to 17	18 to 25	26 to 34	>35	12 to 17	18 to 25	26 to 34	>35
Any illicit drug*	23.7	48.0	53.1	29.0	16.7	26.8	14.6	5.3	9.0	15.6	8.4	2.9
Marijuana and hashish	16.8	44.0	50.5	27.0	13.0	23.8	11.3	3.8	7.1	13.2	6.3	2.0
Cocaine	1.9	10.2	20.9	8.9	1.4	4.7	3.5	0.9	0.6	2.0	1.5	0.4
Crack	0.7	3.0	4.4	1.6	0.4	1.3	1.1	0.4	0.2	0.6	0.5	0.2
Inhalants	5.9	10.8	8.3	3.6	4.0	3.0	0.7	0.3	1.7	1.0	0.3	0.1
Hallucinogens	5.6	16.3	15.4	7.3	4.3	6.9	1.1	0.2	2.0	2.3	0.2	0.1
PCP	1.2	2.3	4.2	3.4	0.7	0.5	0.0	0.1	0.2	0.1	†	0.0
LSD	4.3	13.9	11.7	5.8	2.8	4.6	0.5	†	0.8	0.9	0.1	†
Heroin	0.5	1.3	1.3	1.2	0.3	0.9	0.2	0.0	0.2	0.4	0.1	0.0
Nonmedical use of any												
psychotherapeutic*	6.8	12.7	13.4	8.3	4.7	6.7	4.2	1.8	1.9	2.9	1.9	0.9
Stimulants	2.2	4.3	6.5	4.7	1.5	2.0	1.3	0.4	0.5	0.6	0.4	0.3
Sedatives	1.1	1.3	2.9	2.5	0.4	0.7	0.5	0.2	0.2	0.3	0.2	0.0
Tranquilizers	1.7	5.0	5.8	3.1	1.0	2.6	1.6	0.7	0.2	0.9	0.5	0.4
Analgesics	5.5	8.9	7.5	4.2	3.7	4.9	2.5	1.1	1.5	2.0	1.1	0.5
Any illicit drug other than marijuana <sup>§</sup>	13.0	26.6	30.2	15.1	9.3	12.7	7.2	2.7	4.6	6.3	3.6	1.4
Alcohol	38.8	83.8	90.3	87.8	32.7	75.3	77.2	64.9	18.8	60.0	61.6	51.7
"Binge" alcohol use <sup>¶</sup>	— <sup>†</sup>	—	—	—	—	—	—	—	7.2	32.0	22.8	11.3
Heavy alcohol use <sup>‡</sup>	—	—	—	—	—	—	—	—	2.9	12.9	7.1	3.8
Cigarettes	36.3	68.5	73.8	77.8	24.2	44.7	39.2	29.1	18.3	38.3	35.0	27.0
Smokeless tobacco	10.0	23.4	24.4	14.8	4.6	9.7	7.2	2.9	1.9	6.1	4.9	2.3

\* Use at least once of marijuana or hashish, cocaine (including crack), inhalants, hallucinogens (including PCP and LSD), heroin, or any prescription-type psychotherapeutic used nonmedically.

† Low precision; no estimate reported.

‡ Nonmedical use of any prescription-type stimulant, sedative, tranquilizer, or analgesic, does not include over-the-counter-drugs.

§ Use at least once of any of these listed drugs, regardless of marijuana use, marijuana users who also have used any of the other listed drugs are included.

¶ Drinking five or more drinks on the same occasion on at least 1 day in the past 30 days. "Occasion" means at the same time or within a couple hours of each other. Heavy alcohol use is defined as drinking five or more drinks on the same occasion on each of five or more days in the past 30 days, all heavy alcohol users are also "binge" alcohol users.

† Not available.

From National Household Survey on Drug Abuse, Substance Abuse and Mental Health Services Administration (SAMHSA) Office of Applied Studies, Department of Health and Human Services, preliminary data, June 1997.

