

## Substance abuse: the designer drugs.

by Diane K. Beebe and Elizabeth Walley

**Drug abuse can be defined as the use of a chemical in an inappropriate way or in an inappropriate amount to achieve a desired pharmacologic effect. Family physicians should be able to recognize the signs of designer drug use. These drugs, synthetic derivatives of existing federally controlled drugs, are currently very popular. They are produced by illegal laboratories and sold on the black market. There are four major classes of designer drugs: mescaline analogs (amphetamines, methamphetamines, and MDMA, nicknamed "ecstasy"); synthetic opioids ("China white," "Mexican brown" and "Persian white"); arylhexylamines (including PCP, or "angel dust"); and methaqualone (Quaalude) derivatives. Crack, a form of cocaine, is also considered a designer drug. Abuse of methaqualone derivatives has declined and is not discussed here. Drugs synthesized from opium, morphine and heroin are the deadliest of these drugs of abuse. The street names and the effects of the drugs are discussed, and the adverse effects and physiological effects of overdose are described. The treatment of intoxication is detailed for each class of drug. Physicians should be aware of the signs and symptoms of drug abuse so that the diagnosis can be made before there is serious mental or physical damage. Immediate treatment should be followed by counseling and rehabilitation, which are required for long-term success. (Consumer Summary produced by Reliance Medical Information, Inc.)**

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Designer drugs, chemically altered compounds derived from federally controlled substances, have become a major cause of addiction and overdose deaths. These drugs include mescaline analogs, synthetic opioids, arylhexylamines, methaqualone derivatives and crack, a new form of cocaine. Sudden changes in mood, weight loss, depression, disturbed sleep patterns, deteriorating school or work performance, marital problems, and loss of interest in friends and social activities may be signs of drug addiction. Life-threatening complications of acute intoxication, such as hyperthermia, seizures, combative and psychotic behavior, and cardiorespiratory collapse, require prompt diagnosis and supportive intervention.

Drug abuse permeates our society, affecting persons at every socioeconomic level and jeopardizing every aspect of life. Among the most popular contemporary drugs of abuse are the designer drugs, which are synthetic derivatives of federally controlled substances.(1), These new, untested drugs are created by slight alterations in the molecular structures of existing drugs and are produced illegally in black market laboratories.

Family physicians need to be able to recognize the various clinical presentations of designer drug intoxication. This article reviews the pharmacology of the newer illicit drugs and discusses the signs, symptoms and treatment of acute intoxication.

### Epidemiology

The ever-changing nature of designer drug abuse makes it difficult to obtain accurate, current information. The most recent statistics from the U.S. Department of Health and Human Services represent data collected in 1988.(2) According to these figures, approximately 21.2 million Americans have used cocaine at least once in their lives, and 8.2 million used cocaine during 1988. Overall, 72.5 million Americans 12 years of age and older have tried marijuana, cocaine or other

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illicit drugs at least once. It is important to note that these statistics do not address the rising popularity of the designer drugs. Furthermore, since polysubstance abuse has become increasingly common, designer drugs are undoubtedly being used with greater frequency in combination with other drugs.

### Classes of Designer Drugs

The four major classes of designer drugs are the mescaline analogs, the synthetic opioids, the arylhexylamines and the methaqualone derivatives (Table 1). Because of the increasing availability and popularity of crack, a new form of cocaine, it is now included as a designer drug.

Mescaline analogs, the most extensively studied class of designer drugs, include amphetamines, methamphetamines (speed, crank, meth, crystal or ice) and a variety of compounds known by the abbreviations of their long chemical names. The most popular mescaline analog is 3,4-methylenedioxymethamphetamine (MDMA), commonly known as ecstasy.<sup>(3)</sup>

The synthetic opioids are perhaps the deadliest of the designer drugs. These narcotics mimic the classic opiates opium, morphine and heroin.<sup>(3)</sup>

The arylhexylamines are easily synthesized and have been the source of numerous street-drug analogs.<sup>(3)</sup> The best known arylhexylamine is phencyclidine (PCP).

