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Stephen M. Stahl, Meghan M. Grady, Nancy Muntner
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Stahl's Illustrated | Chapter 1

Substance Use and Addiction: An Overview

From a behavioral perspective, addiction can be conceptualized as an impaired ability to inhibit drug seeking in response to environmental information that should normally suppress the behavior. Neurobiologically, this is linked to alterations in reward and other circuitry that may precede initial drug use (e.g., genetic risk factors) and/or be caused by chronic drug exposure itself.

In this book, we provide the biological background that will enable the reader to understand not only how chronic drug exposure is thought to alter reward circuitry, but also how currently available treatments for various substance use disorders work in the brain. We also review screening, treatment, and general management strategies for patients with addiction to various substances of abuse. In addition, we briefly touch on impulse control disorders that may have neurobiological similarities to drug addiction.

This chapter serves as an introduction to these topics by providing clinical definitions of the various terms used to describe substance use and addiction as well as an understanding of the behavioral progression from occasional, impulsive drug use to compulsive use and addiction.

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Substance Use Terms

Misuse	Use of a medication other than as directed, whether willful or not
Abuse	Use of a drug/medication for nonmedical purposes (e.g., getting high)
Aberrant Behavior	Medication-related behavior that departs from adherence to the prescription plan
Addiction	Chronic neurobiological disease characterized by impaired control over drug use, compulsive use, continued use despite harm, and/or craving
Pseudo-addiction	Mimics true addiction, but symptoms resolve with adequate pain relief
Dependence	Pharmacological adaptation characterized by drug class-specific withdrawal
Tolerance	State of adaptation in which exposure to a given dose of a drug induces biological changes that result in the drug's diminished effects over time; often leads to dose escalation

TABLE 1.1. Terms related to drug use, addiction, and dependence have historically been used interchangeably; however, this has the potential to create confusion. In this book, we use the term "addiction" when describing the neurobiology of the disease, whereas we generally state "use disorder" when discussing the clinical characteristics and management. Dependence is reserved for describing physiological dependence.

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Substance Use Disorder:
Proposed DSM-V Criteria

Maladaptive pattern of substance use leading to significant impairment/distress
(2 or more of the following within 12 months; 2–3 = moderate, >3=severe)

- Recurrent use leading to failure to fulfill major obligations
- Recurrent use in hazardous situations
- Continued use despite persistent or recurrent social problems caused or exacerbated by effects of substance
- Tolerance
- Withdrawal
- Taken in larger amounts or for longer periods than intended
- Persistent desire or unsuccessful efforts to control, reduce, or stop
- Great deal of time spent obtaining, using, or recovering
- Important activities given up or reduced because of substance use
- Continued use despite knowledge of physical or psychological problem likely caused or exacerbated by substance
- Craving or urge to use substance

FIGURE 1.1. Though not finalized yet, the proposed criteria for a substance use disorder in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) integrate criteria for abuse and dependence, with the term dependence now limited to physiological dependence (i.e., evidence of tolerance and/or withdrawal). The criteria are the same regardless of the particular substance being used. Separate criteria are still projected to exist for substance-induced intoxication, delirium, and withdrawal.

