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CRACK COCAINE ABUSE: An Epidemic with Many Public Health Consequences[1]

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ABSTRACT

In the mid-1980s a new, smokable form of cocaine, called crack, was introduced in the United States. Soon thereafter, it became apparent that crack cocaine abuse was a serious and important public health concern. Over the past several years, crack cocaine use has increasingly been associated with a myriad of immediate and long-term adverse effects. Duing this same period, crack cocaine use has progressively moved away from experimentation and recreational use to chronic and compulsive drug use.

The aim of this chapter is to present several topics concerning compulsive crack cocaine use that have particularly important consequences for public health. Crack cocaine use associated with pregnancy and with sexually transmitted diseases is highlighted.

WHAT IS CRACK?

Despite the widespread use of crack cocaine, there is quite a bit of confusion among the lay public regarding its definition. Therefore, it is important for health care providers to educate the public that crack is cocaine that is in a smokable form.

Until the late 1970s, the usual form of cocaine available on the street was cocaine hydrochloride. This salt form of cocaine is usually sniffed (snorted)

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nasally or mixed with water and injected intravenously. Occasionally, cocaine hydrochloride is combined with heroin and the mixture (called a "speedball") is injected. The hydrochloride salt can not be smoked because it is quickly destroyed at high temperatures. Cocaine is smokable in its freebase alkaloid form which is easily extracted from the hydrochloride salt (30). Freebase cocaine is generally prepared by one of two techniques. In one method the hydrochloride salt is first mixed with buffered ammonia, then the alkaloidal cocaine is extracted from the solution using ether, and finally the ether is evaporated to yield cocaine crystals. When heated the crystals liberate a vaporized cocaine that can be inhaled. Upon heating, the crystals make a popping sound and it is this characteristic sound that is the origin of the term "crack". This form of cocaine is very pure and is generally called "free base" on the street. The other method of producing free base cocaine is to combine cocaine hydrochloride with sodium bicarbonate (baking soda) and heat the solution until a solid forms. The resultant pieces of the solid, also called "rock", when heated release vaporized cocaine (30). Since the mid-1980s this has been the preferred method of production for smokable cocaine because it is simpler and safer than the ether extraction method. Today most of the available crack cocaine in the United States has been produced in this manner.

HISTORY

It is ironic yet important to know that our country had suffered through a previous cocaine epidemic. From the 1880s to the early 1900s, there was an epidemic of cocaine use in the United States and also in Europe. Some of the purported therapeutic uses for cocaine began to appear in the early 1880s. In his 1884 paper entitled *On Cocaine,* Sigmund Freud recommended that cocaine be used as a local anesthetic, an aphrodisiac and as a pharmacotherapy for depression, alcoholism and morphine addiction (18). Unfortunately, some of the patients who had substituted cocaine for either alcohol or morphine, subsequently became addicted to cocaine. By 1887 Freud had changed his opinion on the merits of cocaine and wrote an article in which he said that cocaine was much more dangerous for public health than morphine (5). During this time there was widespread use of cocaine and it was touted as a treatment for almost every imaginable illness. Cocaine could be found in a variety of goods ranging from patent medicines and tonics to soft drinks, In 1886 John Styth Pemberton, a druggist, formulated the syrup base for Coca-Cola. He blended a whole-leaf extract of coca with an extract from the African kola nut which is also a stimulant. Coca-Cola was initially manufactured and marketed as medicine. Later it was touted as a temperance drink despite the fact that cocaine was still a key ingredient. The manufacturer believed that their product should not only be strongly associated with cocaine by the product name but also by

the product package. Thus, the unique shape of the Coca-Cola bottle was originally intended to resemble the shape of a coca bean. In reality, the bottle shape resembles a cocoa bean because the production artists mistakenly used a cocoa bean, instead of a coca bean, as the model for the bottle design. In 1903, soon after the dangers of cocaine were publicized, the manufacturer of Coca-Cola removed cocaine from its formulation (23, 40). Congress passed The Harrison Narcotic Act of 1914 as a method of controlling the manufacture, sale, distribution and prescription of narcotics. Interestingly, cocaine, a stimulant, was included in the list of narcotics covered by these federal narcotic regulations. Consequently, cocaine was only available through a doctor's prescription. The public perception that cocaine was a dangerous drug was reinforced by these restrictions. Cocaine use decreased and remained low through the 1960s. In the early 1970s, cocaine abuse re-emerged, particularly among middle-class Americans. As Gold noted (23) all that had been learned about the dangers of cocaine from the previous epidemic had been forgotten.

