<table>
<thead>
<tr>
<th>Attribute</th>
<th>Caffeine</th>
<th>Marijuana</th>
<th>Lysergic acid diethylamide</th>
<th>Chlorpromazine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discriminable interoceptive (subjective) effects</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Produce dose-related increases in self-reported &quot;liking&quot; scores</td>
<td>Griffiths, Bigelow, Liebson et al. (1990), Chait and Griffiths (1983), Griffiths and Woodson (1988b)</td>
<td>+</td>
<td>+</td>
<td>?</td>
</tr>
<tr>
<td>Produce elevated response on MBG (euphoria) scale of ARC inventory</td>
<td>Chait and Griffiths (1983)</td>
<td>-</td>
<td>Higgins and Stitzer (1986), Cone et al. (1986)</td>
<td>-</td>
</tr>
<tr>
<td>Positive reinforcer in animal drug self-administration studies</td>
<td>Deneau et al. (1969), Griffiths and Woodson (1988b)</td>
<td>-</td>
<td>Harris et al. (1974)</td>
<td>-</td>
</tr>
<tr>
<td>Place conditioning</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Attribute</td>
<td>Caffeine</td>
<td>Marijuana</td>
<td>Lysergic acid diethylamide</td>
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<tr>
<td>Therapeutic use in treatment of medical disorder</td>
<td>+ AMA (1983), Gilman et al. (1980), Medical Economics Company (1987), and others</td>
<td>+ AMA (1983), Gilman et al. (1980), Medical Economics Company (1987), and others</td>
<td>+？ AMA (1983), Gilman et al. (1980), Medical Economics Company (1987), and others</td>
<td>+？AMA (1983), Gilman et al. (1980), Medical Economics Company (1987), and others</td>
</tr>
</tbody>
</table>

NOTE: + indicates that drug administration produces the effect; – indicates that drug administration does not produce the effect; ? indicates that available scientific data are inadequate to draw a conclusion.

* Further discussion can be found in other chapters of this Report.

1 *As aid to stop cigarette smoking and to treat nicotine dependence.*

2 As topical anesthetic (rarely used) for ear, nose, eye, and throat.

3 (1) As strong analgesic for treatment of both acute and chronic pain; (2) treatment for myocardial infarction (analgesia, anxiolysis, and reduced left ventricular work load and myocardial oxygen requirements); (3) for obstetric analgesia; (4) as preanesthetic medication to smooth induction; (5) treatment for pulmonary edema; (6) as cough suppressant; (7) treatment for severe diarrhea.

4 (1) As antiseptic agent on skin, (2) intravenously to treat premature labor (uterine relaxant), (3) treatment of spasticity by local or intrathecal injection of dilute absolute alcohol solution, (4) as vehicle in dermatologic preparations (antiseptic action, astringent action, cooling effect), (5) treatment of alcohol withdrawal.

5 (1) Incorporated with over-the-counter analgesics (e.g., aspirin) to treat ordinary headache and relieve inflammatory pain (scant scientific data to substantiate); (2) in combination with ergot alkaloids to treat migraine headache; (3) in combination with sympathomimetic amines possessing anorectic properties in weight-loss medications; (4) as stimulant; (5) treatment (clinical trials) for preterm infant apnea of undetermined origin; (6) rarely for treatment of central nervous system depressant poisoning.

6 (1) As antihemorrhagic for cancer chemotherapy patients; (2) glaucoma treatment.
TABLE 8.—Continued

* None at present, but several proposed in past: (1) as psychotherapy aid, (2) as adjunct in alcohol and opioid addiction treatment, (3) as adjunct in terminal cancer patient therapy to reduce opioid analgesic need and induce tranquility.

* (1) Management of psychotic disorder manifestations, (2) treatment for nausea and vomiting, (3) relief of presurgery restlessness and apprehension, (4) treatment for acute, intermittent porphyria, (5) as adjunct in tetanus treatment, (6) to control mania manifestations in manic-depressive illness, (7) treatment for intractable hiccups, (8) treatment of children’s severe behavioral disorders characterized by combativeness or hyperexcitable behavior, (9) possible second-line treatment for nonpsychotic anxiety.

† “Liking” was not measured, but the increased scores on a tension and anxiety scale suggested dose-related “disliking.”
severe mood swings (Mello and Mendelson 1970; Mello 1968; Isbell et al. 1950); erratic supplies of opioids may be associated with sociopathic drug-seeking and withdrawal-related mood effects (Jasinski 1977); erratic supply of tobacco can also result in disruption of ongoing activities in an effort to obtain tobacco or as a consequence of withdrawal symptoms.

Consideration of multiple factors such as the dependence potential of a drug, the extent of its actual use, and the degree to which it produces adverse effects can be used to assess the overall liability associated with the use of a drug (i.e., "abuse liability") (Brady and Lukas 1984; Griffiths et al. 1985; Yanagita 1987). For example, caffeine produces only minimal (if any) disruptive behavioral or physiological effects and is not generally regarded as posing a serious public health problem even though self-administration may be widespread (e.g., caffeine in tea or coffee) (Griffiths and Woodson 1988a,b). In contrast, drugs which produce disruptive physiological and behavioral changes even when self-administered infrequently may be considered to represent a more serious health hazard (e.g., LSD). Drugs may fall anywhere on the continuum defined by these parameters, and the relative impact on health is most effectively determined by a comprehensive assessment of these interactive behavioral and physiological dimensions (Griffiths, Brady, Snell 1978b; Griffiths et al. 1986; Brady and Lukas 1984; Yanagita 1987).

