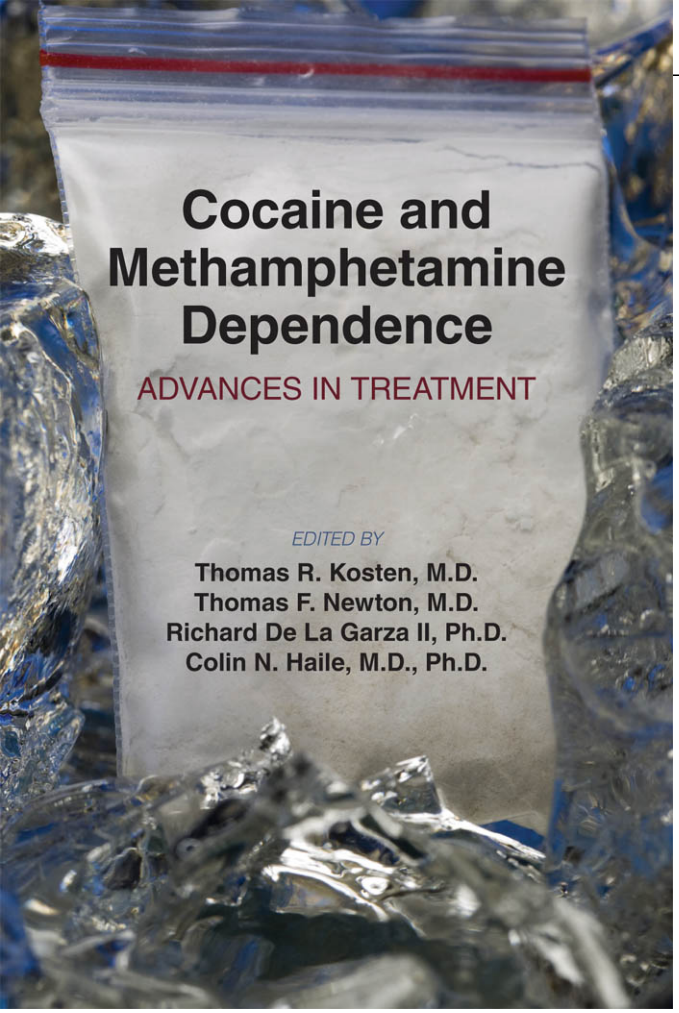
Cocaine and Methamphetamine Dependence
ADVANCES IN TREATMENT
EDITED BY
Thomas R. Kosten, M.D.
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Richard De La Garza II, Ph.D.
Colin N. Haile, M.D., Ph.D.

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Advances in Treatment

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Contents

Contributors vii
Foreword ix
Herbert D. Kleber, M.D.

1 **Epidemiology and Psychiatric Comorbidity** 1
Thomas R. Kosten, M.D.
Thomas F. Newton, M.D.

2 **History, Use, and Basic Pharmacology of Stimulants** 13
Colin N. Haile, M.D., Ph.D.

3 **Diagnoses, Symptoms, and Assessment** 85
Thomas R. Kosten, M.D.

4 **Behavioral Interventions** 105
Jin H. Yoon, Ph.D.
Rachel Fintzy, M.A.
Carrie L. Dodrill, Ph.D.

5 **Pharmacotherapy** 143
Thomas F. Newton, M.D.
Richard De La Garza II, Ph.D.
Ari D. Kalechstein, Ph.D.

6 **Polydrug Abuse** 155
Richard De La Garza II, Ph.D.
Ari D. Kalechstein, Ph.D.

7 **HIV and Other Medical Comorbidity** 175
Valerie A. Gruber, Ph.D., M.P.H.
Elinore F. McCance-Katz, M.D., Ph.D.

8 **Summary and Future Directions** 193
Thomas F. Newton, M.D.
Colin N. Haile, M.D., Ph.D.