EPIDEMIOLOGY

Cocaine abuse in the United States has maintained epidemic status since the early 1980s. Estimates from a recent National Household Survey on Drug Abuse (50), based on a sample of 22,181 individuals, indicate that in 1994 there were 1.4 million current cocaine users in the United States. The estimated number of crack abusers was 500,000. This represents a marked reduction in cocaine usage compared to peak use, 5.8 million persons, in 1985, and is also a significant decrease from the 1.9 million users in 1991. Almost all of the reduction in use is accounted for by occasional cocaine users, people who used in the past year but less frequent than monthly (Figure 1). Despite the dramatic change in pattern of cocaine consumption, the number of frequent cocaine abusers, defined as those who use cocaine on a weekly basis during the past year, has remained constant since 1985 at about 640,000 persons. Most of the current cocaine users were in the age bracket 18 to 34. Men used cocaine twice as frequently as women. With regard to ethnicity, blacks and Hispanics had higher rates of cocaine use, 1.3% and 1.1%, respectively, compared to whites who used at a rate of 0.5%. In terms of absolute number of current cocaine abusers, whites accounted for 62%, blacks 22%, and Hispanics 16%.

Cocaine abuse and dependence appear even more serious considering that chronic cocaine users are developing a significant number of medical and psychosocial problems. According to data from the Drug Abuse Warning Network (51), cocaine-related hospital emergencies continue to increase, especially for individuals 35 years of age and older (11).

Unlike the United States, European countries have not experienced dramatic increases in cocaine abuse. Ingold et al (29) describe an overall low level of

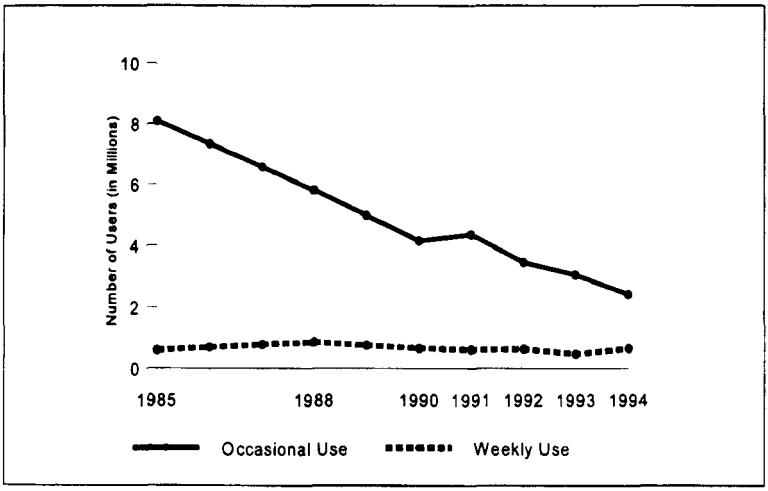

Figure 1 Cocaine use in past year, 1985–1994

crack cocaine use in France; however, in the last few years there has been a progressive increase in the number of crack abusers. In 1991 there were 51 known crack abusers in all of France but by 1993 there were 226 abusers in Paris alone. These authors believe that France and other European countries may be on the eve a crack cocaine epidemic. Recently, there has been research directed at understanding the meaning of the reported differences in prevalence rates of cocaine use for the race/ethnic demographic characteristic. In the last two National Household Surveys on Drug Abuse (NHSDA), the prevalence rates for lifetime use of crack cocaine for African Americans were more than twice those for white Americans. In a recently reported study (39), investigators conducted a reanalysis of the original data for the 1988 NHSDA to examine the extent to which cocaine smoking is associated with race/ethnic factors. The hypothesis was that the reported racial/ethnic group differences might be an artifact of environmental risk factors. In the reanalysis the survey respondents were grouped into neighborhood clusters. In this manner, shared characteristics such as drug availability and social conditions could be held constant. The results showed that the odds of cocaine use did not differ by race and ethnicity. In other words, environmental influences increase the risk of cocaine use regardless of race and ethnicity.

COCAINE AND ADDICTION

Cocaine abuse refers to a pattern of drug use that produces recurrent and significant adverse consequences related to repeated use of the drug. Cocaine

addiction, which is also referred to as dependence, involves compulsive drug use that causes interference with normal activities and may include tolerance and physical dependence. Crack cocaine smoking and intravenous cocaine are associated with a rapid progression from cocaine use to cocaine abuse and addiction. Over the past two decades, health care providers and researchers have increasingly used criteria of the *Diagnostic and Statistical Manual of Mental Disorders* of the American Psychiatric Association (1) to characterize individuals with substance use disorders. The reader is referred to this manual for a full discussion of these specific diagnostic criteria.