Identification of Dependence-Producing Drugs

Independent of whether use of a substance has been observed to lead to addiction, it is possible to directly and objectively test a chemical to determine if it is addicting. Such tests provide data used by Federal (e.g., FDA, Drug Enforcement Administration) and International (e.g., WHO) agencies as to how to regulate chemicals. In fact, new drugs are usually evaluated and regulated ("scheduled") before they are ever made available for medical application. Such decisions rely heavily upon the known properties of addicting drugs and on the methods used to test for such properties (both described in this Chapter). Although the physicochemical structure of the drug is one determinant of the stimulus effects produced by drug administration, simply knowing the drug structure is rarely sufficient to predict the nature and magnitude of possible drug effects (Barnett, Trsic, Willette 1978); behavioral and physiological testing in animals and humans is usually necessary. When there is convergent evidence from multiple measures of dependence potential, then the drug is appropriately regarded as addicting or dependence producing. Whether humans outside the laboratory actually become addicted will depend on additional factors such as availability, price, and social acceptability of the drug (US DHHS 1987; also see discussion by Katz and Goldberg 1988).
Table 6 provides a comparison of several drugs in terms of the major measures that have been reviewed in this Chapter. As shown in the table, drugs known to produce widespread problems in a given population are characterized by positive responses with most of these measures (cocaíne, morphine-like drugs, alcohol, and nicotine). Conversely, drugs not contributing to such problems have fewer positive responses on the various tests (chlorpromazine). Intermediate drugs are associated with intermediate levels of difficulty in management of use.

Comparison Among Drugs

Within a given class of drugs, it is sometimes possible to rate their relative efficacy as reinforcers by how much behavior was affected (e.g., how many lever presses would occur or how much money would be paid) (Griffiths et al. 1981; Yanagita 1987). For instance, the slower onsetting/offsetting formulations of opioids, barbiturates, stimulants, and nicotine appear to have a lower dependence potential than the quicker onsetting and offsetting formulations (Jaffe 1985).

The practical generality of such comparisons, however, is limited because many other factors determine the overall level of dependence that might develop, the extent of social and/or personal damage, and the resulting level of social concern (Yanagita 1987; Katz and Goldberg 1988). For example, the increasing availability and decreasing relative price of cocaine in recent years are major factors contributing to increased levels of use and resultant social damage (US DHHS 1987). Analogously, the widespread ready availability and the relatively low cost of tobacco products and alcohol have probably contributed to the much higher rates of addiction and mortality associated with alcohol and tobacco than with drugs such as cocaine, even though cocaine may appear to be a more effective reinforcer in animals. Social or cultural factors may also contribute to the spread and levels of drug use. For example, sensational press reporting may have contributed to the popularization of barbiturates in the 1960s (Brecher 1972), and the mass marketing and advertising of tobacco products is likely to have contributed to the use of these products, especially among women and especially in the case of smokeless tobacco products (Ernster 1985, 1986; Warner 1986b; Davis 1987; Tye, Warner, Glantz 1987).

Four examples of drugs associated with striking changes in the prevalence of use among various populations as well as associated morbidity are: alcohol, for which use and associated diseases decreased during the Prohibition years early in the 20th century; lysergic acid diethylamide (LSD), for which use and associated hospitalizations were elevated during the 1960s; cocaine, for which use and associated hospitalizations increased during the 1970s
tobacco, in which consumption of smokeless tobacco products increased among youth in 1970s and cigarette consumption increased sharply among women in the 1950s and 1960s (US DHHS 1981, 1986; Appendix A). As discussed in the aforementioned references, the changes in use of these drugs were not due to changes in the pharmacologic actions of the drug or sudden changes in genetic constitution of the populations, but rather to changes in factors such as availability, cost, social acceptability, regulatory controls, marketing efforts, and general perceptions about the risks associated with use.

Finally, various other factors contribute to the level of social concern and may be only indirectly related or unrelated to the pharmacologic properties of the drug itself. For instance, the observations on transmission of AIDS by way of shared needles among i.v. drug users and on cancer caused by tobacco smoke carcinogens have greatly increased the liability of use attributed to these drugs in recent years.

Environmental Determinants of Drug Dependence Including Behavioral Conditioning

A common feature of use of all dependence-producing drugs is that the positive (satisfaction symptoms) and negative (e.g., withdrawal symptoms) effects may become conditioned responses to associated environmental stimuli. The implications of this are important for understanding the chronic and self-sustaining nature of drug dependencies. Such conditioning is a powerful behavioral mechanism by which the drug comes to control an increasing amount of the behavior of the drug user (Thompson and Schuster 1968; Goldberg 1976a).

Some of the important environmental determinants of drug dependence are discussed elsewhere in this Chapter in the context of drug self-administration studies. These factors include: (1) the behavioral or economic cost of the drug itself or of taking the drug, (2) direct pressure to take the drug by making other reinforcers contingent upon drug taking, and (3) the other ongoing activities of the person (e.g., demanding work schedule) that tend to enhance drug taking. The focus of the present Section is on environmental stimuli that may contribute to drug dependence by evoking urges to use drugs, and by eliciting bodily responses that mimic the usual effects of either drug taking or drug withdrawal reactions.
Drug Taking as a Learned Behavior

