ADVERSE HEALTH CONSEQUENCES OF COCAINE ABUSE

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Cocaine creates a strong physical addiction and is becoming recognized as one of the most dangerous illicit drugs abused today. The myth is that cocaine is harmless and nonaddictive. An estimated 30 million Americans have used cocaine, but the number may be as high as 40 million. Five to six million individuals are compulsive users. A review of the current literature revealed multiple reports of acute myocardial infarction and cerebrovascular accident with a temporal relation to cocaine use. Cocaine has also been associated with acute rupture of the aorta, cardiac arrhythmia, and sudden death. Cocaine has multisystem toxicity involving neurologic, psychiatric, obstetric, pulmonary, dermatologic, and gastrointestinal systems. The dopamine depletion hypothesis may explain why cocaine is repeatedly administered; cocaine produces a transient increase in synaptic dopamine. Alterations in dopamine neurotransmission may be responsible for the development of compulsive use patterns. When cocaine use becomes compulsive, psychosocial dysfunction, deviant behaviors, and a wide spectrum of social, financial, and family problems invariably result. Addiction, major medical complications, and death are true hazards of cocaine use.

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Cocaine creates a strong physical addiction and is becoming recognized as one of the most dangerous illicit drugs in common use today. Believing cocaine was harmless and nonaddictive, millions of people tried it and cocaine abuse proliferated. It is estimated that 30 million Americans have used cocaine,[1] and 6 million are compulsive users.[2,3] In the past, cocaine was expensive and price served as a barrier to widespread use. Users often believed that cocaine use gained them entry into an elite group. Recently, cocaine has become less expensive and its availability and purity have increased. The purity of cocaine purchased on the street may vary from 25% to 90%. Although the effects of cocaine are unpredictable, regardless of its purity, there is widespread belief that cocaine is a safe and nonaddicting substance. As a result cocaine use has rapidly escalated in American society.

The earliest known use of cocaine dates back to 600 AD, evidence of which—in the form of coca leaves—has been found in tombs of South American Indian mummies.[2,4] For centuries, the large Indian population of Peru has chewed coca leaves. Although the first medicinal use of the coca leaf was reported by a Spanish physician in 1596, it was not until 1855 that cocaine was isolated from coca leaves. In 1884, Freud published the first major report on the effects of cocaine.[5,6] Cocaine is prepared from the leaves of the plant *Erythroxylon coca*, which is grown in South America high in the Andes Mountains.[4] Most of the cocaine that enters the United States comes from either Colombia or Peru. More than half of the raw material (cocaine hydrochloride) reaching the United States is cultivated in the upper Huallaga River Valley in Peru.

During the late 1970s and early 1980s, cocaine abuse reached alarming proportions in the United States and crossed all racial, social, geographic, and economic

barriers.[7] Drug use is usually inversely proportional to age (National Institute on Drug Abuse, unpublished data, May 1985), but cocaine abuse appears to be an exception. Data suggest that the intensity of cocaine abuse among blacks is of significant proportions. These data further suggest that black persons may suffer adverse consequences of cocaine abuse disproportionate to their representation in the general population (National Institute on Drug Abuse, unpublished data, May 1985). The prevalence of reported drug abuse is obviously much higher in urban areas. Blacks are more likely to reside in inner cities and may be at a greater risk for the negative social and adverse health consequences associated with cocaine abuse.

Five patterns of cocaine use have been described: experimental, social/recreational, circumstantial/situational, intense, and compulsive (addictive).[8] Patterns of use between 1970 and 1978 involved primarily social/recreational intranasal doses ranging from 1 to 4 grams per month. From 1978 to 1983, doses increased to 1 to 3 grams per week, with increased use by freebase smoking. Between 1982 and 1984, episodes of concentrated binding became more common as did the development of experimental practices, including intranasal cocaine freebase and the smoking of coca paste.[8] The purity of cocaine increased between 1982 and 1984 and concomitantly the price dropped to pre-1977 levels of approximately $85 per gram.[8-10]

Cocaine is a potent peripheral vasoconstrictor and by this action may prevent its own absorption.[4] It is a central nervous system stimulant comparable to amphetamines with respect to neurochemical and clinical effects. The major difference that pertains to abuse is the duration of action. The effects of cocaine include garrulousness, euphoria, excitement, heightened energy, increased self-esteem, a sense of well-being, enormous self-confidence, and lower anxiety and social inhibitions. Many users report that cocaine increases sexual desire and performance. Cocaine may be administered intranasally ("snorting"),[11] or injected subcutaneously, intramuscularly, or intravenously. It may also be used orally, vaginally, sublingually, or rectally,[8,9] and can also be smoked. Intranasal use is the most common route of administration in the United States.