Drugs that reliably produce pleasure (euphoria) are more likely to be taken repeatedly. Reinforcement refers to the quality of drugs to produce effects that make the user wish to take them again. The more strongly reinforcing a drug is, the greater the likelihood that the drug will be abused. Studies in animal models have associated reinforcement with the ability to increase extracellular levels of the neurotransmitter dopamine in critical brain areas, particularly the nucleus accumbens. Cocaine, amphetamine, ethanol, opioids and nicotine all reliably increase extracellular dopamine levels in the nucleus accumbens region. In contrast, drugs that block dopamine receptors generally produce unpleasant feelings. Neither laboratory animals nor humans will spontaneously take such drugs. The abuse liability of a drug is enhanced if it has a rapid onset of action. Effects that occur soon after administration are more likely to initiate the chain of events that lead to loss of control over drug taking. The time that it takes the drug to reach critical receptor sites in the brain and the concentrations achieved can be influenced by the form of the drug, route of administration and rate of absorption, metabolism and entry into the brain.

The history of cocaine illustrates the changes in abuse liability of the same compound, depending on the form and the route of administration. Coca leaves can be chewed and the alkaloidal cocaine is slowly absorbed through the oral mucosa. This method produces low cocaine blood levels and correspondingly low levels in the brain. The mild stimulant effects produced by the chewing of coca leaves have a gradual onset, and this practice has produced little, if any, abuse or dependence despite thousands of years of use by natives of the Andes mountains. Natives in several of the cocaine-producing countries in South America use coca paste which is the product of a crude extraction of the coca plant. This paste, which is locally called basulca, is smoked. Basulca frequently contains leftover hydrocarbons and chemicals which when smoked exposes the user to the additional dangers of inhaling these contaminants.

Beginning in the late nineteenth century, scientists isolated cocaine hydrochloride from coca leaves and the extraction of pure cocaine became possible. Cocaine could be taken in higher doses by oral ingestion or by absorption through the nasal mucosa, producing higher cocaine levels in the blood and a more rapid onset of stimulation. Subsequently, it was found that a solution

of cocaine hydrochloride could be administered via the intravenous route giving the ultimate in rapidity of blood levels and speed of onset of stimulatory effects. With each "advance" in cocaine administration, there was an associated increment in blood level and speed of onset of the drug. Consequently, the drug became more likely to produce addiction. In the 1980s, the availability of cocaine to the American public was increased further with the invention of crack cocaine. Crack, which is sold at a very low price on the street ($1 to $3 per dose), is alkaloidal cocaine (free base) that can be readily vaporized by heating. Simply inhaling the vapors produces blood levels comparable to intravenous cocaine. The pulmonary route is highly effective because the lungs provide a large surface area for absorption into the pulmonary circulation. The cocaine-containing blood then enters the left side of the heart and reaches the cerebral circulation without dilution by the systemic circulation. The pulmonary route rapidly delivers the drug to the brain and is also the preferred route for users of nicotine and cannabis. Inhalation of crack cocaine is thus more likely to produce addiction than chewing, drinking or sniffing cocaine.

The behavioral effects of a cocaine "high" are manifested by an extreme euphoria, increased sense of self-confidence, hyperalertness, hyperactivity, restlessness, decreased appetite, decreased need for sleep and impaired judgment (30). Users frequently report that when cocaine is available it is difficult to avoid using it and that it is almost impossible to resist completely ingesting all of the cocaine that is available. The effects of cocaine are so powerful that the abuser often neglects personal care and health, sleep, employment and even child care (23). The cocaine high lasts only for about 10-20 minutes, and is quickly followed by anxiety, depression and an immense craving to re-experience the high. These symptoms are relieved by taking more cocaine.

Only a minority of cocaine-dependent persons who discontinue use manifest cocaine withdrawal symptoms. When present, cocaine withdrawal occurs within hours to days after the last dose and is manifested by dysphoria, depression with suicidal ideation, fatigue, hypersomnia, and increased appetite. These symptoms usually do not require specific treatment, other than rest, and they usually subside within 3 to 4 days.

TOXICITY

Cocaine abuse has been associated with a variety of systemic complications involving all the major organ systems. Cardiovascular, neurologic, psychiatric, pulmonary, gastrointestinal, musculoskeletal and dermatologic manifestations have been reported. Several reviews of cocaine toxicity are available (23, 37, 38, 53).