The interface between a drug and its effects is the behavior of obtaining and ingesting the drug. Such behavior is learned behavior, and as discussed earlier in this Chapter, many of the factors that modulate this behavior are similar to those which modulate other learned behaviors including eating, exercise, and occupational skills (Thompson and Schuster, 1968). Technically, drug taking is "operant behavior" and includes "respondent" or "classically conditioned" components. The basic governing principle of operant behavior is that it occurs in the context of certain stimuli and is either strengthened or weakened by the nature of the consequence (a positive reinforcer strengthens the response and a punisher weakens the response) (Skinner 1938, 1953). Thus, for example, a friend might offer a drug (antecedent stimulus); the drug is ingested (operant behavior or response); and the effects of the drug strengthen the behavior (positive reinforcement). Respondent conditioning occurs simultaneously and further contributes to the strength of the behavior (Bouton and Swartzentruber 1986). A drug might serve as an unconditioned stimulus which elicits a relatively involuntary response (e.g., nicotine and morphine can elicit feelings of pleasure and/or nausea); when physical dependence has occurred, drug abstinence can also elicit certain responses (e.g., anxiety and urges to take the drug). Any environmental or even internal stimulus can become part of this conditioning process by repeated association with the elicited response. For example, the taste of alcohol, the smell of smoke, "thinking" about use of the substance, and the sight of cocaine- or opioid-associated paraphernalia can elicit feelings associated with either the administration or withdrawal of the drug (Childress, McLellan, O'Brien 1986a,b; Ludwig 1986; Ludwig and Stark 1974; Erben 1977; Gotestam and Melin 1983; Pickens, Bigelow, Griffiths 1973; Rickard-Figueroa and Zeichner 1985; Levine 1974).

The simultaneous operation of both operant and respondent conditioning can converge to generate and maintain powerful chains of behavior over which the individual may have little control. As shown earlier in this Chapter, highly addicting drugs are those which are very effective at reinforcing behavior and eliciting responses. Their power can be increased by factors such as drug deprivation, which may be associated with a discomforting withdrawal syndrome. In the presence of withdrawal, the person may behave in a way to relieve the discomfort of a withdrawal syndrome; in this case the withdrawal syndrome itself may be said to be functioning as a negative reinforcer. When drugs are readily available, as with tobacco for most people or opioids for physicians, these behavioral conditioning processes may be very subtle because the drug can be taken in a pattern that avoids excessive discomfort. For example, early interoceptive or subjective withdrawal cues that
are evident upon waking in the morning signal that "it is time to smoke a cigarette," and thus the smoker neither "forgets to smoke" nor experiences pronounced withdrawal symptoms.

As implied by the foregoing discussion, the strength and persistence of drug-seeking behavior are not just functions of the drug itself or of withdrawal. Rather, they are determined by many factors, such as the number of times that certain responses are associated with certain stimuli, the presence or absence of such stimuli, the subjective discomfort occurring as part of withdrawal, and the availability of the drug. The convergence of so many environmental and subjective forces can result in extremely persistent behavior that may appear disproportionate to the pleasure actually experienced when the drug is taken (e.g., the few minutes of pleasure from the postdinner cigarette or when heroin is taken after 8 to 12 hr of deprivation). In fact, the subjective pleasure itself may be very mild, and the person may describe the role of the drug as "simply maintaining feelings of normalcy or comfort" and not as "getting high" per se. The scientific basis for these observations has been actively and systematically studied since the pioneering work of Wikler and others (Wikler 1973) and has been reported and reviewed in detail elsewhere (Goudie and Demellweek 1986; O'Brien, Ehrman, Ternes 1986; Grabowski and Cherek 1983; Grabowski and O'Brien 1981; Childress, McLellan, O'Brien 1986a,b; McLellan et al. 1986; Wikler 1973; Meyer and Mirin 1979).

**Drug-Associated Stimuli Modulate Drug Seeking**

Stimuli associated with drug effects may come to elicit ("trigger") those same effects or sometimes opposite effects (withdrawal responses). For example, increased heart rate induced by stimulant administration may become associated with multiple environmental stimuli—the color of the tablet, the individual who provided it, and the office environment in which the drug was taken. These stimuli may act alone or in concert. One stimulus may produce a slight heart rate change; two such stimuli may produce a larger change; and the presentation of many such stimuli may have a synergistic effect. Other stimuli may counteract or facilitate these effects (Schindler, Katz, Goldberg, in press).

The response produced in relation to environmental correlates may differ qualitatively from the direct drug effect. For instance, the direct effect of a drug may be a heart rate increase, whereas the conditioned or learned response to drug-associated stimuli may be either a decrease or an increase in heart rate. Changes may be particularly evident for agents with biphasic effects such as nicotine. Whatever the direction of change in response value, the events may be of physiological and behavioral significance (for example, see Childress, McLellan, O'Brien 1986a,b; O'Brien, Ehrman, Ternes...
1986; Stewart, de Wit, Eikelboom 1984; Grabowski and O'Brien 1981; Childress et al., in press). These complex conditioning processes which can function to precipitate drug taking appear to function similarly for a variety of drugs including opioids and tobacco (Ternes 1977).

Since the 1960s many researchers have shown that the role of associated stimuli is important for diverse biological reinforcers such as drugs, food, and sex. For example, Thompson and Schuster (1964) demonstrated that environmental stimuli paired with drugs could themselves come to generate drug seeking in monkeys. Schuster and Woods (1968), Davis and Smith (1976), and Carnathan, Meyer, and Cochin (1977) demonstrated that stimuli previously associated with drug taking could generate much drug-seeking behavior in animals during extinction of use when the drug is no longer available. Similar findings were obtained in a study of i.v. cocaine self-administration in which human volunteers emitted high rates of lever pressing in the presence of cocaine-associated stimuli when the drug was not available (Katz and Goldberg 1988).

Goldberg (1976b) reported that environmental stimuli associated with drug taking could help sustain substantial behavioral repertoires in monkeys often far in excess of the behavior that was maintained when just the drug was given. Similarly, Meisch found that the taste and smell of alcohol, which were normally found to be highly aversive to rats, became highly effective stimuli in their own right in the maintenance of alcohol-seeking behavior, even when alcohol was not actually available for the rats to consume (Meisch 1977). Lal and colleagues (1976) demonstrated that environmental stimuli previously associated with drug effects could, by producing drug-like responses, attenuate opiate withdrawal signs in rats. These and many other studies have shown conclusively that specific environmental stimuli associated with drug taking exert control over drug seeking, drug taking, and characteristics of the drug response itself.