Index 205

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Foreword

This book provides a comprehensive summary of what a clinician needs to know about stimulant dependence and its treatment in order to move beyond the basics of this complex disorder as presented in *The American Psychiatric Publishing Textbook of Substance Abuse Treatment* (Galanter and Kleber 2008). The textbook covers the material that a general psychiatrist or primary care physician needs for appropriate referral and initial management of patients with these complex disorders, for which no U.S. Food and Drug Administration (FDA)–approved pharmacotherapies yet exist, but treatments for these disorders are evolving rapidly. The present volume more closely examines stimulant abuse and its changing epidemiologies and treatment models.

As outlined in Chapter 1 of this volume, cocaine, methamphetamine (METH), and amphetamine (AMPH) abuse and dependence differ substantially in geographic distribution among North American cities and rural areas, as well as in Europe and Asia. The Philippines have the world's highest rates of AMPH abuse, with estimates that over 2.9% of the population are abusers (Ahmad 2003).

The criminal justice responses to these stimulant epidemics have produced some enlightened and humane linkages between the criminal justice system and treatment, such as "drug courts," where judges order legally supervised treatment for stimulant abusers rather than sending them to prison. Treatment has also been introduced into the prisons themselves and includes options for reducing the duration of imprisonment through work-release programs. These legal innovations are critical for the estimated 1.6 million current (on any given day) cocaine abusers and 502,000 current METH abusers (2009 estimates; Substance Abuse and Mental Health Services Administration 2010b). Another intervention initiated by the criminal justice system rapidly reduced small clandestine METH laboratories from more than 16,000 in 2004 to about 5,000 by 2007 as law enforcement efforts to control supplies of the ephedrine precursors and to find and destroy these laboratories were effective. These efforts increased the price of METH by

over 80% while its purity decreased by 26%, and the indicators in almost all metropolitan areas showed stable or reduced METH use (although there appeared to be somewhat of a rebound in METH availability during 2008).

Despite such efforts, there is still a steady number of new users and casualties from stimulant use: the 30-day prevalence of cocaine abuse among eighth, tenth, and twelfth graders increased more than twofold between 1991 and 1998 and recently increased again in 2009 and 2010 (Johnston et al. 2010).

Overall, cocaine dependence complications are common, being involved in one of every three drug-related emergency department visits, and cocaine has substantial social and economic impacts on those afflicted (McLellan et al. 2000; Substance Abuse and Mental Health Services Administration 2010b). Moreover, from 2007 through 2009, the United States had 2.5 million cocaine abusers using regularly, and in 2007 only 809,000 of them received treatment (Substance Abuse and Mental Health Services Administration 2010c). Coroners' reports (Graham and Hanzlick 2008; Kaye et al. 2008) relate stimulants to the direct cause of death in 25% of cocaine overdoses and 68% of METH overdoses, or identify stimulant use as an antecedent of cardiovascular or other medical problems, leading to death, in another 20% of these abusers.

The epidemiology of stimulant abuse is changing because of the increase in pharmaceutical abuse attributable to several factors: 1) increasing numbers of prescriptions have led to greater availability; 2) attention to this form of abuse by the media and in advertising on television and newspapers has stimulated adolescents' interest in it; 3) easy access through family and friends has made this type of abuse cheap and attractive; and 4) lack of proper monitoring of adolescents and of disappearance of drugs in the home or elsewhere has led to underrecognition of addiction (Substance Abuse and Mental Health Services Administration 2010a).

Cocaine and METH abuse and dependence frequently co-occur with other major (i.e., Axis I) mental illnesses, especially schizophrenia, major depression (Hughes et al. 1986), and posttraumatic stress disorder (PTSD) (Jacobsen et al. 2001). Many types of drug use are more common among patients with mental illnesses than among the general population. Patients with mood and anxiety disorders are at less risk for smoking and perhaps for stimulant abuse than patients with schizophrenia, but patients with any of these comorbid disorders smoke at higher rates than control subjects, and many biological and social factors are involved. Psychotic symptoms secondary to METH abuse may not abate after the METH use has stopped and may be associated with heavy alcohol use.