Cardiovascular

The most frequently occurring toxic complications involve the cardiovascular system and are manifested by arrhythmias, coronary vasospasm, myocardial ischemia, myocardial infarction, and cardiomyopathy. Cocaine is a powerful vasoconstrictor whose effects are dose dependent. The toxic effects of cocaine are the result of direct stimulation of the cardiovascular system and the prolonged catecholamine stimulation following reuptake blockade (16).

Several studies have reported an increased incidence of strokes in persons who smoke crack cocaine (12, 32). In most cases strokes occurred in young adults who had few, if any other, risk factors for stroke. Cerebral hemorrhages and ischemic infarcts are seen with about equal frequency.

The pressor effects of cocaine can cause a sudden increase in arterial pressure that may cause a cerebral vessel to rupture. In addition, cocaine may cause constriction of cerebral vessels and lead to ischemic brain infarction. In persons who have risk factors for stroke, such as hypertension, renal failure and diabetes mellitus, the additional risk of smoking crack cocaine may be particularly harmful.

Neurological

Seizures are the most frequent neurological complication associated with cocaine use. The seizures occur because cocaine, through its local anesthetic action, lowers the seizure threshold. The seizures usually occur within minutes after cocaine use, are generalized tonic-clonic type, and have a short duration (30, 44, 52)

Several studies have found evidence of the neurotoxic effects of cocaine (28, 46, 54). Cerebral atrophy, between 20% and 40%, has been described for a chronic cocaine abusers (46). Strickland et al (54) studied cerebral perfusion and neuropsychological function in a group of 8 chronic cocaine abusers who had been abstinent for at least 6 months. All the subjects showed abnormal brain perfusion and neuropsychological deficits. Hypoperfusion, which varied in location and severity, was observed in all 8 subjects during single-photon emission computed tomography (SPECT) studies. Deficits in attention, concentration, and new learning were seen in all subjects.

Pulmonary

Difficulty breathing is a frequent complaint of crack cocaine smokers and often leads the abuser to seek medical attention. There are a variety of reported pulmonary problems associated with the inhalation of crack cocaine. Pulmonary pathology and crack cocaine use has been reviewed elsewhere (37). This review emphasized that cocaine abuse may cause several diverse, pulmonary disorders such as pulmonary hemorrhage, pulmonary edema, asthma, and

barotrauma manifested as pneumothorax, pneumomediastium and pneumopericardium.

COMBINATIION OF COCAINE WITH ALCOHOL

Between 60% and 90% of cocaine abusers also abuse alcohol (24, 49). Cocaethylene, an ethyl ester of benzoylecgonine, is formed in the liver when cocaine and alcohol are consumed together. High blood levels of cocaethylene following cocaine and alcohol use have been found in persons admitted to the emergency room and in persons who died as a result of cocaine overdose (25). This metabolite has behavioral effects similar to those of cocaine. It is as potent as cocaine in animal self-administration studies and thus it has significant abuse potential (31). Cocaethylene is more toxic than cocaine and its half-life is twice as long as that of cocaine (15, 26). Compared to using cocaine alone, a person who consumes both alcohol and cocaine may experience more intense pleasurable sensations, but he may also develop the combined toxicities of cocaine and cocaethylene (26).

SEXUALLY TRANSMITTED DISEASES

Several investigators have described an increased incidence of sexually transmitted diseases (STD), including human immunodeficiency virus (HIV) infection, in crack cocaine abusers as a consequence of these abusers participating in high risk sexual behaviors (4, 9, 19, 43). Two recently reported studies, each involving a large patient cohort, provide additional clinical evidence that links crack cocaine abuse to infections with STD. Edlin et al (14) investigated the relationship between crack cocaine addiction and HIV infection in crack cocaine abusers in three cities. The study consisted of interviewing and testing for HIV all participants. Subjects for this study were adults, 18 to 29 years of age, who either smoked crack cocaine regularly or who had never smoked crack cocaine, and who were recruited from inner-city areas in New York, Miami and San Francisco. The reported findings were for 1967 participants who had never injected drugs. Of these, 1137 were regular (at least 3 days a week during the prior 30 days) crack cocaine users and the remaining 830 had never smoked crack. Half the subjects in each group were males. African Americans represented 87% of crack smokers and 81% of nonsmokers. The crack users had been smoking crack for a median of 5 years, used crack regularly (at least 3 days a week) a median of three years, and had used crack a median of 28 of the prior 30 days.