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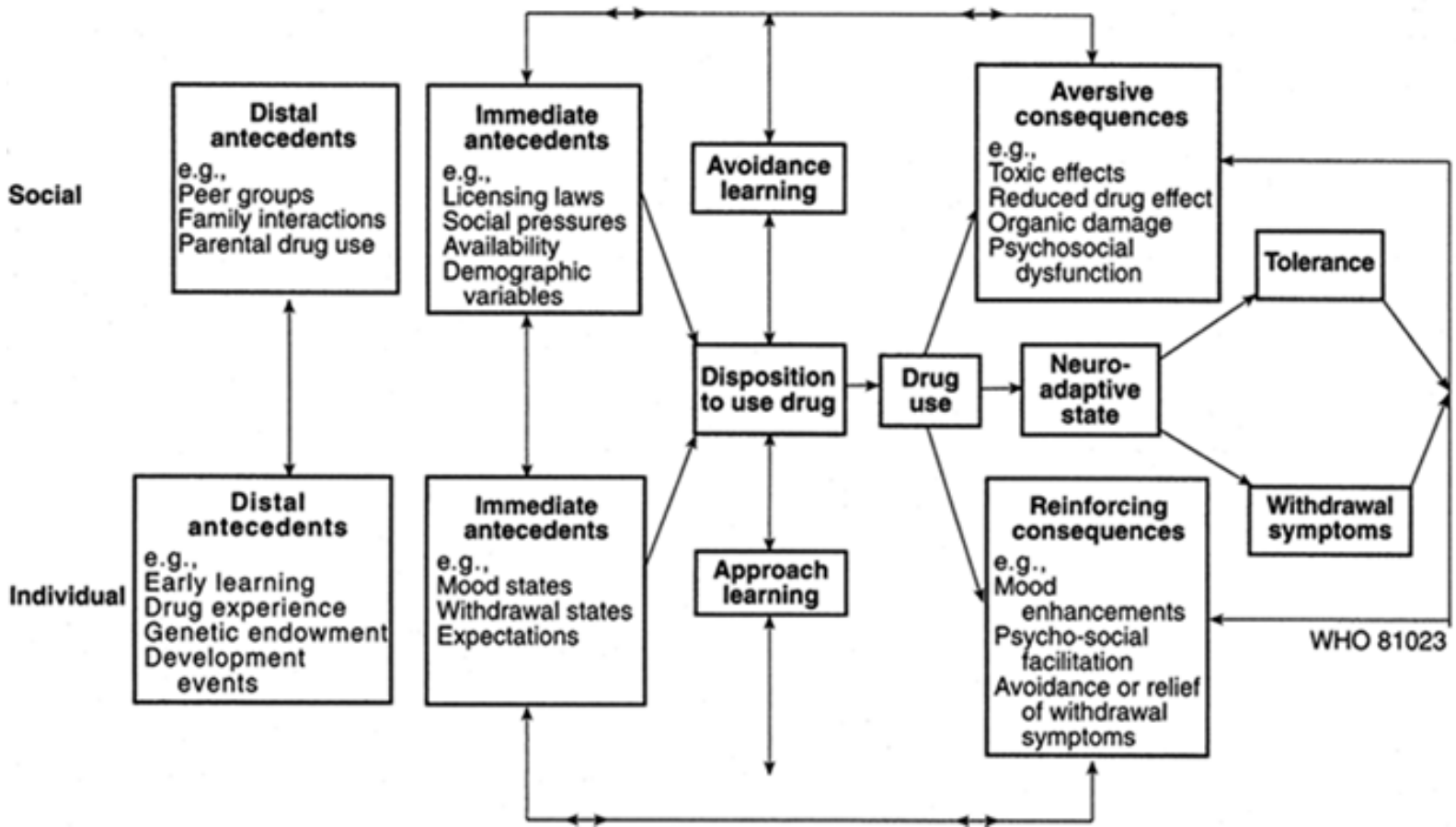
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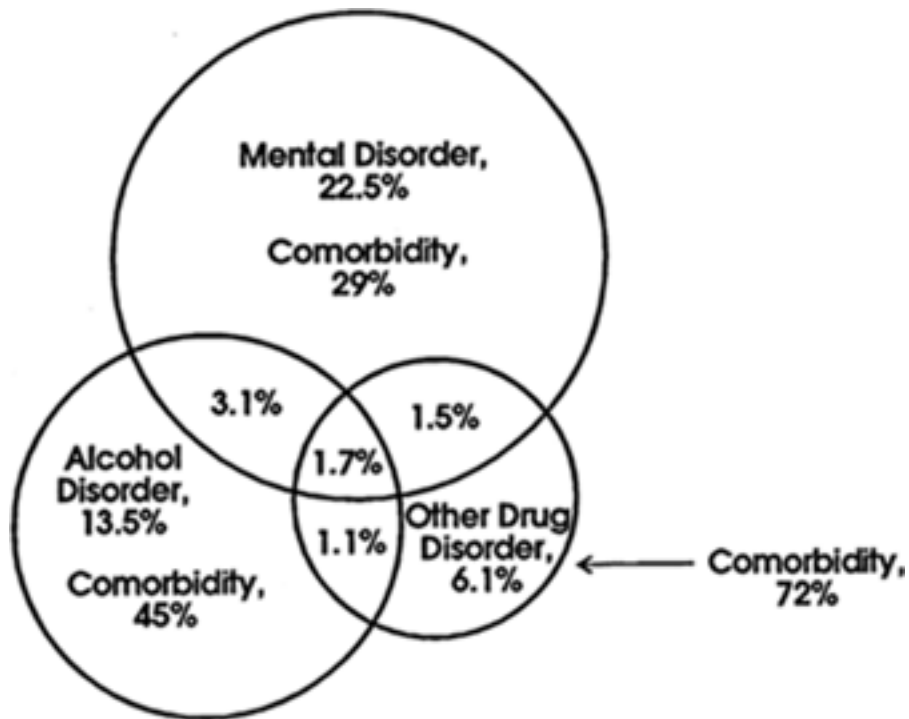
**SOCIAL AND INDIVIDUAL ANTECEDENTS**

**SOCIAL AND INDIVIDUAL CONSEQUENCES**



**FIGURE 11.1-1** WHO schematic model of drug use and dependence. (Reprinted with permission from Edwards G, Arif A, Hodgson R: Nomenclature and classification of drug- and alcohol-related problems. A WHO memorandum. Bull WHO 99:225, 1981.)

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**FIGURE 11.1-2** Lifetime prevalence of comorbid mental and addictive disorders in the United States, combined community and institutional five-site Epidemiologic Catchment Area data, standardized to the U.S. population. (Reprinted with permission from Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK: Comorbidity of mental disorders with alcohol and other drug abuse. JAMA 264:2511, 1990.)

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