Chapter 2, on the complex pharmacology of stimulants, is outstanding, although not readily summarized in a brief Foreword.

Chapter 3, on symptoms and diagnosis, introduces the plan for DSM-5 to drop the distinction between abuse and dependence, which is a useful change in considering stimulants. In addressing teenage drug use information reports, the author emphasizes the limitations of self-reports; even if anonymous or confidential, they can lead to underreporting because respondents will still give socially acceptable but untruthful answers, such as "I don't" use drugs. A recent study in teens found that hair specimens were 52 times more likely to identify cocaine use compared with self-report. Furthermore, parent hair analyses for cocaine use were 6.5 times more likely to indicate drug use than was parental self-report (Delaney-Black et al. 2010). The SBIRT (Screening, Brief Intervention, and Referral to Treatment), a national program for screening and brief interventions with drug abusers, indicates that such urine screening in emergency departments has particularly high yields for detection and for reductions in health care utilization with even a single 10- to 15-minute intervention focused on the substance abuse.

Subjective and behavioral responses to stimulants, including both tolerance of and sensitization to behavioral effects, are also detailed in Chapter 3. Sensitization for AMPH-induced psychosis may persist despite long periods of abstinence and may be characterized by delusions, paranoid thinking, and stereotyped compulsive behavior. Dependence and withdrawal syndromes are reviewed, and treatments for the range of stimulant complications are considered (Gay 1982).

A comprehensive assessment of the patient involves the management of aberrant behaviors such as intoxication, violence, suicidality, impaired cognitive functioning, and uncontrolled affective displays. Suicidal ideation may be intense but may clear within hours. In the case of intoxication, blood and urine tests can help to determine the relevant stimulant(s) involved, as well as to identify withdrawal from another drug that is masked or exacerbated by concurrent stimulant dependence. Differences in developmental, gender, and cultural presentations in the natural history of stimulant dependence are also considered in Chapter 3.

The differential diagnosis of stimulant-induced intoxication and withdrawal can require distinguishing these from a wide range of psychiatric disorders, and up to a month of abstinence may be required for clear distinctions to be made. However, the introduction of pharmacological treatments, such as antidepressants, does not require such a lengthy delay. Thus, therapeutic and diagnostic distinctions may require different time frames during evaluations of the patient. For example, the symptoms of stimulant withdrawal frequently overlap with those of depressive disorders, and this diagnosis can be particularly difficult to distinguish from protracted withdrawal, which can include sleep and appetite disturbance as well as dysphoria that mimics affective disorders. A clinical vignette addresses whether a patient with stimulant

dependence in remission with a confirmed diagnosis of residual attention deficit disorder should be given a trial of methylphenidate.

Chapter 3 closes with a review of biomarkers for stimulant, and particularly cocaine, dependence. These biomarkers include abnormalities in neurotransmitter receptors and transporters that have been noted in animal models and confirmed in human neuroimaging studies of both the dopamine (DA) and serotonin (5-HT) neurotransmitter systems (Volkow et al. 1990), although none of these neuroimaging, neurohormone, or genetic biomarkers have entered general clinical use.

Later chapters focus on treatment and emphasize that the most important component of stimulant treatment involves behavioral therapies, often in combination with adjunctive medications (see Chapters 4 and 5). Although no medications have been FDA approved for use in stimulant dependence, a range of candidate medications, with varying mechanisms of action, have shown some efficacy. Distinguishing among the effectiveness of available behavioral treatments based on outcome has been difficult. A large multisite study showed little difference between drug counseling and two more intensive behavioral therapies, cognitive and supportive-expressive; however, these therapies retain patients in treatment and can lead to abstinence (Crits-Christoph et al. 1999). Overall, these therapies form the platform for any pharmacotherapy in order to engage the patient and facilitate more long-term changes, including prevention of relapse (Carroll 1997; Carroll et al. 2000).