The authors stated that the study has three limitations: (*a*) study participants were recruited from the streets and thus, there is probably an overrepresentation of people who live or spend a lot of time in public places; (*b*) participants were

either regular crack cocaine users or nonusers, therefore no information was collected regarding infrequent and former crack cocaine smokers; and (*c*) information regarding drug use and sexual behaviors were from the participants' self-reports. Overall these limitations did not seriously weaken the importance of the findings from this study.

Several important findings were cited: prevalence of HIV infection among crack smokers (15.7%) was 2.4 times that of the nonsmokers (5.2%); the highest prevalence of HIV infection was among the women crack smokers in New York (29.6%) and Miami (23%). The lowest prevalence was among nonsmoking women; in women there was a stronger association between crack smoking and HIV infection than among men; four sexual practices were the strongest risk factors for HIV infection and accounted for the higher prevalence of HIV infection among the crack cocaine smokers. The four high-risk sexual practices are: (*a*) sexual work (meaning sex in exchange for money or drugs) at any time; (*b*) recent unprotected sexual work, (*c*) anal sex between men; and (*d*) homosexual anal intercourse with 50 or more male partners. Women who used crack were more likely than men who used crack to report high risk sexual practices.

The authors conclude that crack cocaine smoking is associated with high-risk sexual practices, which in turn results in the transmission of HIV. Eighty percent of the crack smokers reported having had a sexually transmitted disease.

The females who abused crack were also more likely to report ever having had a sexually transmitted disease, in particular genital ulcer disease. DeHovitz et al (13) studied a group of 372 sexually active inner-city women in Brooklyn, New York in order to determined the prevalence of untreated sexually transmitted diseases. Women 18 to 50 years old who had at least one male sex partner in the prior year were eligible for the study. Women with a history of intravenous drug use or a positive HIV antibody test were excluded.

Each participant had an extensive evaluation that included questionnaires to collect demographic data and historical information regarding alcohol consumption, drug use and sexual practices, medical history, physical examination, pelvic examination, routine laboratory blood studies, and a urine toxicological analysis. STD's were assessed using medical history, culture, serologic analyses.

Three-hundred and seventy-two women were studied, of whom 92% were black and 49% were US-born. Thirty-five percent of all the women had at least one STD. The rate of STD among US-born women was 50% compared to a rate of 22% among foreign-born women. A total of nine women (2.4%), seven US-born and two foreign-born, had a positive HIV antibody test. All seven US-born reported recent crack cocaine use and three reported having six or more sexual partners during the prior year. The researchers found large

differences between crack cocaine use, sexual behavior, and place of birth, and consequently they examined the US-born and foreign-born groups separately. Among the US-born women, 61% of the cocaine users had an STD compared to 34% of nonusers. Recent crack cocaine use was the strongest predictor of syphilis infection.

The authors summarized the study findings as showing three important relationships: (*a*) that undiagnosed and untreated STD was significantly associated with a history of crack cocaine use; (*b*) and to a lesser extent to a history of multiple sex partners; and (*c*) that there was a very strong association in women between crack cocaine use and syphilis and HIV.

PREGNANCY

It is reported that in urban areas as many as 18% of all newborns infants are delivered to women who in the prenatal period test positive for cocaine (17). It is difficult to gather accurate self-report data from pregnant women who use cocaine because they fear that they may lose custody of their newborn because of their drug use. This is also a principal reason that they delay or avoid seeking prenatal care. One report found that 25% of prenatal mothers currently abusing cocaine denied drug use (17).

Over the past decade there have been several reports of the negative effects on the infant of prenatal cocaine exposure (7, 8, 42). The detrimental effects included depressed growth manifested as low birth weight, a variety of neurological abnormalities, and behavioral disturbances. Richardson et al (48) found that many of the reported studies on the effects of prenatal cocaine exposure have significant methodological problems such as failure to control for the prenatal use of other drugs, or the failure to control for other important variables such as prenatal care and environmental conditions. In one recent study, when these types of confounding variables were controlled, the analysis revealed no difference between infants of women who abused cocaine and those who did not use cocaine (48).

Lutiger et al (41) performed a meta-analysis of studies on the effects of prenatal cocaine use on fetal development. They found that of all the reported detrimental effects, only low birth weight could be specially attributed to the mother's prenatal use of cocaine. Although a significant number of pregnant women use cocaine, it is not clear what effects this intrauteral cocaine exposure has on the fetus, infant, and child.