There has been a recent increase in intravenous administration of heroin and cocaine together (a "speedball"), as well as an increase in cocaine ("freebase") smoking. Freebase is made by extracting cocaine using an alkaline solution and adding a solvent such as ether. The mixture separates into two layers; the top layer contains cocaine dissolved in the solvent. The solvent mixture can then be evaporated leaving relatively pure cocaine crystals.[10,12,13] The most common method of preparing cocaine freebase is by using baking soda and water. This method eliminates the need for chemicals and special glassware. The baking soda and water method is preferred by some as it is rarely associated with nasal complaints.[10] The cocaine alkaloid, known as freebase, volatilizes at low temperatures.[13] Many cocaine freebase users prepare their own freebase from cocaine hydrochloride. Cocaine freebase called "rock" has been found on the market in Los Angeles and Oakland, California.[14] Cocaine freebase called "crack" has been gaining popularity in the Northeast, particularly in Boston, New York City, and Washington, DC. The belief that the freebase technique removes contaminants is not true. Freebase can be mixed with tobacco in a cigarette and smoked or heated in a water pipe and inhaled.[13] Smoking freebase provides effective respiratory absorption of cocaine and a rapid increase in cocaine plasma concentration with subjective and physiologic effects comparable to those achieved by injecting cocaine intravenously.[12] The main effect is a euphoria similar to that produced by amphetamine-like drugs. Cocaine's effects are short, lasting about 15 to 20 minutes when smoked as freebase. Intranasal administration may provide effects lasting as long as 1½ hours.

The average cocaine user is a young male with higher than average income. Many are professionals and in positions of authority requiring a high degree of responsibility.[15] Among blacks and whites, the highest prevalence rates of cocaine use are among young males (ages 18 to 25 years) living in the northeast and western United States.[1] The young adult black cocaine user is likely to use the drug occasionally and be a frequent user of alcohol or marijuana. It is not unusual for the black cocaine user to combine marijuana and cocaine use.[1] Cocaine use among black women is increasing and is often connected with issues of sexuality and relationships with men. Many black women receive cocaine as a gift from men, as they would candy or flowers, and this practice has become incorporated into courtship rituals.[16]

As stated previously, cocaine has become widely recognized as one of the most dangerous illicit drugs (*New York Times,* July 30, 1986).[17-20] Data from animal studies suggest that it may be more harmful than heroin. Cocaine has been found to be a powerful reinforcing drug.[21,22] The reinforcing properties of cocaine coupled with effective delivery systems and a relatively short half-life may lead to a pattern of compulsive use. This can cause disruptions in family life and job performance

as well as physical and mental deterioration. These patterns may lead to use of cocaine by more dangerous routes of administration and in higher doses, which increase the risk of untoward effects due to, for example, the cardiovascular actions of cocaine.[23] Until recently, little information was available about the cardiovascular effects of cocaine.[17,18,24-29] Cocaine-related cardiovascular events and deaths have increased because of the drug's popularity and increased availability.[30-33] To date, however, cocaine's greatest dangers have not been adequately recognized by either the physician or the general public.[17,18]

PHARMACOLOGY

Cocaine is prepared from the leaves of the *Erythroxylon coca* plant; the formula is $C_{17}H_{21}NO_4$ (benzoylmethylecgonine).[5,6] Cocaine hydrochloride is prepared by dissolution in hydrochloric acid to form a water soluble salt. This preparation is sold for medicinal purposes. The molecular weight of cocaine hydrochloride is 330.81. It is marketed in the form of crystals, granules, or a white powder that is slightly bitter to taste and numbs the tongue and lips. Cocaine hydrochloride is 89% cocaine by weight, decomposes on heating, melts at 195°C, and is soluble in ether and oils.

The cocaine alkaloid, known as freebase, is soluble in alcohol, acetone, oils, and ether. It is a colorless, odorless, transparent crystalline substance almost insoluble in water.[4] It dissolves in dilute acids to form salts. Freebase melts at 98°C, vaporizes at higher temperatures, and does not decompose on heating. The molecular weight is 303.36; aqueous solutions are alkaline on litmus test. The wider use of crack is due to increased availability and decreased price of cocaine, which make it profitable to convert cocaine hydrochloride to the alkaloid.[34] Freebase is well absorbed by mucous membranes and the gastrointestinal tract. Cocaine freebase is absorbed slowly through mucous membranes, resulting in delayed onset of its effects and sustained duration of action. This delay in absorption is responsible for the prolonged therapeutic effect in ointments, oily solutions, and topical preparations.