Environmental conditions in many forms can contribute to sustained drug use, and specific stimulus conditions can have well-defined drug-like properties. This phenomenon, which has been well documented in laboratory settings, is recognized as being powerful in clinical pharmacology, in which "placebo" effects (conditioned responses to drug-taking conditions) may be dramatic and difficult to separate from so-called direct drug effects. Both direct drug effects and those established through learning influence physiology and behavior, thereby contributing to the strength of addictive behaviors. Recent reports suggest that conditioned effects can be attenuated for some individuals through effective treatment specifically designed to extinguish, or alter through learning, these responses (Childress, McLellan, O'Brien 1986a,b; McLellan et al. 1986).
The stimuli associated with drug effects also may generate further drug seeking and drug taking. Wikler (1973) and more recently Meyer and Mirin (1979) contributed substantially to both the conceptual framework and the data describing these complex phenomena. These investigators found that environmental stimuli which correlated with direct drug effects are pertinent to the acquisition, maintenance, and elimination of opioid taking by humans. Similar findings were observed in an intensive study of an alcoholic subject: alcohol-associated stimuli produced orderly responses including urges to drink and even drinking itself (Pickens, Bigelow, Griffiths 1973). A series of studies by Goldberg and his colleagues (Goldberg 1970; Goldberg, Kelleher, Morse 1975; Goldberg and Kelleher 1977; Goldberg, Spealman, Kelleher 1979) showed that environmental stimuli occasionally associated with morphine injections or with early withdrawal effects could lead to increased drug seeking and/or drug taking.

**Conditioned Withdrawal Symptoms May Precipitate Drug Seeking**

Wikler (1948) first described the discomfort of long-abstinent patients on their return to environments in which they had previously used drugs and experienced withdrawal symptoms. Subsequently, Wikler (1973), O'Brien (1975) and colleagues (O'Brien, Ehrman, Ternes 1986; O'Brien et al. 1975), and several other researchers (Siegel 1975, 1976, 1978; Eikelboom and Stewart 1979; Stewart, de Wit, Eikelboom 1984; Childress et al., in press) have made fundamental contributions to the identification of the complex interplay of factors modulating the physiological and behavioral components of abstinence. These and other studies have shown that the conditions established by abrupt withdrawal after chronic administration of a drug can serve as setting conditions which may result in further drug taking. In other words, for some individuals the onset or anticipation of abstinence symptoms may be strongly linked to reinitiation of drug self-administration. In turn, the drug effect reinforces the reinitiation of drug taking (Stewart, de Wit, Eikelboom 1984). Withdrawal symptoms and drug taking may thus become closely associated with a range of environmental stimuli. These stimuli then come to elicit abstinence symptoms and generate drug taking through a variety of powerful biobehavioral mechanisms. In fact, McNeill and colleagues (1986) have concluded that the pattern of abstinence symptoms itself may be in part determined by conditioning factors.

Environmental stimuli can lead to drug seeking by eliciting distressing conditioned withdrawal effects. Several thorough reviews on conditioning factors in drug dependence indicate that correlated behaviors and stimuli dramatically alter drug effects, withdrawal
symptoms, and other features of substance use behaviors (Goudie and Demellweek 1986; O'Brien, Ehrman, Ternes 1986; Grabowski and Cherek 1983; Grabowski and O'Brien 1981). These interacting factors have also been described in a number of prominent medical and scientific texts (Jaffe 1986, 1987), as well as in the recent Second Triennial Report to Congress from the Secretary, Department of Health and Human Services (US DHHS 1987).

One of the clearest observations of the contribution of environmental factors in tobacco withdrawal was made by Hatsukami, Hughes, and Pickens (1985). They noted that the number of withdrawal signs increased substantially when cessation occurred in the natural environment. Parallels exist in both laboratory research and naturalistic observation. Stitzer, Bigelow, and McCaul (1983) reviewed this literature and noted that individuals restrained from access to drugs for prolonged periods tend to return to use when the agents are again available; the implication is that environmental stimuli contribute to relapse. In a laboratory study, Thompson and Ostlund (1965) found that relapse to self-administration occurs rapidly for animals removed from, and then after extended periods returned to, the original environment but not for animals that undergo extinction of self-administration within that environment. In a reverse situation in humans, Robins, Davis, and Goodwin (1974) reported that individuals who experienced initial drug use in the stressful and ready-access conditions of the Vietnam war tended not to continue use on return to the United States.

**Relapse to Drug Dependence**

For many drug-dependent persons, achieving at least brief periods of drug abstinence is a readily achievable goal. Maintaining abstinence, or avoiding relapse, however, poses a much greater overall challenge. There is a substantial base of data for these conclusions. Treatment outcome reviews concerning opioid (Platt 1986), alcohol (Miller and Hester 1986a; Peele 1987), and tobacco (Brownell et al. 1986; Lichtenstein 1982; Schwartz 1987) dependence show that clinical interventions are often successful in producing short-term cessation of drug use but that relapse to use is a frequent posttreatment occurrence (Hunt, Barnett, Branch 1971; Brownell, Marlatt et al. 1986).

An important issue in the contemporary study of addictions is the degree to which relapse and recovery are generalizable across categories of substances (US DHHS 1986; Tims and Leukefeld 1986; Marlatt 1979; Miller and Hester 1986a,b; Schwartz 1987). This Section examines rates and predictors of relapse across drug classes with emphasis on comparisons among alcohol, opioids, and tobacco.
Implications of these observations for the prevention of relapse will be described in the next Section of this Chapter.