TREATMENT

Detoxification is simply accomplished by abstinence. Cocaine withdrawal symptoms are not life-threatening and rarely require treatment.

Psychosocial Therapies

RELAPSE PREVENTION The therapeutic goal of relapse prevention is to achieve and maintain abstinence from drugs and alcohol. Psychosocial treatments are the modal form of therapy for cocaine dependence. Most of the treatment programs last about 30 days and have been patterned after alcohol treatments (2). Treatment is usually provided through a variety of modalities, and urinary drug screens are an integral part of the program. Group and individual therapies are combined in varying amounts, with family/couples therapy and self-help groups (20).

Treatment results from research studies on cocaine dependence indicate that long-term care is needed because brief treatments are ineffective (33). A typical protocol may require a short in-patient stay or an intensive outpatient program; then treatment is tapered and continued for one to two years.

Recent reports for outcome studies involving intensive psychosocial treatments for cocaine dependence show good rates of abstinence: Alterman et al (2) 60% for 7 months; Carroll et al (6) 30% for a year; Higgins et al (27) report that for patients who received behavioral treatment with an added incentive program, 55% achieved 10 weeks of continuous abstinence and 30% achieve 20 weeks. Although these kinds of programs appear effective, they are not practical as standard treatments for huge numbers of patients because they are very expensive, long-term and require specialized staff. On the other hand, they are less expensive than long-term inpatient care.

Medication

Many patients are unable or unwilling to undergo therapy without the support of medication. Unfortunately, there is no medication clearly identified as an effective pharmacotherapy for cocaine-dependent persons.

Our current understanding of the neurochemical changes that result from chronic stimulant use has been the basis for the selection of potential pharmacotherapies for cocaine dependence. The nucleus accumbens is an important part of the brain reward pathways. Cocaine administration, in rats, results in increased levels of dopamine in the region of the nucleus accumbens. Cocaine and other abused substances that increase nucleus accumbens dopamine also decrease the threshold for brain-stimulation reward (34).

Medications for the treatment of cocaine dependence must be considered separately from medications used to treat complications involved in cocaine abuse such as depression and psychotic reactions. Although a withdrawal syndrome for cocaine dependence has been proposed (21), this withdrawal generally consists simply of tiredness, somnolence, lack of energy, craving for cocaine and periods of depression. It usually resolves spontaneously over several days but there is evidence from brain imaging studies that receptor changes and even brain metabolic effects from chronic cocaine may persist

for weeks or months after the last dose of cocaine. Several types of medications have been used in an effort to correct the biochemical changes that are thought to play a role in relapse to compulsive cocaine use. Antidepressant medications have been used, based on the theory that they, like cocaine, block reuptake of biogenic amines and therefore, may correct some of the deficit produced by the abrupt withdrawal of cocaine (11). The antidepressant medication most studied has been desipramine. It has also yielded the best results in specific populations. Several double-blind studies with desipramine (22) indicate that it has a modest effect, at best, in inducing abstinence from cocaine. Two recently reported studies of Arndt et al (3) and Kosten et al (35) both involved methadone maintenance patients who were abusing cocaine, mainly intravenously, and they did not find desipramine to be an effective pharmacotherapy. Possibly cocaine abusing methadone patients who primarily use cocaine by the intravenous route may be more difficult to treat and less likely to respond to desipramine. Research is needed, particularly in nonintravenous abusers, in order to determine which population of cocaine abusers benefits most from desipramine pharmacotherapy.

Another approach has been based on animal studies that indicate that cocaine can produce kindling of seizure activity. Kindling is an electrical phenomenon that refers to the increase in seizure activity when a standard sub-threshold stimulus is applied repeatedly to certain brain structures, especially the amygdaloid nucleus. Small doses of cocaine applied to the amygdala have also been shown to produce kindling and thus, the drug carbamazepine which blocks the production kindling (47), might have a role in the treatment of cocaine dependence. Thus far, double-blind studies have not shown any benefit from carbamazepine in preventing relapse to cocaine use (10, 36, 45).

SUMMARY

This review has briefly described the history of cocaine use over the past century in the United States. Although crack cocaine is a relatively recent development, it has already been shown to be highly addicting and associated with numerous medical problems. Treatment of compulsive users is difficult, but behavioral treatments have achieved success with about half of the cocaine addicts requesting treatment. There is a great deal of interest in finding a medication that will improve the treatment of cocaine addiction, but so far no medication has been consistently successful in controlled clinical trails.

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