Cocaine is detoxified by liver and plasma cholinesterase to water soluble metabolites (benzolyecgonine and ecgonine methylether) that are excreted in the urine.[35] Plasma cholinesterase activity is genetically determined and therefore varies greatly between individuals. Cholinesterase activity is much lower in the fetus, infants, elderly males, individuals with liver disease, and during pregnancy.[35] Succinylcholine-sensitive individuals and those with congenital cholinesterase deficiency may have impaired hydrolysis of cocaine in plasma.[36] Cocaine may persist in the urine of an adult for 24 to 36 hours depending on the route of administration and cholinesterase activity. Assays for the urine metabolites of cocaine are useful markers of cocaine use.[37,38]

Dopamine is a precursor of norepinephrine, and the body synthesizes norepinephrine from this compound. The central nervous system neurons use norepinephrine or dopamine as a neurotransmitter. Norepinephrine is present in the hypothalamus, which regulates appetite, thirst, body temperature, sleep, and sexual arousal. Electrical stimulation of other areas of the hypothalamus produces euphoric sensations.

Cocaine can produce sensitization to catecholamines. It is a potent vasoconstrictor and by this action may prevent its own absorption. Epinephrine and norepinephrine both potentiate the effects of cocaine.[4]

Cocaine belongs to a class of compounds known as local anesthetics and is similar to procaine and lidocaine. Introduced in 1884 as the first local anesthetic, cocaine gained popularity in ophthalmology, surgery, and dentistry.[6] Cocaine is a weak base and the hydrochloride salt solution is quite acidic. The addition of alkali to a local anesthetic leads to greater potency and increased toxicity. The local anesthetic effect is due to cocaine's ability to block the conduction of electrical impulses within nerve cells.[4] The electrical impulse generated in these nerve cells at the synapse is responsible for the release of a transmitter. Cocaine acts primarily on norepinephrine found in the central and peripheral nervous system blocking the reuptake of norepinephrine and producing an excess of neurotransmitter in the synapse to stimulate receptors.[4,39] Higher norepinephrine levels produce vasoconstriction, tachycardia, and an acute rise in blood pressure, ventricular arrhythmias, and seizures. Cocaine also activates the sympathetic nervous system. Its specific physiologic effects include dilated pupils, increased heart rate and blood pressure, vasoconstriction of blood vessels, hyperglycemia, and hyperthermia.

The dopamine depletion hypothesis states that the pathophysiology underlying repeated cocaine administration is the drug's ability to increase synaptic dopamine transiently.[40] Chronic cocaine use appears to deplete brain dopamine. Alterations in dopamine neurotransmission may be responsible for the development of compulsive use patterns. Compulsive cocaine use results in psychosocial dysfunction, deviant behaviors, and a wide variety of social, financial, and family problems. Chronic, compulsive use leads to major medical complications or death.[19]

CARDIAC CONSEQUENCES OF COCAINE

Acute Myocardial Infarction

Twenty-four patients who suffered acute myocardial infarctions (mean age 32 years, range 19 to 44) with a temporal relation to the use of cocaine were reported between 1982 and early 1986.[41-54] Thirteen reports of myocardial infarction associated with cocaine occurred in persons with pre-existing angina or a prior myocardial infarction unrelated to cocaine use. These patients had underlying fixed or spastic coronary artery disease. The remaining patients were all less than 45 years of age and had no prior history of heart disease. Seven had normal coronary arteries demonstrated by selective coronary arteriography.[44-47,52,53] Coronary artery spasm could not be induced by ergonovine maleate in four patients. Four patients left the hospital before the coronary angiography could be performed.[49-52] Recently, an additional eight patients with myocardial infarction have been reported in the literature.[55-59]

Cocaine represents a potential hazard to anyone with underlying fixed coronary artery disease by virtue of predictable increases in double product (heart rate times systolic blood pressure) and myocardial oxygen demand.[46] The pathophysiology of coronary occlusion remains uncertain, but current evidence suggests a transient focal coronary event, ie, spasm and/or thrombus. Acute myocardial infarction occurring in any young patient who does not have the usual coronary risk factors should raise the suspicion of coronary spasm related to recreational cocaine use.[44-46] Coronary artery thrombosis may cause acute myocardial infarction despite anatomically normal coronary arteries,[60-62] but whether cocaine can induce coronary thrombosis is unknown. Coronary artery embolization is remote in the absence of other systemic emboli or an identifiable source.[46] Cocaine may be mixed with a variety of different diluents including lidocaine, procaine, phencyclidine (PCP), antihistamines, lactose, or amphetamines.[10] Amphetamines are potent sympathomimetics with vasoconstrictor properties but acute myocardial infarction and coronary artery spasm have not been attributed to abuse of these drugs.[63]