**Definition of Relapse**

In general, relapse refers to resumption of drug use following abstinence from such drug use; however, the criterion for abstinence and resumption of drug use must be specified. Principles for such specification are generally similar among drugs; however, there are drug-specific issues which complicate comparisons of data and will be discussed in this Section. Only when an individual has achieved criteria for abstinence is he or she "eligible" for the possibility of relapse. Defining abstinence over some time period as the eligibility criterion is useful because it permits distinctions to be drawn between continuous users and those who are able to "quit" drug use, however briefly. Definitions of "quit episodes" differ dramatically among published studies, leading to quite different interpretations of subsequent relapse. With regard to tobacco, a consensus conference, held under the auspices of the National Heart, Lung, and Blood Institute, recommended 24 hr of continuous abstinence from tobacco as the criterion for defining a quit episode and establishing eligibility for relapse to tobacco use (see Chapter VII). With regard to other dependence-producing drugs, patients of residential alcohol and drug abuse treatment facilities are usually deemed eligible for relapse at discharge without reference to the duration of treatment or abstinence.

Two general ways of defining relapse after a period of abstinence have appeared in the literature. Relapse has been defined as a discrete event occurring with the single use of a drug or as a process developing over time (Wesson, Havasy, Smith 1986). When relapse is defined as a discrete event, distinction is often made between first use of the primary drug of dependence and first use of any other psychoactive agent. Return to use of the primary drug holds clear potential for return to addiction (Hubbard and Marsden 1986). However, there has been less consensus regarding whether use of a substitute drug should be defined as relapse. When relapse is defined as occurring over time, the endpoint of the process has been variously defined as daily drug use for a specified period, a return to drug use at or above pretreatment or baseline level, a consequence of drug use such as readmission for treatment, a return to dependence defined by one or more diagnostic instruments, or a return to drug use at levels above criteria specified in terms of quantity and/or duration of drug use (APA 1987; Litman et al. 1983; Ossip-Klein et al. 1986; Simpson and Marsh 1986).

The choice of definition is also influenced by the treatment modality being evaluated and by the theoretical orientation of the investigator. For example, relapse is usually discretely defined in
clinical applications of aversive counterconditioning to treatment of alcohol and tobacco dependence (Boland, Mellor, Revusky 1978; Schwartz 1987). In contrast, investigations of skills training approaches to alcohol, tobacco, and other drug use treatment typically employ continuous or process measures of relapse, e.g., number of days of abstinence (Chaney, O'Leary, Marlatt 1978; Marlatt and Gordon 1985) because new skills are not lost after a slip but rather could be used repeatedly to reestablish abstinence (Catalano and Hawkins 1985).

Measurement of Relapse

Relapse is usually assessed by one of two measurement procedures (Wesson, Havassy, Smith 1986). Current drug use measures ascertain drug use at selected posttreatment intervals (e.g., 3, 6, and 12 months). Intermittent drug use occurring between these time intervals may not be captured by this procedure. Continuous status measures ascertain whether there was drug use at any point in the posttreatment interval. Current use measures typically yield higher abstinence rates than continuous status measures, because of the variable course of drug abuse careers (Pickens et al. 1985). Current use measures provide point-in-time estimates of relapse status among a sample of treated users, while continuous status measures allow for determining the percentage of individuals who have managed to achieve relatively enduring abstinence (Ossip-Klein et al. 1986). The implications of different measurement approaches for interpretation of relapse phenomena have been reviewed (Wells, Hawkins, Catalano, in press; Brownell et al. 1986).

While self-reported drug use status has been the primary method of detecting relapse, detection of the drug in biological fluids or in expired air is being used as an adjunct with increasing frequency (Wesson, Havassy, Smith 1986). As discussed earlier in this Chapter, biochemical methods of assessing drug use vary widely in their sensitivity and in the period during which drug use can be detected (Walsh and Yohay 1987).

Rates of Relapse

Hunt and his colleagues were the first to investigate commonalities in relapse processes among substances (Hunt, Barnett, Branch 1971; Hunt and Bespalec 1974; Hunt and General 1973; Hunt and Matarazzo 1970). They compared relapse rates for clients discharged from opiates, alcohol, and tobacco dependence treatment programs and noted the remarkable similarity of the relapse curves they obtained (Figure 2). Relapse was defined as any use of the primary drug of abuse. They then formulated a learning theory of relapse that was presumed to operate in alcohol, opioid, and tobacco dependence.
Although attempts to base theories of relapse on cumulative survival curves, such as those depicted in Figure 2, are complicated by a variety of factors (Litman, Eiser, Taylor 1979; Sutton 1979; Brownell et al. 1986), such curves do possess heuristic value. They indicate that abstinence rates fall precipitously in the early post-treatment period; that most treated smokers, alcoholics, and heroin addicts relapse to at least single use of the primary drug of use by 3-month follow-up; and that those who have maintained abstinence for at least 6 months are much less likely to relapse.

Similar large-scale reviews of relapse rates for multiple substances have not been published in recent years. Instead, a voluminous
literature has accrued regarding treatment effectiveness (Schwartz 1987; Miller and Hester 1986a; Platt 1986; Simpson and Sells 1982). However, data from studies of alcohol, opioid, and tobacco relapse consistently support the similarities in relapse rates and patterns across these three forms of drug dependence, as well as the operation of similar determinants of relapse. For instance, high rates of relapse characterize most treatment programs for dependence to opioids (Maddux and Desmond 1986; Platt 1986; McAuliffe 1975; McAuliffe et al. 1986; Waldorf 1983), alcohol (Belasco 1971; Bruun 1963; Robson, Paulus, Clarke 1965; van Dijk and van Dijk-Koffeman 1973; Vaillant 1982; Imber et al. 1976; Kendell and Staton 1966; Orford and Edwards 1977), and tobacco (Brandon, Tiffany, Baker 1986; Erickson, Rugg, Tunstall, Jones 1984; Hunt and Matarazzo 1973; Marlatt and Gordon 1985; Shumaker and Grunberg 1986; Schwartz 1969; see also Chapter VII). The remainder of this Section will address the parallel in the correlates of relapse to these three substances.