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The Addiction Cycle

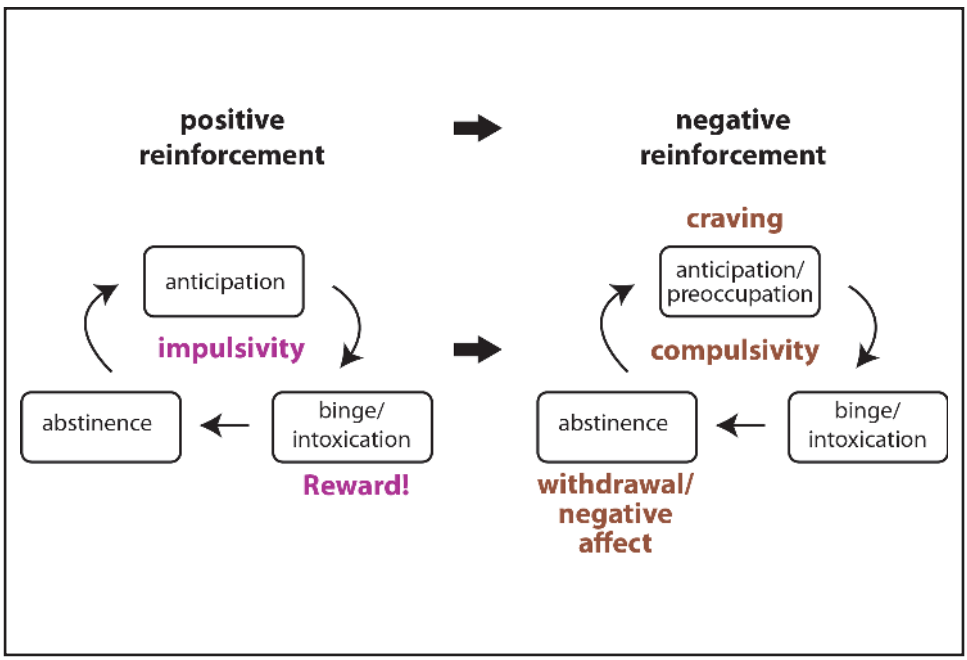

FIGURE 1.2. Addiction can be understood both as a progression from positive to negative reinforcement and as a progression from an impulsive to a compulsive disorder. That is, with initial drug exposure (left), an individual will experience pleasure/reward. This experience "teaches" the brain to anticipate reward on subsequent exposure to the drug. When the drug is taken, pleasure/reward will again be experienced, although this may be followed later by regret.

For most individuals, occasional and controlled drug use remains an impulsive choice driven by positive reinforcement from the drug's rewarding effects. However, for those with risk factors for addiction or excessive drug exposure (see Figure 1.3), this occasional drug use causes neurobiological changes that lead to the development of drug craving, reduced reward on drug exposure, and withdrawal/negative affect state during abstinence (right). Thus, drug addiction can be conceptualized as a compulsive disorder driven by negative reinforcement, wherein the withdrawal symptoms and negative affect during abstinence lead to craving and preoccupation with the drug, with drug use providing relief from these symptoms.

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Risk Factors for Addiction

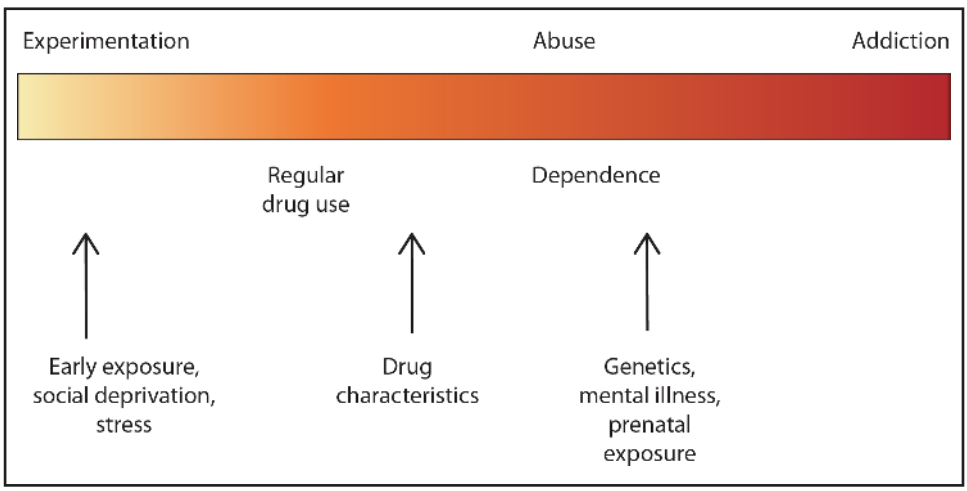

FIGURE 1.3. The risk for developing addiction is affected by multiple factors, including environment, characteristics of the particular drug, and genetics. Environmental risk factors include prenatal exposure, early exposure (e.g., due to parental use in the home or peer use during adolescence), early use, early social deprivation, and psychological stress. The presence of mental illness is also a risk factor for addiction. Drug characteristics include the specific drug used as well as the method of administration (which affects the rate of uptake).

Genetics are also known to affect the vulnerability to addiction; however, there is no single gene linked to addiction. Instead, the data to date suggest that genetic contributions to addiction are the result of the interaction of numerous genetic factors, much like with other psychiatric disorders. It is also possible that epigenetic mechanisms (i.e., changes in gene expression rather than in the genes themselves) contribute to the risk for addiction. For example, early life experiences (e.g., prenatal or early life stress) can cause changes in gene expression that can alter the brain's circuitry and thus increase the risk for the development of addiction.

In general, the risk for the initiation of drug use is associated more with psychosocial factors, whereas the risk for progression to addiction is associated more with neurobiological factors.