Methaqualone derivatives, which include Quaalude, have become less popular in recent years. Since these drugs no longer constitute a significant abuse problem,<sup>(3)</sup> they are not discussed in this article.

### Ecstasy

Ecstasy or MDMA, also known as Adam, XTC, MDM or M & M, was synthesized in the early part of this century as a relative of 3,4-methylenedioxyamphetamine (MDA), which was popularized in the 1960s as the "love drug."<sup>(1)</sup> Similar in structure to lysergic acid diethylamide (LSD), ecstasy produces mild intoxication, euphoria and hallucinations. By 1972, ecstasy had appeared on the streets. As the drug became more popular, black market laboratories produced the drug and distributed it to at least 21 states and Canada.<sup>(1)</sup> In recent years, ecstasy has been associated with numerous deaths.

In the late 1970s and early 1980s, small doses of MDMA were used legally as an adjunct to psychotherapy.<sup>(3)</sup> The drug was also considered for use as an appetite suppressant; however, this application was never approved by the U. S. Food and Drug Administration.<sup>(4)</sup>

Despite recognition of ecstasy's potentially lethal effects, the drug was not permanently classified as a Schedule I controlled substance until November 1986.<sup>(4)</sup> In the same year, the Controlled Substance Analogue Enforcement Act, an amendment to the Controlled Substance Act, was adopted. This legislation was aimed at restricting chemicals with structures similar to those of drugs that were already federally controlled. Stimulants such as ecstasy and its derivatives were specifically included in the amendment. Despite this measure, the Drug Enforcement Administration expects more analogs of federally restricted drugs (particularly mescaline analogs) to appear on the streets.<sup>(3)</sup>

### PHARMACOLOGY

Ecstasy is generally taken orally. In its purest form, it is a white powder that can be packaged in clear gelatin capsules. More commonly, the drug is sold as a light-yellow or white pill that has been adulterated with any of several amphetamine compounds. Cost ranges from \$10 to \$35 per dose.<sup>(1)</sup>

Ecstasy acts pharmacologically as a sympathomimetic. <sup>(5)</sup> With low doses, users become euphoric and experience an increased sense of self-esteem and intimacy. Although users may perceive visual changes, they experience no true hallucinations. Ecstasy and amphetamine overdoses have similar presentations, including tachycardia, hypertension, hyperthermia, hyperreflexia, tremors, agitation and mydriasis. Core temperatures may reach 40[Degrees]C (104[Degrees]F).

Most deaths from acute ecstasy intoxication are the result of arrhythmias (supraventricular and ventricular), hyperthermia

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with seizures, or intracerebral hemorrhage. Underlying diseases may be exacerbated. Additional deaths may be attributed to these disease complications or to inadequate gastrointestinal elimination of the drug.(3)

Chronic abuse of ecstasy can lead to a paranoid psychosis that is clinically indistinguishable from schizophrenia; this psychosis is usually reversible after a prolonged drug-free state.(3) For this reason, speculation exists about the drug's neurotoxicity. Ecstasy has been found to destroy serotonin-producing neurons in the brains of rats and monkeys. In these animals, a single oral dose of the drug produces a 60 percent depletion of serotonin neurons. Whether ecstasy produces similar effects in humans and whether these effects may be permanent remain to be determined.(5)

### TREATMENT

The first step in the management of acute ecstasy intoxication is gastric lavage and the administration of activated charcoal. Aggressive blood pressure control and temperature maintenance are the mainstays of supportive therapy.

Hypertension is best treated with alpha blockers, combined alpha and beta blockers or vasodilators. (1,3) Chlorpromazine (Thorazine) has been proposed as an antidote for acute toxicity. In canine studies, the intravenous administration of chlorpromazine, 10 mg per kg, was found to hasten restoration of normal blood pressure, heart rate and temperature.(5) Benzodiazepines may be useful in the treatment of extremely agitated patients. They should be used with caution, however, since mental status is an important parameter in assessing central nervous system changes.