Correlates of Relapse

Factors found to be associated with relapse fall into three domains. Background or pretreatment factors are those that seem to heighten the individual's vulnerability to relapse (Shiffman et al. 1986). These variables may be measures of fixed pretreatment characteristics such as demographics and drug use history. Pretreatment factors appear to account for between 10 and 20 percent of the variance in posttreatment relapse (Cronkite and Moos 1980; Simpson, Savage, Lloyd 1979; Simpson and Sells 1982). Variables measured during treatment are also thought to influence the probability of relapse at posttreatment. These include treatment length, intensity, setting, type, and compliance with treatment. Treatment factors appear to account for 15 to 18 percent of the variance in drug abuse outcome studies (Simpson, Savage, Lloyd 1979). Posttreatment factors are those associated with the subject's posttreatment environment or internal state. These include degree of family support, drug use among peers, involvement in work and leisure activities, and emotional states. Posttreatment factors have been shown to account for roughly 50 percent of the variance in posttreatment relapses (Finney, Moos, Mewborn 1980) and thus may be the most important focus for relapse prevention efforts. The rest of this Section will review prominent relapse factors that have been systematically studied for opioids, alcohol, and tobacco.

Pretreatment Correlates of Relapse

Severity of Drug Dependence

Severity of pretreatment drug dependence is one determinant of the likelihood of relapse. Several studies have found that light
smokers are more likely to succeed at abstinence than heavy smokers (see Table 7 and Chapter VII). Similarly, with regard to opioid dependence, a shorter pretreatment period of dependence is associated with better posttreatment outcomes (Riordan et al. 1976), and level of drug craving was directly related to the amount of variance in relapse (McAuliffe et al. 1986). Estimating the contribution of severity of alcohol dependence to relapse is more problematic because there has been such a wide variety of measures (e.g., severity of social harm, illness, withdrawal, or craving) used among studies. Thus, the seven alcohol studies cited in Table 7 provide equivocal results, and it is unclear whether there is actually no relationship or whether variability in measurement among studies precludes meaningful conclusions. Furthermore, there is some evidence that predictions of relapse based on severity of dependence are moderated by age, marital status (Polich, Armor, Braiker 1981), and gender (Hesselbrock et al. 1983).

A factor that complicates the relationship between duration of drug dependence (as a measure of severity) and likelihood of relapse is that the age of the individual is directly related to remission (see discussion of spontaneous remission earlier in this chapter). Millman, Khuri, and Nyswander (1978) reported that length and intensity of addiction were positively associated with relapse, except that older opioid-dependent persons were more successful at avoiding relapse than younger ones. In a followup study of 38 treated methadone clients, Riordan and colleagues (1976) found that relapsed subjects were more likely than nonrelapsed subjects to have been addicted longer prior to treatment.

**Psychiatric Impairment**

As previously discussed, both depression and anxiety are commonly observed as dual diagnoses in persons dependent on alcohol and other psychoactive drugs. These diagnoses are also predictive of high rates of relapse and poor treatment outcomes. As shown in Table 7, several studies suggest that overall severity of psychiatric symptomatology may be an important predictor of treatment outcome. For example, McLellan and colleagues (1983) evaluated 6-month posttreatment outcomes for 460 alcoholics and 282 opioid addicts drawn from 6 rehabilitation programs. Using an intervention-based assessment of the severity of psychiatric symptomatology, they observed that patients with low psychiatric severity improved in every treatment program, while patients with high psychiatric severity showed almost no improvement in any treatment program. Patients with midrange severity levels of psychiatric disorder showed differential responses as a function of treatment modality.
<table>
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<th>Factors</th>
<th>Tobacco Studies</th>
<th>Opioids Studies</th>
<th>Alcohol Studies</th>
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TABLE 7.—Continued

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<td>Negative physical states</td>
<td>Pomerleau (1979), Shiffman (1979)</td>
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Demographic Factors

Demographic correlates of relapse have been widely studied. Consistent demographic predictors of relapse, either within or among substances, have not been identified (Tucker, Vuchinich, Harris 1985 and see Table 7). It is possible that the wide historical diversity of methods and definitions used contributes to greater apparent diversity when data are evaluated both within and among drug classes.

Treatment Correlates of Relapse

In treatment studies of opioid-dependent persons, it has been found that treatment type and duration as well as treatment expectancies affect posttreatment relapse. Length of time in treatment has been positively associated with outcomes across modalities of drug dependence treatment (McLellan et al. 1983; Simpson and Sells 1982). In addition, treatment completers have shown more positive outcomes than those who do not complete treatment regimens (DeLeon, Wexler, Jainchill 1982). Expectations of positive treatment outcome have also been related to lower relapse rates (Simpson and Sells 1982). Finally, modality of treatment has been related to treatment outcome in opioid addicts. Methadone maintenance, long-term inpatient treatment, and outpatient drug-free programs have all produced better outcomes than detoxification treatment or no treatment in both a followup study (Simpson and Sells 1982) and a prospective study (Bale et al. 1980). In the alcohol treatment literature, however, few differences have been detected among the most popular treatment techniques, including residential and outpatient modalities (Emrick 1974, 1975; Miller and Hester 1986a).

Schwartz (1987) has recently examined the effectiveness of more than 20 types of smoking cessation interventions (see Table 2 in Chapter VII). Seven methods showed good short-term results: educational techniques, nicotine chewing gum when combined with behavioral treatment, group hypnosis, physician intervention with cardiac patients, rapid smoking, satiation, and contingency contracting. Multicomponent programs that combined several interventions appeared to produce especially encouraging outcomes.