Contingency management (CM) procedures are given significant attention in this book. The authors emphasize that effective CM requires treatment providers to identify an appropriate target as well as a method for assessing the occurrence of the target behavior. Additionally, treatment providers must choose appropriate and effective reinforcers and decide the optimal way to deliver those reinforcers. Positive contingencies have been used to initiate abstinence and prevent relapse, and this approach has been quite successful for managing individuals who abuse cocaine or AMPH (Higgins et al. 1994b, 2000a, 2000b; Petry 2005; Silverman et al. 1996; Weinstock et al. 2007). The goal of this approach has been to decrease behavior maintained by drug reinforcers and increase behavior maintained by nondrug reinforcers by presenting rewards contingent on documented drug abstinence (positive contingencies) and withdrawing privileges contingent on documented drug use (negative contingencies).

Studies illustrate how positive CM procedures facilitate initial abstinence in cocaine-dependent persons. In a 24-week study (Higgins et al. 1994a), cocaine-dependent individuals were randomly assigned to receive either behavioral treatment without incentives or behavioral treatment with incentives (i.e., vouchers exchangeable for goods and services) during weeks 1–12. Then,

during weeks 13–24, clients in both groups received a $1.00 lottery ticket for every drug-free urine sample, in addition to behavioral treatment. The group that received the incentives showed significantly greater treatment retention and longer duration of continuous abstinence than the group not receiving the incentives. In a 12-week clinical trial among methadone-maintained cocaine abusers (Silverman et al. 1996), the CM group also achieved significantly longer duration of sustained cocaine abstinence than control subjects. Overall, these findings suggest that incentives contingent on drug abstinence can be a powerful intervention tool for facilitating cocaine abstinence in cocaine- and methadone-maintained cocaine abusers.

Recent studies have further reinforced that abstinence-based incentive procedures are efficacious in improving retention and associated abstinence outcomes in substance abusers. CM interventions implemented in community-based settings, for example, have been successful in improving retention and associated abstinence outcomes (Petry 2005). Combining CM with pharmacotherapies such as bupropion may significantly improve treatment outcomes for cocaine addiction as well (Poling et al. 2006). There is, however, a significantly higher cost associated with the incentives group versus usual-care group (Olmstead et al. 2010). In order to determine the cost-effectiveness of implementing CM to improve patient outcomes in real-world situations, researchers need to determine threshold values for patient outcomes in substance abuse treatment.

As discussed in Chapter 4, cognitive-behavioral therapy (CBT) is also an efficacious intervention for the treatment of stimulant abuse. CBT for stimulant abuse includes functional analyses to determine the client's historical and current triggers for drug use, along with skills training in the management of drug cravings, effective drug-refusal techniques, and general problem-solving and decision-making strategies. Computerized delivery of CBT may effectively address issues commonly associated with regular in-person therapy sessions, such as scarcity of qualified mental health professionals in less populated regions, scheduling problems, transportation issues, and financial constraints.

In a recent pilot study, CBT was examined in conjunction with pharmacotherapy to evaluate length of treatment, drug-free urinalyses, and reduction of alcohol and cocaine craving. Although subjects who received CBT remained in treatment longer than subjects who received CBT and either disulfiram or naltrexone, the combination treatment groups achieved significantly greater reductions in cocaine-positive urinalyses (Grassi et al. 2007). In a study comparing CBT with CM, CM was found to be efficacious during treatment application. While CM may be useful in engaging substance users, retaining them in treatment, and helping them achieve abstinence, CBT has comparable longer-term outcomes (Rawson et al. 2006). Results of previous

research also suggest that cognitive deficits predict low retention in outpatient CBT treatment programs for cocaine dependence (Aharonovich et al. 2003, 2006). Future studies should examine the potential impact of differences in cognitive functioning on treatment outcomes and should test group counseling approaches, which offer various assumptions and models to match the needs of specific individuals.