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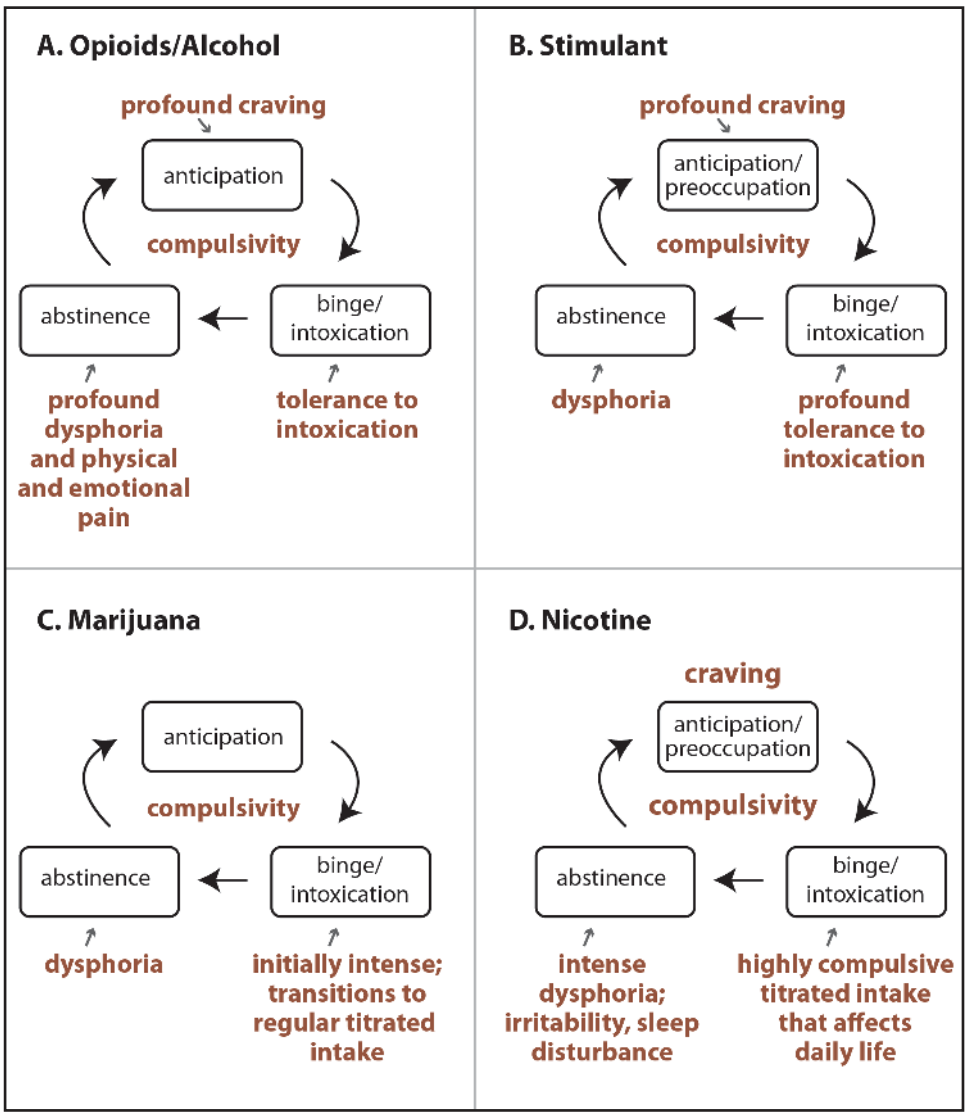
Patterns of Addiction by Drug



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Patterns of Addiction by Drug (cont'd)

FIGURE 1.4. The addiction cycle is the same for all drugs of abuse; however, both the risk of developing addiction and the specific pattern of addiction-related symptoms can vary depending on the particular substance.

(A) Opioids and alcohol initially cause intense intoxication; however, with chronic use, profound tolerance occurs (though some intoxication does remain). This generally results in the escalation of use. Abstinence from opioids/alcohol can lead to serious withdrawal with profound dysphoria and physical and emotional pain.

(B) Stimulants can also cause intense intoxication and binging upon initial use, but, as with opioids/alcohol, profound tolerance to intoxication occurs with chronic use. Preoccupation and craving is generally profound with stimulant addiction. Withdrawal is generally not as intense as with some other substances, although dysphoria can occur.

(C) Marijuana use typically begins with an intense binge/intoxication stage that transitions to regular titrated intake. Dysphoria can occur during abstinence, but craving is not usually profound.

(D) The pattern of nicotine use is generally highly compulsive and titrated, affecting one's schedule of daily activities; however, there is not generally much intoxication. Abstinence can lead to intense dysphoria, irritability, sleep disturbance, and craving.