Expectations regarding alcohol’s effects may enhance susceptibility to relapse. Eastman and Norris (1982) examined this relationship in 89 persons participating in outpatient treatment for alcohol dependence. At a 2-month followup, 71 percent of subjects with positive expectations about alcohol’s effects had relapsed (any level of consumption was the criterion), compared with only 7 percent of subjects with negative expectations about the effects of alcohol. Analogously, in cigarette smokers, expectations regarding one's
ability to successfully abstain may also predict relapse to tobacco use (Brandon, Tiffany, Baker 1986; Chapter VII).

Posttreatment Correlates of Relapse

Evidence from a number of sources suggests that posttreatment experiences are particularly important to the relapse process. For example, Finney, Moos, and Mewborn (1980) found posttreatment factors to account for roughly half of all variance in treatment outcome. Further, recent investigations of the effectiveness of aftercare in the treatment of drug and alcohol abuse suggest that interventions which target the posttreatment interval may be particularly effective (Ahles et al. 1983; Catalano and Hawkins 1985; Catalano et al., in press; Marlatt and Gordon 1985). Specific categories of posttreatment factors associated with relapse are described below.

Family Support Factors

Family support has been a strong predictor of posttreatment success for opioid users, alcoholics, and cigarette smokers (Table 7). For example, Orford and colleagues (1976) found a marital cohesion factor to predict treatment outcome for drinking variables measured 12 months later. Similarly, in a survey of 219 subjects who were interviewed at 1-year followup after treatment in a minimal intervention smoking cessation program, abstainers reported significantly more support from spouses, parents, family, and friends than did relapers (Horwitz et al. 1985). Similarly, Orford and colleagues (1976) found that high marital discord was a predictor of relapse drinking at the 12-month followup among treated alcoholics, whereas Burton and Kaplan (1968) found reduction in the number of areas of disagreement between the alcoholic and his or her spouse to be associated with improvement in drinking behavior. These observations are consistent with the retrospective reports of relapsed subjects indicating that interpersonal conflict that was family or peer related was a trigger for drug use following a period of abstinence (Marlatt and Gordon 1980). Taken together, these data suggest that family support plays an important role in preventing relapse to substance use and that family conflict and lack of support for posttreatment recovery may increase levels of relapse for treated users of alcohol, opioids, and tobacco.

Drug Use Among Peers

Relapse to drug use following a period of abstinence after treatment often occurs when there is peer pressure to use drugs or when drugs are offered by the nonabstinent peer. A series of reports by Marlatt, Chaney, and their associates (Chaney, O’Leary, Marlatt
1978; Chaney, Roszell, Cummings 1982; Marlatt 1979; Marlatt and Gordon 1980, 1985) examining determinants of relapse for various substances suggested that social pressure is a factor for approximately 15 to 40 percent of relapse episodes among alcohol and opioid users. In a followup study of treated heroin users, Hawkins (1979) found that 69 percent of those who returned to heroin use after drug treatment reported that they did so in response to informal pressure from peers, suggesting an even stronger effect of social factors on relapse among opioid users. Similarly, living with smokers (Shiffman 1982) and failure to avoid smoking peers (Graham and Gibson 1981) are related to relapse in treated smokers. Specifically, Shiffman (1982) found that 30 percent of the relapse cases of 183 ex-smokers were associated with the presence of other people smoking. Other investigators have also found the presence of other smokers (Lichtenstein, Antonuccio, Rainwater 1977) or social pressure to smoke (Cummings, Gordon, Marlatt 1980) to be a risk factor for relapse (Chapter VII).

**Involvement in Work and Leisure Activities**

Although active employment and involvement in leisure activities may be distinguished (as shown in Table 7), there are similarities in their effects on relapse. Furthermore, the factors are similar in that both may be incompatible with active involvement with some dependence-producing drugs. In brief, research on posttreatment experiences of both opioid users and alcoholics has shown a consistent positive relationship between involvement in active recreational leisure activities (sports, hobbies, crafts, and volunteer work) and reduced use of opioids, alcohol, and tobacco (Table 7). Similarly, unemployment is associated with relapse to opioids and alcohol (Table 7).

**Negative Emotional States**

One of the most consistent findings from retrospective studies of relapse is the involvement of negative emotional states in relapse episodes. Data supporting this conclusion regarding tobacco use are discussed in detail in Chapters VI and VII and are only briefly summarized in this Section to enable a comparison of findings with opioids and alcohol. Ludwig (1972) interviewed 161 relapsed alcoholics and reported that 25 percent relapsed in response to "psychological distress." Marlatt (1978) interviewed 48 alcoholics who relapsed within 90 days of discharge from treatment and found that 10 percent relapsed in negative mood states and 29 percent in situations arousing frustration or anger. Negative emotional states are also prominent determinants of relapse to cigarette smoking. For instance, Marlatt and Gordon (1980) reported that 43 percent of the
relapse episodes of 35 subjects who had completed a smoking cessation program were in response to negative mood states.

Drug use has also been reported as a means of alleviating negative emotional states. For example, Stephens and Cottrell (1971) studied 236 opioid users who had received 6 months of inpatient methadone treatment. One-quarter of the clients they studied relapsed, reportedly using the drug to alleviate stress or to combat personal faults or depression. Consonant with these findings, reports of former drug users suggest that approximately one-fourth to one-third of the incidents of first drug use following treatment are precipitated by negative emotional states (Cummings, Gordon, Marlatt 1980; Marlatt and Gordon 1980).

Potential sources of negative emotions cited by relapsers include stressful interpersonal interactions (e.g., anger, frustration) and negative life events such as death, illness, job loss, or change. The role of negative life events has long been recognized as an important factor that can influence psychopathology, illness, and drug dependence; recently, systematic studies of these latter factors have also been conducted (Bloom 1985). For example, Moos, Finney, and Chan (1981) found that relapsed alcoholics reported nearly twice as many negative events and approximately one-half as many positive events as either recovered alcoholics or controls (Hull and Young 1983; Vuchinich and Tucker 1985).