Any agents used in treating drug intoxication should be rapid-acting and easily titratable. As with all amphetamines, renal clearance of ecstasy can be enhanced by acidifying the urine with oral ascorbic acid or ammonium chloride. However, acidification increases the risk of myoglobinuria in the renal tubules.

### Synthetic Opioids

Synthetic heroins became popular in the early 1980s after increased law enforcement activities during the late 1970s reduced the volume of imported opium and heroin.(3) Figure 1 shows the relationship among the opioids and their derivatives.

Fentanyl (Sublimaze), a potent narcotic approximately 100 times stronger than morphine, was introduced in 1968. Today, this drug is used as an analgesic and a tranquilizer in about 70 percent of the surgeries performed in the United States. Synthetic heroins are analogs of fentanyl.

Alpha-methyl fentanyl, or China White, was the first of the synthetic heroins; and it is still perhaps the most widely known of the fentanyl derivatives. This synthetic opioid, which is 200 times stronger than morphine, is often contaminated and sold as heroin, cocaine or speed. Since the term "China White" originally referred to pure Southeast Asian heroin, buyers of the synthetic form are often misled.(1)

Other fentanyl derivatives are 3,000 times stronger than morphine and 1,000 times stronger than heroin.(1,3) These drugs have accounted for numerous deaths since they appeared on the streets between 1979 and 1985. Dosages as small as 1[micro]g can produce the desired euphoric effects. Street names for fentanyl derivatives include Mexican Brown and Persian White. These derivatives can be easily altered, with deadly results. One toxic byproduct of a synthetic opioid, 1-methyl-4-phenyl-1,2, 3,6-tetrahydropyridine (MPTP), produces severe parkinsonian effects.(1,3,6)

### PHARMACOLOGY

Synthetic opioids are most commonly taken intravenously, although they can be smoked or snorted. The user's euphoria depends on the dose and the route of administration. Since the plasma half-life of heroin is four to six hours, and the half-life of the fentanyls is even shorter, the euphoria induced by these agents is generally intense but short-lived.

The fentanyls, like the classic opiates, act primarily on the CNS and the gastrointestinal tract. These drugs produce analgesia, euphoria, drowsiness and respiratory depression.

The most acute toxic effect of the fentanyls is respiratory depression, which reaches its maximum effect five to ten

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minutes after administration and resolves within 30 minutes.(1,3) Blood pressure may drop as much as 20 percent, with a concomitant 25 percent decrease in pulse rate. Massive pulmonary edema has been reported.(3) Cardiovascular collapse and death can occur.

Long-term use of synthetic opioids depletes the body's natural supply of endorphins and dopamine, producing prolonged depression. Evidence suggests that with chronic synthetic opioid use, the brain's dopamine receptors can be permanently damaged. Both tolerance and physical dependence develop.(1)

### TREATMENT

Naloxone (Narcan) is the specific antagonist for the synthetic opioids. In cases of drug overdose, naloxone should be used in conjunction with other supportive measures..(3)

### Phencyclidine

PCP, the most commonly abused arylhexylamine, is frequently called angel dust or dust, although it has numerous other street names, including lovely, kools, mist, T and crystal.(2,7-9) This drug was originally developed in the late 1950s as an analgesic and anesthetic agent. However, in clinical trials, PCP caused postoperative thought disturbances and agitation. Consequently, it was never approved for use in humans.

In the mid-1960s, PCP appeared on the streets, where it was known as the "Peace Pill." The drug continued to be used as a veterinary anesthetic until April 1979, when all legal manufacture ceased.(1,7) PCP is synthesized easily and inexpensively. Numerous analogs have been produced, many with greater potency than the parent compound.