The complex pharmacology and pharmacodynamics of cocaine's action, from the molecular to the behavioral level, is described in Chapter 5 as a foundation for a review of current pharmacotherapies (see also Chapter 2 for a discussion of basic neuropharmacology of stimulants). A key concept for acute reinforcement and euphoria is that different forms of cocaine and AMPH differ in their addictive potency based on how quickly the drug traverses the blood-brain barrier and affects key limbic circuits. Chronic stimulant abuse induces aberrant synaptic plasticity on brain circuits linked to reward learning as well as on other brain circuits. Specifically, cocaine-dependent individuals have decreased DA synthesis, reduced endogenous DA levels, blunted stimulant-induced DA release, reduced D_2/D_3 receptor availability, and increased DA transporter and cortical norepinephrine (NE) transporter levels. These abnormalities have been shown in human neuroimaging studies of limbic brain areas related to DA neurotransmission. Furthermore, vulnerable phenotypes prone to develop cocaine dependence are being noted in both neuroimaging and genetic studies. These abnormalities are defining the brain disease substrate of cocaine dependence and helping researchers to identify appropriate targets for treatment. Newer clinical studies have switched their focus from DA to the NE and glutamate (GLU) neurotransmitter systems in order to develop new pharmacotherapies. A substantial number of clinical trials have identified compounds that theoretically may correct deficiencies in neural circuits and attenuate the reinforcing effects of cocaine in cocaine-dependent individuals. Some compounds also appear to block drug cue–induced craving that relates to relapse. These medications include DA releasers such as sustained-release formulations of medications used to treat attention-deficit/hyperactivity disorder; mixed DA reuptake inhibitors (modafinil); DA precursors (L-dopa); NE synthesis blockers (disulfiram); and drugs that potentiate GLU neurotransmission (*N*-acetylcysteine). The difficulty of defining the appropriate therapeutic target to produce positive clinical results, as well as the cost of development, has led to inadequate involvement by the pharmaceutical industry. Although some agonist therapies have shown promising results, it remains controversial whether their potential abuse liability would outweigh their possible clinical efficacy.

Chapter 6 covers polydrug abuse. Substance abuse comorbidity is common with alcohol, marijuana, and opiates. Common psychiatric comorbidity includes depression, psychosis, and personality disorders.

Medical comorbidity and HIV are addressed in Chapter 7. A substantial problem with medical comorbidity is that despite evident extreme examples of health problems resulting from cocaine or METH use, these comorbid conditions often are not credible to users. Many well-controlled studies link stimulant use to a number of medical problems, some of which are fatal. Knowledge of these problems can help stimulant users and health care providers respond to symptoms earlier, but the denial of these major medical complications among the stimulant users is a significant challenge.

The list of complications begins with stimulant overdose (Centers for Disease Control and Prevention 2010), which manifests initially with symptoms such as agitation, increased heart rate, and hyperthermia (Kosten and Kleber 1988). Hyperthermia is particularly lethal through progression to rhabdomyolysis and renal failure. Long-term stimulant use increases the risk of hypertension, atherosclerosis, vasospasm, thrombosis formation, myocardial infarction, and stroke. Rarely, vasoconstriction can also cause corneal ulcers and scarring, resulting in blindness. Smoking crack or METH harms the lungs, exacerbates asthma and chronic obstructive pulmonary disease, and increases vulnerability to tuberculosis. Cocaine and especially METH can cause gum disease and tooth decay via vasoconstriction, dehydration, reduced salivary flow, poor dental hygiene, and poor diet. Cocaine and METH use can lead to dehydration and nutritional deficiencies that result in dry, itchy skin. In addition, some users have tactile or visual hallucinations involving their skin (e.g., feeling bugs under their skin) that exacerbates damage to the skin through their picking at it (Gawin and Ellinwood 1988).