Another potential source of negative emotions is illness or somatic discomfort from a variety of sources. In this regard, drug dependence researchers have documented the tendency of some drug users to use drugs as a form of self-medication (see Chapter VI for tobacco-specific data). For instance, opioid dependence may develop during the course of treatment for chronic pain (Khatami, Woody, O'Brien 1979) and other forms of somatic discomfort (Marlatt and Gordon 1980; Chaney, Roszell, Cummings 1982). Similarly, physical symptoms, including allergies, back pain, headache, and insomnia, during the posttreatment period were related to opioid and alcohol use in a sample of treated alcoholics (Finney, Moos, Mewborn 1980; Moos et al. 1979). A possibly related finding is the suggestion from a number of studies that protracted withdrawal symptoms are factors in relapse to opioid (Martin 1972) and tobacco (Pomerleau 1979; Shiffman 1979) use.

As shown in this Section, relapse is characteristic among persons treated for opioid, alcohol, nicotine, and other forms of drug dependence. Rates and patterns of relapse appear to vary more as a function of treatment characteristics, client parameters, and posttreatment environmental factors than as a function of drug type when alcohol, opioids, and nicotine are compared.

Posttreatment factors appear to be the most important determinants of treatment success and relapse avoidance for users of
tobacco, opioids, and alcohol. These are summarized in Table 7. Specifically, the most common predictors, similar for alcohol, opioids, and nicotine, include posttreatment family support factors, peer substance use factors, leisure and recreational activities, and occurrence of stressful or negative affect situations in the form of intrapersonal mood states, somatic complaints, negative life events, or stressful interpersonal interactions. Additional factors that appear important include pretreatment severity of use (tobacco and opioids), length of treatment (opioids), and type of treatment (tobacco and opioids).

**Treatment of Drug Dependence**

Scientifically based methods of helping drug dependent persons to achieve and maintain drug abstinence are available and can be efficacious. The methods are being continually refined, however, as new data are collected on how to better address the needs of clients or patients and how to make treatments more readily available and acceptable for those who want help. This Section briefly reviews some of the kinds of treatment approaches that are available for the various drug dependencies.

Treatment strategies designed to address dependence on opioids, alcohol, nicotine, and many other dependence-producing drugs are remarkably similar. This phenomenon provides additional evidence that the processes that determine addiction are similar for the various dependence-producing drugs. Some of the differences in treatment are related to variations in detoxification strategies, which depend on the route of drug administration and on differences in the duration of drug action. There is also need to tailor the content and/or intensity of treatment delivered to groups with different substance dependencies. For example, the need for medical intervention to alleviate acute withdrawal symptoms varies among and within drug classes as a function of the physical dependence level. This Section will discuss the goals of treatment for drug dependence and three types of interventions that are commonly employed: (1) pharmacologic substitution therapy designed to suppress withdrawal, (2) interventions designed to redress deficits in skills and/or deficits in social support that are potentially related to relapse, and (3) interventions designed to bolster or sustain motivation for abstinence. These kinds of intervention strategies are not mutually exclusive, and are often used in combination to yield better overall rates of success than any single approach (Grabowski et al. 1984).
Goals of Treatment

Reducing or eliminating self-administration of the substance to which the person is dependent is the primary goal of treatment. Traditionally, there has been a tendency for treatment programs to rely on a goal of complete abstinence rather than reduction of use to manageable or nonproblematic levels. The appropriateness of this goal may, in part, vary by drug class, as well as by severity of dependence. For example, problems associated with alcohol use vary considerably, and it would appear that many persons with low levels of dependence are able to maintain stable levels of "social drinking," whereas persons with more severe levels of dependence must maintain total abstinence (Miller and Joyce 1979; Miller 1979). Because it has been estimated that only about 10 to 15 percent of adults (United States) who drink warrant the designation "problem drinker" and only a subset of these warrant the designation "alcoholic," such variation in treatment goals is not surprising (Cahalan 1970; Miller 1979). Analogously, it appears that only a small fraction of caffeinated beverage (e.g., coffee and tea) drinkers display distinct adverse consequences and apparent loss of control over caffeine intake (Griffiths and Woodson 1988)—observations consistent with the rapidly growing decaffeinated beverage market.

On the other hand, with drugs for which any nonprescription use is illicit (e.g., opioids) or on which the overwhelming majority of users are dependent (e.g., only 10.6 percent of current smokers smoke 5 or fewer cigarettes/day according to the 1985 National Health Interview Survey (unpublished data, Office on Smoking and Health)), a goal of reduction of use may be especially problematic (Chapter VII). Two additional problems with low-level cigarette use as a therapeutic goal are that no level of cigarette smoking has been found safe (US DHHS 1986) and that even if the smoker is only smoking a few cigarettes, by taking more puffs per cigarette and by inhaling the smoke more deeply, the smoker might actually maintain substantial levels of tobacco toxin intake and nicotine dependence (Kozlowski 1981; Benowitz et al. 1983; Chapter IV). The percentage of persons using amphetamine or cocaine who are unable to control their intake is unknown, but because nonmedical use of these drugs is illicit and because animal and human research indicates that these drugs are powerful reinforcers (US DHHS 1987), total abstinence is similarly recommended (US DHHS 1987).

Maintenance of abstinence or avoidance of relapse is another major treatment goal. Because relapse factors can remain functional for many years in individuals who are abstaining from use of a drug to which they had been dependent (Chapters VI and VII), designing a long-range program to minimize the impact of such factors is an integral part of many drug treatment programs (e.g., Thompson, Koerner, Grabowski 1984; Stitzer et al. 1984). These factors may