Cardiac Arrhythmias

Cardiac arrhythmias can occur as a result of cocaine abuse and may be attributed either to a direct effect of the drug or, more likely, to its effects on catecholamines. Cocaine blocks the reuptake of norepinephrine by presynaptic nerve endings which may be important in enhancing beta stimulation of the myocardium. Arrhythmias associated with cocaine use include sinus bradycardia, sinus tachycardia, ventricular premature depolarizations, ventricular tachycardia/fibrillation, and asystole.[4,23,64] Arrhythmias may also occur after cocaine-induced myocardial infarction. In addition, cocaine is known to produce hyperpyrexia, which can lead to seizures and possibly also to cardiac arrhythmias. A general autonomic outpouring may precede many of the prefatal and fatal events associated with cocaine use.

Cardiac arrhythmias may be life-threatening and require prompt treatment with anti-arrhythmic drugs.[65] Propranolol and amitriptyline have been recommended for treatment of ventricular arrhythmias by some investigators.[14,29,64,66-68] Recently, calcium channel blockers have been shown to be effective in rats. Nitrendipine (a calcium channel blocker) has been found to be an effective antagonist to the cardiotoxic effects of cocaine.[69,70]

CENTRAL NERVOUS SYSTEM COMPLICATIONS OF COCAINE

Cerebrovascular Accidents

Seventeen patients who had cerebrovascular accidents with a temporal relation to cocaine abuse having a mean age of 32 years (range 22 to 51) have been reported since 1977.[71-79] In six cases, subarachnoid hemorrhage occurred within minutes of intranasal administration of cocaine. Two patients had an aneurysm of the anterior communicating artery, three had an aneurysm of the right posterior communicating artery, and in two patients bleeding was from an arteriovenous malformation. Two additional patients probably had an occlusion of the anterior branch of the left middle cerebral artery. This occurred between one and two hours after intramuscular administration of cocaine. Computerized tomography revealed diffuse subarachnoid hemorrhage in five other individuals, but cerebral angiography was not performed and the anatomy is unknown.[79] Cerebral angiography failed to demonstrate any anatomical lesion in four patients.

Three additional adult patients with strokes have been reported with temporal uncertainty.[71,75] Recently, Chasnoff et al reported an infant who developed cerebral infarction after birth.[76] The mother had used cocaine intranasally 15 hours before delivering the infant. After delivery, the infant experienced seizures, intermittent tachycardia, hypertension, and decreased tone in the right arm, shoulder, and hip. Computerized tomography (noncontrast) of the brain showed an acute infarction in the distribution of the left middle cerebral artery. The exact timing of the cerebral infarction is unknown, but prenatal occurrence is likely because the infant had right-sided weakness at birth.

Tachycardia and blood pressure elevation occur within minutes of taking cocaine intranasally.[73] The mechanism of cerebrovascular accidents is probably related to adrenergic stimulation and a sudden surge in blood pressure. Sudden increases of blood pressure in otherwise normotensive persons may precipitate spontaneous bleeding.[73] The incidence of subarachnoid hemorrhage from the use of cocaine is unknown but is probably low. However, any person with an arteriovenous malformation or an aneurysm of a cerebral vessel may be at risk. Cocaine use during pregnancy may place the fetus at risk for a cerebrovascular accident.[76] Maternal cocaine use should be included in the differential diagnosis of neonates with perinatal cerebral infarction. Physicians caring for patients with headaches that follow cocaine use should be aware of the possibility of intracranial hemorrhage.[18,73] The risk of stroke from intravenous use with bolus effect is unknown.

Seizures

Convulsions were among the earliest known adverse effects of cocaine[6,10] and can be induced after a single dose of the drug.[80] Hyperpyrexia can occur after cocaine use and can lead to seizures, possibly cardiac arrhythmias, and even death.[81,82] Because cocaine lowers the seizure threshold, seizures can be primary or secondary.[22,68] There is excellent evidence that cocaine has the capacity to "kindle" neurons (reverse tolerance) in the animal experimental models.[83,85] Repetitive subthreshold electrical stimulation of the limbic system produces increasing effects on electrical activity and behavior, eventually resulting in major convulsions. Seizures may also be secondary to central nervous system-induced cardiac events such as ventricular tachycardia/fibrillation. A general autonomic outpouring may precede many of the prefatal events associated with cocaine use.