Behavioral complications of chronic stimulants extend from the neonatal and pediatric periods to older adulthood (Delaney-Black et al. 2010). Children who are exposed prenatally to cocaine or METH are at increased risk for neurobehavioral problems and should receive regular developmental and mental health assessments and referrals as needed. Cocaine and METH use is associated with increased risk of violence toward and from intimate partners, even after other risk factors are taken into account. Unprotected sex and the resuse of previously used needles, syringes, and possibly pipes can transmit HIV and hepatitis C virus. Poor skin hygiene when injecting can result in infections of the skin (abscesses), heart (endocarditis), or other organs. The adulterant levamisole, found in most cocaine, can result in neutropenia and life-threatening infections. Finally, cocaine and possibly METH increase HIV disease progression, even after taking into account other risk factors. To reduce this disparity, it is important to engage stimulant users in HIV care and addiction treatment as early as possible.

The continued high levels of cocaine and METH/AMPH abuse and the destructive effects of such abuse call for renewed efforts to improve treatment results. This comprehensive volume brings together what is known

about these drugs and points the way to such improvement. As such, it is an important contribution to the addiction field.

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Chapter 1

Epidemiology and Psychiatric Comorbidity

Thomas R. Kosten, M.D.
Thomas F. Newton, M.D.

Epidemiology and Background

The epidemiology of cocaine, amphetamine (AMPH), and methamphetamine (METH) abuse and dependence reflects substantial differences in distribution, with cocaine being supplied through ports of entry from sources in South America and AMPH and METH coming from more "home-grown" sources, at least until recently. Cocaine from Colombia and its neighboring countries typically arrived in urban areas, where its use became epidemic in North American cities in the 1980s. Cocaine was rarely exported to rural areas. Now, increasing amounts of cocaine are being smuggled through the Mexican border into California, Arizona, and Texas, although cocaine, unlike METH, remains primarily an urban problem. Most METH is now imported into the United States from Mexico, and METH from this source is fast replacing METH of local manufacture, which predominated until the later 2000s. This shift in distribution appears to be due to policies initiated to restrict importation of precursor chemicals such as pseudoephedrine into the United States, whereas such chemicals continue to be imported into Mexico.

A steady decline in U.S. METH lab seizures from 2004 to 2007 with a slight increase in 2008 reflects aggressive policing measures.

METH distribution networks are separate from those for cocaine, with METH predominating in rural, western, and southern regions of the United States. Information on geographic trends in drug abuse comes from sources such as the National Institute on Drug Abuse Community Epidemiology Work Group, which in June 2009 reported that primary METH abuse treatment admissions were declining for nearly all U.S. cities being monitored (Figure 1–1) (National Institute on Drug Abuse 2010). This decline likely stems from reductions in local production, as noted above.

This geographic distribution for abuse of these drugs can also be shown through community-wide drug testing of wastewater samples as a population measure of community drug use. Such studies indicate that cocaine use peaks at weekends, as would be expected given its generally intermittent use. A report of a Belgian study of cocaine index wastewater loads (milligrams/person/day) included a map suggesting greater urban than rural use, as was also found in an Oregon study of cocaine metabolites, which were significantly higher in urban areas and below detection in many rural areas (Banta-Green et al. 2009). Conversely, METH was present in the wastewater of all Oregon municipalities, with no significant differences in index loads by urban versus rural area. Wastewater METH index loads also indicate higher usage of METH in the United States than in Europe, which is consistent with findings from other epidemiological surveys. Overall, the fast-moving and geographically influenced trends in abuse epidemics of METH and cocaine are difficult to monitor in real time with existing drug use indicators, and these novel public health approaches are finding some use for projections of drug-related crime levels and prevention and treatment needs.

Our chapter is focused on the current cocaine epidemic and its course, but this is not the first epidemic of cocaine use in the United States, as documented by David Musto in his classic book *The American Disease.* Cocaine was a significant public health problem as early as the turn of the twentieth century and led to drastically punitive legal measures (Musto 1999). The more recent U.S. epidemic, spanning the 1980s, also produced a substantial criminal justice response but has resulted in more humane linkages between the criminal justice system and treatment. Examples include "drug courts," where judges offer the convicted cocaine or METH abuser the option of engaging in legally supervised treatment rather than going to prison. Treatment has also been introduced into the prisons themselves and includes options for reducing the duration of imprisonment through work-release programs. These work-release programs allow legally supervised treatment beyond the typical limitations of parole programs, with their overwhelming caseloads of 400 or more parolees per supervisor.