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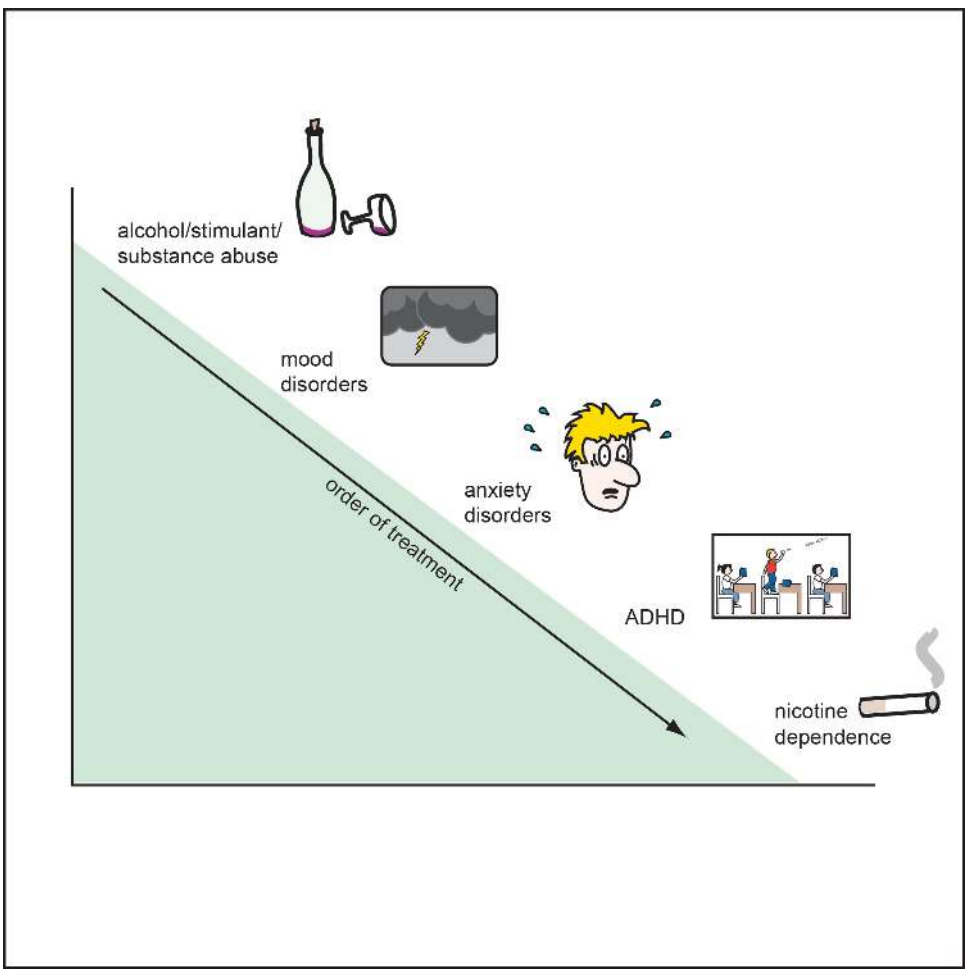
Clinical Considerations



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Clinical Considerations (cont'd)

FIGURE 1.5. It is common for individuals with a substance use disorder to use more than one substance. This can complicate the management of patients; unfortunately, there is limited research regarding the treatment of patients who use multiple substances.

Individuals with substance use disorders also have an increased risk of suicide, aggressive behavior (see Figures 10.5 and 10.6), and comorbid psychiatric disorders.

When psychiatric illness and substance use occur comorbidly, it is generally necessary to treat both disorders; in other words, successful treatment of the psychiatric disorder cannot be assumed to resolve the substance use problem. Research and expert clinical opinion support the integrated treatment of both substance use and psychiatric illness. However, depending on the severity of individual disorders, patients may sometimes do better if treatment is sequential rather than simultaneous. In some cases (e.g., major depression), this may mean that the substance use disorder is better treated first, so that one can differentiate between substance-induced symptoms and other symptoms. In many cases, however, it may be better to treat the psychiatric illness first, particularly if symptoms are severe. In general, adherence to psychiatric medication is better if the substance use disorder is treated first. This decision generally needs to be made on a patient-by-patient basis.

The presence of a substance use disorder does not generally affect the medication selection for a psychiatric disorder, although there are some exceptions to this. For example, one would not generally prescribe a benzodiazepine for anxiety for a patient who is actively abusing alcohol; agents that prolong the QTc interval should be avoided in patients abusing stimulants; some medications (olanzapine, clozapine, and others) are metabolized by CYP450 1A2, which is induced by cigarette smoking; and tricyclic antidepressants may be of greater concern in patients with SUDs because of the risk of seizures.

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The Neurobiology of Reward and Drug Addiction

The goal of neurobiological drug abuse research is to identify the mechanisms that mediate the progression from occasional and impulsive drug use to compulsive drug use, as well as how these mechanisms contribute to the high risk for relapse even after prolonged abstinence. It is known that chronic drug use affects not only dopamine and the reward circuit, but also other neurotransmitters and circuits involved in memory, motivation, executive function, and stress. Thus, the mechanisms by which addiction may develop are widespread, and although research is plentiful and rapidly expanding, many unanswered questions still remain.

This chapter covers what is best understood about the neurobiology of the reward system and the acute effects of drug exposure; chronic drug exposure and the progression to addiction; and the neurobiology of tolerance, withdrawal, and the risk for relapse.

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