The Dade County autopsy study included 36 deaths due to cocaine alone and in 13 individuals, seizures were witnessed prior to death.[15] The conventional anticonvulsant drugs may not be helpful in preventing cocaine-related seizures.[4] Diazepam, administered intravenously, is the drug of choice for the treatment of acute seizures.[68]

Wetli et al reported fungal cerebritis in three intravenous cocaine abusers.[86] They suggest that a diminished immune response may be responsible for this opportunistic infection. These patients developed a fulminant fungal cerebritis without other identifiable predisposing factors. Two patients died and on autopsy, no predisposing causes were found. A primary fungal infection of the brain is uncommon without a predisposing risk. Fungal cerebritis may represent a variant of the acquired immune deficiency syndrome.

OTHER ADVERSE MEDICAL CONSEQUENCES OF COCAINE

Obstetrical Complications

Six occurrences of abruptio placentae, at a mean age of 22 years, have been reported in association with cocaine use.[87,88] Five patients had the onset of labor and vaginal bleeding immediately after intravenous cocaine. In the sixth patient, contractions and vaginal bleeding occurred within several hours of intranasal administration of cocaine. All were subsequently found to have a large retroplacental clot. All coagulation parameters were normal. The patients displayed alterations in blood pressure consistent with the acute phase of cocaine use modified by their specific gestational physiology.[87] The association of cocaine with immediate but transient hypertension is well established[4] and may have contributed to abruptio placentae. Placental vasoconstriction with decreased blood flow to the fetus and increased norepinephrine levels leading to uterine contractility due to cocaine use have also been reported.[87]

Cocaine exerts a deleterious influence on the outcome of pregnancy.[88] Hypertension and vasoconstriction could be responsible for abruptio placentae, given the documented association between hypertension and this condition. Obstetricians should be aware of the potentially serious consequences of recreational abuse of this drug during pregnancy and that cocaine-induced transient hypertension may be wrongly interpreted as a physiologic alteration of blood pressure during pregnancy.[87] Women who use cocaine during pregnancy have a rate of spontaneous abortion even higher than that of women using heroin during pregnancy.[88] Current data suggest that infants exposed to cocaine are at risk for higher rates of congenital malformations, perinatal mortality, and neurobehavioral impairments.[88-90] The long-term effects of cocaine on cerebral function of infants born to cocaine-abusing mothers are unknown.

Intestinal Ischemia

Few data have been published about ingested cocaine despite widespread use. There is a common misconception that cocaine is hydrolyzed in the gastrointestinal tract and rendered inactive[91]; however, there is evidence to the contrary. Cocaine administered by the oral route is at least as effective as the same dose taken intranasally. The subjective "highs" are greater after oral than intranasal administration.[92] Two patients with intestinal

ischemia following ingestion of a large quantity of cocaine have been reported.[91] One patient in whom gangrene of the bowel developed required repeated surgical resections and subsequently died. The second patient had less severe ischemia, and the bowel returned to normal after several days. The diagnosis of ischemic bowel was confirmed by exploratory laparotomy in both patients.

The mechanism by which ingested cocaine causes severe bowel ischemia or gangrene is related to the basic pharmacology of the drug. The intestinal vasculature contains alpha-adrenergic receptors that are stimulated by norepinephrine, leading to an increase in intestinal vasculature resistance. Cocaine-induced catecholamine stimulation of alpha receptors in mesenteric vasculature causes intense vasoconstriction and reduced blood flow, which can lead to ischemia.[92] The diagnosis of bowel ischemia should be considered whenever a cocaine user presents with severe abdominal pain. The presence of marked leukocytosis in such a patient supports the diagnosis of bowel gangrene, which demands prompt surgical intervention.[91]

Other deaths have resulted from the accidental rupture of bags of cocaine in individuals ("body-packers" or "mules") who were attempting to transport them through customs.[15,91,93-99] Gastrointestinal obstruction and rupture are major problems related to cocaine-packet ingestion.