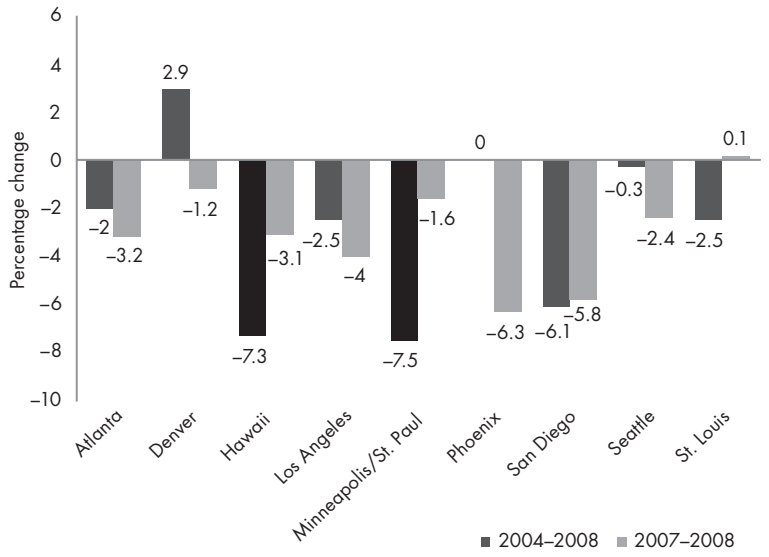

FIGURE 1–1. Primary methamphetamine treatment admissions in nine Community Epidemiology Work Group reporting areas as a percentage of primary drug admissions, excluding primary alcohol admissions.
Source. National Institute on Drug Abuse 2010.

Other legal interventions have been less enlightened. Most notable is the establishment of substantially more severe penalties for crack than for powder cocaine possession and sale. Crack cocaine is the base form of the drug, whereas powder cocaine is the hydrochloride salt. These two forms of cocaine are pharmacologically equivalent and have the same addictive potential. Such a distinction in penalties seems to reflect a bias against minorities, as inner-city cocaine abusers are more likely than suburban whites to smoke and sell the crack form of the drug. Thus, we have made some sociopolitical progress in our approach to the abuse and the abusers of stimulants, but more enlightened policies and approaches to demand reduction beyond policing are needed.

The U.S. cocaine epidemic had its peak in 1985 and produced an estimated 2.5 million lifetime stimulant abusers. We now have about 1.4 million current cocaine abusers and 350,000 current AMPH abusers (Johnston et al. 2010a). These 2.5 million lifetime abusers contribute some long-term users to the total, from the peak of the epidemic 25 years ago, but a steady stream of new users also adds to the current number of users. Between 1991 and 1998, the 30-day prevalence of cocaine abuse among eighth, tenth, and twelfth graders increased more than twofold, and the 2009 Monitoring the Future study of

U.S. secondary students found that 3.4% of twelfth graders had used cocaine in the previous year and 1.3% had used crack (Johnston et al. 2010b).

Casualties from stimulant use also continue to accumulate, as cocaine involvement in emergency department (ED) accident and violence cases remains prominent. Drug Abuse Warning Network (DAWN) 2009 data, derived from representative EDs, shows 482,000 mentions of cocaine compared with 1,000,000 for alcohol and 1,900,000 for all legal and illegal drugs (Substance Abuse and Mental Health Services Administration 2010). The number of deaths from cocaine overdose has also risen steadily, from 3,500 in 1999 to 7,000 in 2006 (Centers for Disease Control and Prevention 2010). The numbers of new abusers of cocaine, stimulants (including METH), and ecstasy (3,4-methylenedioxymethamphetamine; MDMA) remain high compared with the number of new users of marijuana, as shown in Table 1–1. Overall, cocaine dependence complications are common, involving one of every three drug-related ED visits, and cocaine has substantial social and economic impacts on those afflicted (McLellan et al. 2000; Substance Abuse and Mental Health Services Administration 2010). From 2007 through 2009, the United States had 2.5 million cocaine abusers, and only 809,000 of them were treated in 2007 (Johnston et al. 2010a).