Cocaine Intoxication

Dysphoric agitation may be the first symptom of cocaine intoxication. It can develop rapidly and may be fatal.[100] Cocaine intoxication (resembling drunkenness) has been associated with myriad effects. The spectrum of intoxication ranges from euphoria, alertness, decreased appetite, sleep disorders, and feelings of enhanced energy to assaultive behavior, paranoid ideation, delirium, syncope, nausea, vomiting, chest pain, tremors, seizures, hypertension, respiratory paralysis, cardiac arrhythmias, and death.[68-70,101-107] Intoxication can be self-limited in which case recovery can take place within 24 hours. Treatment is usually supportive and symptomatic.[101-108] Benzodiazepines have been found to be helpful in decreasing the stimulatory effects.[30,102,103]

Miscellaneous Complications

Other medical complications of cocaine abuse depend on the route of administration. Loss of sense of smell, atrophy of the nasal mucosa, and necrosis and perforation of the nasal septum can occur with intranasal administration.[109,110] Inhaling or smoking freebase cocaine is reported to produce a significant reduction of carbon monoxide-diffusing capacity of the lungs.[111,112] Lung damage, pneumonia, and pulmonary edema have also been reported in freebase smokers.[10,113-116] Spontaneous pneudomediastinum and pneumopericardium have also been reported after freebase smoking.[117-125] The smoking of freebase involves deep, forced, and prolonged inspiratory efforts with Valsalva's maneuver. Spontaneous pneumomediastinum occurs as a consequence of alveolar rupture when there is a sudden rise in intra-alveolar pressure.[119]

Cellulitis, cerebritis, wound abscess, sepsis, arterial thrombosis, thrombotic phenomena, renal infarction, thrombophlebitis, infective endocarditis, hepatitis, and human immunodeficiency virus infection are some of the common medical complications seen in parenteral cocaine abusers.[86,126-133] Other complications reported include thallium poisoning, rhabdomyolysis, retinal artery occlusion, dermatologic problems, and muscle and skin infarction.[134-137]

Cocaine may interfere with antihypertensive properties of guanethidine and related drugs because of their sensitizing effect on catecholamines.[22] Blood glucose levels may also become abnormal because of poor food intake, medication noncompliance, and sensitization of the individual to epinephrine, which can mobilize glucose.[22] Many individuals with compulsive use patterns have eating disorders and can experience massive weight loss.[138] Hyperthermia can be induced by hyperactivity and the vasoconstrictive effect of cocaine on the temperature-regulating center.[81] Hyperthermia can be severe enough to cause death.[82]

Bilateral loss of eyebrows and eyelash hair in a male with AIDS-related complex was recently reported. He had used freebase cocaine in the form of crack.[139] Crack vapors are often inhaled in a glass pipe, and these hot vapors can singe the eyebrows and eyelashes. Tames et al suggest that madarosis should be considered along with chronic rhinitis, rhinorrhea, and nasal septic ulceration and perforation as symptoms that could alert clinicians to illicit cocaine use.[139]

Sexual dysfunction is one of the primary motivating factors for seeking treatment for compulsive use of cocaine. A common myth is that cocaine is an aphrodisiac and enhances sexual performance. At low doses, cocaine can delay ejaculation and orgasm as well as cause elevated mood and heightened sensory awareness. These effects together can often produce an improved sexual experience.[140] Chronic male users, particularly those using high doses, may have difficulty maintaining an erection and ejaculating. Many males have frequent

periods of complete sexual disinterest[141] and some women have difficulty in achieving orgasm.[140] Chronic high doses of cocaine can result in aberrant sexual behavior such as compulsive masturbation and multiple partner marathons.[140] Cocaine-induced sexual dysfunction is probably related to alterations in dopamine neurotransmission.[142] The sexual excitement produced by cocaine may result from amygdaloid and dopamine effects. Cocaine administration has been reported to cause spontaneous ejaculation without genital stimulation.[67,143,144]

PSYCHIATRIC COMPLICATIONS OF COCAINE

A variety of psychiatric complications and clinical syndromes have been seen with cocaine abuse. Psychiatric complications include euphoria, dysphoria, agitation, anxiety, suicidal ideation, paranoid psychosis, and severe depression. In some cases, psychiatric illness may be the presenting manifestation of cocaine abuse.[145-148] Cocaine has been associated with multiple psychiatric syndromes rather than a single illness. There is an orderly progression of clinical syndromes with cocaine use that is related to dosage and chronicity.[145] This progression implies that alterations in neurotransmitters may be involved in each of the cocaine-induced syndromes. Clear sequential changes have been documented in animals after increasing dose and duration of exposure to cocaine.

Cocaine's mood-elevating properties have been known for centuries, dating back to the Inca Indians. Intravenously injected cocaine produces an ecstatic high, which is of brief duration but is so pleasurable that the user may repeatedly "shoot-up" at intervals of 10 to 15 minutes until the entire supply of cocaine is exhausted.[145] Continued use of cocaine in escalating doses may lead to increased anxiety, nervousness, suspicion, and dysphoria. Most cocaine abusers do not use only cocaine.[8] Many persons simultaneously use marijuana, opiates, or alcohol to mellow or modulate cocaine's effects.[49] When cocaine has been abused chronically, a paranoid psychosis can develop and this psychosis is indistinguishable from acute paranoid schizophrenia.[145,149] Genetic and environmental factors, preexisting active psychopathology, and stress may be involved in developing cocaine-induced psychosis. Certain individuals more prone to psychiatric disorders may be at even greater risk for developing cocaine psychosis.[14,145]

ADDICTION

Addiction requires tolerance and physical dependence. The myth that cocaine is not addicting because it does not induce physical dependence has been an important factor in fostering widespread acceptance.[150] The issue of physical dependence due to cocaine is still somewhat controversial.[14] Clinicians have observed two types of reactions probably due to cocaine withdrawal: (1) following a short course of high dose cocaine use, there is a two to four day period in which the person is apathetically depressed, fatigued, and exhausted; and (2) following chronic high-dose use of cocaine, the withdrawal period is characterized by an agitated depression, lethargy, insomnia, and irritability.[14,151]

The average social/recreational abuser uses 1 to 4 grams of cocaine per month. Cocaine is purchased in half-gram quantities and consumed over a two to seven day period. The average daily consumption would be approximately 150 mg.[8] The development of a compulsive use pattern and addiction is a major complication of cocaine abuse. Addiction is defined as a compulsion to use a drug, loss of control over the amount used, and the continued use despite adverse health consequences.[14] Cocaine is addicting and only the lack of availability or development of legal, medical, or psychiatric complications limit its use. Many individuals will continue to use cocaine despite the compromise of employment or personal, business, or financial resources and negative impact on their marriages and families.[14]

Many black cocaine abusers have used cocaine for three to four years before they develop compulsive use patterns and finally present for treatment. Many freebase users are middle class individuals who have no previous drug experience. Many of these people present for treatment unaware of their physical dependence.[14] Many users do not believe they can become victims, thus the addictive potential is not a deterrent to use. In fact, cocaine has many attractive attributes for the adventurous: it is illegal, powerful, and dangerous. In the past, the high cost of cocaine served to reinforce its elite and privileged status.[14] The use of freebase cocaine (crack) and the more dangerous routes of administration have served to escalate the growing number of addicted persons.

Deaths have occurred after administration of cocaine by all routes.[12,18,152-154] Individuals with plasma pseudocholinesterase deficiency are at risk for sudden death when using cocaine because this enzyme is essential in the metabolization of the drug. Most deaths are attributed to generalized convulsions, respiratory failure, or cardiac arrhythmias.[1,8,12,14] The medical examiner for Dade County, Florida, which covers a geographical area with 1.7 million people, investigated

unexpected and sudden deaths over a 4.5 year period. Of 240 cases reviewed, 180 were deaths in which cocaine was detected incidentally but did not contribute directly to the cause of death. The remaining 60 deaths were related to cocaine overdose; 36 were due to ingestion of street cocaine alone and 24 were the result of multiple drug overdoses, including cocaine.[15] The incidence of cocaine-related deaths from this study is unknown as the total number of deaths over this period was not recorded.

TREATMENT OF COCAINE ABUSE

As cocaine abuse has escalated, nationwide figures show a sharp increase in emergency room visits, treatment admissions, and cocaine-related deaths.[147] Cocaine-related deaths among blacks tripled between 1982 and 1984 (*New York Times*, May 1985). Emergency room treatment for cocaine overdose can be lifesaving. For acute cocaine overdose, the recommended treatment consists of supportive care, which includes securing an airway, administering oxygen, placing the patient in the Trendelenburg position, administering muscle relaxants if indicated, and if convulsions occur treating them with short-acting barbiturates intravenously (eg, 25-50 mg sodium thiopental).[2,67,101,102,155] Intravenous diazepam can be given for anxiety associated with hypertension and tachycardia. Continuous monitoring of vital signs is essential.