This endemic cocaine abuse in North and South America has more recently spread to Europe, starting in Spain as an epidemic in about the year 2000. This introduction into Spain is not surprising, given the commonality in language with South America. Cocaine abuse has spread rapidly to the rest of Europe and Great Britain, particularly among comorbid opiate abusers who have been injecting amphetamines for many years.

METH abuse is an international public health problem, with two-thirds of the world's 33 million AMPH abusers living in Asia (Ahmad 2003). In Hong Kong, the prevalence of AMPH abuse rose from 1% in 1995 to 17% in 2000. The largest producers of METH are in Southeast Asia and North America, where the majority of users reside (Ahmad 2003). Localized epidemics of METH abuse have developed, particularly in the western United States. The Philippines have the world's highest rates of METH abuse, with an estimated 2.9% or more of the population being abusers. Because of this high rate, METH is the primary drug of concern in the Philippines and several nearby countries in Southeast Asia. A growing market is emerging in South Africa.

AMPH (as opposed to METH) production and use occur primarily in Europe, where injection use is common. Prevalence rates range from 0.7% of the population in Western Europe to 0.2% in Eastern and southern Europe. In the United States, AMPH was available over the counter in inhalers until 1959. AMPH abuse from diverted pharmaceutical sources was a significant problem until 1970, when the drug was moved to the more restrictive Drug Enforcement Agency Schedule II.

TABLE 1–1. Past-year initiates for cocaine, ecstasy, stimulants, and marijuana among persons age 12 or older in 2007

Drug	New abusers
Cocaine	906,000
Ecstasy	781,000
Stimulants	642,000
Marijuana	2,090,000

Source. Substance Abuse and Mental Health Services Administration, Office of Applied Studies, National Survey on Drug Use and Health, 2008.

Abuse of METH has been consistently much more prevalent in the United States since the 1990s, when large quantities of a highly pure, smoked form of METH began to be imported from Asia to Hawaii and then to the West Coast of the United States.

The history and epidemiology of METH in the United States starts with these imported supplies from Asia and then moves to METH production on Mexico and California. A rapid increase in small clandestine laboratories on the West Coast and in the Midwest reached its peak in 2003–2004, when more than 16,000 laboratory incidents per year were recorded. This rate fell dramatically to about 5,000 per year by 2007 as law enforcement efforts to control supplies of the ephedrine precursors and to find and destroy these laboratories were effective (Johnston et al. 2010b). These efforts increased the price of METH by over 80%, while its purity decreased by 26%, and the indicators in almost all metropolitan areas showed stable or reduced use of METH. The national Monitoring the Future study in 2007 also showed a substantial reduction in METH use by twelfth graders, from 2.6% in 2006 to 1.6% in 2007 (Johnston et al. 2010b). Moreover, more recent data from this study in 2009 showed a continued decline in METH use, to 1.2% (Johnston et al. 2010a).

In contrast to this remarkable and rapid reduction in METH use related to these legal interventions, medical and psychiatric complications of METH abuse increased over the longer period from 1995 to 2007. Much of this increase was associated with METH production in Mexico. States on both sides of the Mexican–U.S. border have had substantial increases in METH treatment admissions during these 12 years, from 7% to 25% in Mexico and from 12% to 27% in the U.S. border states. This increased rate of METH admissions was most prominent for western Mexico, while eastern Mexico and Texas had a predominant increase in cocaine treatment admissions during this period.

The abuser often notices few negative health consequences from METH or other stimulants, such as cocaine, but epidemiological data show that