Physicians are seeing increasing numbers of individuals who are seeking treatment for complications of cocaine abuse due to compulsive use patterns. Medical or psychiatric emergencies can develop and cocaine abuse should be considered as a possible hidden cause of both atypical mood and physical complaints.[156] The goal of treatment should be complete abstinence from all mood-altering drugs. Cocaine abuse treatment should be divided into two phases: initiation of abstinence and relapse prevention.[150] Many abusers also use sedative-hypnotics, marijuana, and alcohol. Careful psychiatric evaluation and subtyping of patients may be helpful in designing a treatment protocol. Five subtypes of cocaine abusers have been identified: patients with depression; bipolar or cyclothymic disorder; alteration deficit disorder, residual type; narcissistic and borderline personality disorders; and antisocial personality disorder.[157] Abrupt cessation of cocaine use can result in a variety of symptoms including depression, irritability, appetite changes, nausea, hypersomnia, sleep disturbances, shaking, and psychomotor retardation.[142] Cocaine cravings appear to be the most severe during the first week after discontinuing use.

Blacks are three times more likely to be in treatment for drug abuse-related problems than are whites (*New York Times*, May 1985). Treatment can be initiated on an outpatient or inpatient basis.[151,158] Even with the structure of an outpatient recovery program, many cocaine abusers have great difficulty abstaining. The indications for hospitalization are: (1) chronic freebase or intravenous use, (2) severe impairment in psychomotor functioning, (3) medical or psychiatric complications, (4) physical dependence on other addictive drugs, and (5) inability or unwillingness to stop using cocaine as an outpatient.[159] A complete program must take control of the user, provide a drug-free environment, and frequent drug (urine) testing. A number of pharmacological agents have been tried in various treatment centers. These agents include L-dopa, apomorphine, and bromocriptine. Bromocriptine has been shown to reverse hyperprolactinemia and increased postsynaptic dopamine receptor density that is associated with cocaine abuse.[159,160] In some studies, L-tryptophan, the amino acid precursor to serotonin, in dosages of 2,000 to 6,000 mg per day have been found to be effective in reducing anxiety, agitation, and insomnia associated with cocaine withdrawal.[14] Other studies by Gold et al have shown that tyrosine (an amino acid), desipramine (a tricyclic antidepressant), and bromocriptine may be effective in relieving withdrawal.[142] Woolverton and Balaster demonstrated that when low-dose haloperidol was given to monkeys who were pressing a lever to obtain cocaine, self-administration increased.[161] This finding suggests that neuroleptics should be used with caution in cocaine abusers being treated for psychosis.

Psychological therapy is the most important aspect of treatment for cocaine addiction.[159] Self-help groups and education are effective in treating the majority of patients who are motivated and abstinent. Therapy includes a combination of individual treatment and participation in group sessions and Cocaine Anonymous.[14,159,162] Couple and family therapy may also be included in the treatment plan when indicated. Mandatory urine testing is an essential part of the treatment and can help identify individuals who are unwilling to stop using cocaine.

Despite the high incidence of abuse, cocaine is often misdiagnosed as a psychiatric illness. The laboratory can aid in making a correct diagnosis and eliminating drugs from active consideration as a cause of psychosis, depression, mania, and personality changes.[162] Treatment protocols often rely on the accuracy of the admission drug screen. The appropriate use of analytic technology in drug abuse testing requires an understanding

of available test methodologies. These include drug screens by thin-layer chromatography, comprehensive testing using enzyme immunoassay, and radioimmunoassay.[162]

CONCLUSIONS

Cocaine use has evolved from a relatively minor problem into a major public health threat with important economic and social consequences. Compulsive use is a major complication of cocaine abuse; addiction is a chronic disorder with exacerbations and remissions. That the drug is safe, nonaddicting, and can be used as an aphrodisiac are a few of the many myths associated with cocaine use.[163] The perception that cocaine was only psychologically addicting, and thus less dangerous, contributed to the rapid spread of cocaine dependence. As cocaine abuse has escalated, nationwide figures show an increase in emergency room visits, treatment admissions, cocaine-related cardiovascular events, and deaths due to overdose. It is hoped that scientific understanding and treatment of cocaine abuse will continue to evolve. A national campaign should be mounted to inform the public of the myths, effects, and adverse health consequences surrounding cocaine.[163] Drug testing may be used as an early warning signal that a problem exists and as a means of prevention also.[164-167]

Cocaine abuse is so pervasive at all levels of society that every practicing physician can expect to encounter it. A compulsive user is not likely to disclose the problem but may present with one of the many symptoms of cocaine abuse. It is up to the physician to recognize the signs and ask the right questions.[168] If the present epidemic follows the historical course of drug abuse, lower income individuals, blacks, and other minority groups will be hit last and hardest by the crack epidemic.[150,169] Physicians and other health care professionals have a major responsibility to recognize cocaine abuse, refer these patients for treatment, and clarify the enormous danger cocaine presents for their patients and the American public.[19,170,171]

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