### PHARMACOLOGY

PCP has several routes of administration. Most commonly, it is mixed with marijuana, mint, parsley or oregano and then smoked.(1,7-9) A liquid form of PCP, selling for \$150 to \$400 per ounce, is used for dipping joints or cigarettes; pre-dipped "kools" cost about \$20 each. In powder form, PCP can be ingested or snorted with cocaine. For an equivalent effect, higher doses of PCP are needed if the drug is ingested rather than smoked or snorted.(1) The drug is seldom taken intravenously. In rock-crystal form, PCP resembles cocaine and sells for \$80 to 135 per gram.

The effects of PCP occur within one minute of inhalation or one hour of ingestion, and they may persist for up to six hours. The letdown period can last 24 to 48 hours.(7)

PCP'S mechanism of action is not well understood. Like cocaine and the amphetamines, PCP is known to inhibit presynaptic uptake of norepinephrine, dopamine and serotonin. In low doses of 2 to 5 mg, the drug produces mild depression, which is followed by an acute confusional state. Euphoria and a feeling of depersonalization are accompanied by signs of sympathetic stimulation, such as flushing and perspiration.

Hypertension, one of the earliest signs of acute PCP toxicity, may be accompanied by tachycardia, hyperthermia and hyperreflexia to the same degree as experienced in ecstasy abuse. At this stage of PCP intoxication, horizontal and/or vertical nystagmus is a common finding. Pupils are normal in size and the eyes remain open, even in a comatose state. Some authors suggest that these ocular findings are diagnostic for PCP intoxication. Psychologic effects may include an acute psychosis or schizophreniform state, with autistic and delusional thinking. Auditory hallucinations are common.(1,3,7-9)

In higher doses of 10 to 15 mg, PCP produces altered CNS responses. Patients in this stage of intoxication often become combative and paranoid. They may present to the emergency department in a violent and unpredictable state, with uninhibited muscle activity. Doses of more than 20 mg of PCP can result in seizures, acidosis, catatonia, coma, and respiratory depression or arrest. In this stuporous state, myoclonus with muscle rigidity occurs on stimulation. When death occurs, it most often results from these complications.

### TREATMENT

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Treatment of acute PCP intoxication is mainly supportive. Hypertension should be quickly identified and controlled with propranolol (Inderal), clonidine (Catapres), hydralazine (Alazine, Apresoline), diazoxide (Hyperstat) or prazosin (Mini-press). These drugs have been shown to block a number of the adverse effects of PCP, including hyperactivity.

Since hyperactivity occurs with PCP intoxication, all stimuli should be kept to a minimum. Agitated patients may require diazepam (Valium), particularly if seizures occur. Haloperidol (Haldol) is effective in controlling combative, psychotic patients. Psychotropic medications should be avoided if possible, especially during the first 24 hours of acute intoxication.

Acidification of the urine in PCP intoxication is, as in ecstasy intoxication, a much debated topic; however, it is often recommended. Because significant quantities of PCP undergo gastrointestinal recirculation, repeated doses of activated charcoal may be administered to absorb the PCP secreted in gastric juice.(3,9,10) Because of the potential for electrolyte imbalances, continuous nasogastric suction generally is not recommended. Since PCP has such a large volume of distribution, hemodialysis is ineffective.(3,10)

### Crack

Crack, also called rock, supercoke, gravel and Roxanne, is freebased cocaine. It is the cheapest, most potent form of cocaine. Freebased cocaine was initially made with ether, a dangerously volatile compound. It is now made relatively safely and easily by preparing an aqueous solution of cocaine hydrochloride, ammonia and baking soda. The pure cocaine is then precipitated into crystals by heating. The sound made by the crystals popping when heated is the origin of the name "crack."(1,11,12)

While powdered cocaine is usually 15 to 25 percent pure, crack may be as much as 90 percent pure. The craving that follows the smoking of crack is much more intense than that following the intravenous use of cocaine; thus, crack is highly addictive. One reason for crack's popularity is its low cost, with the price of a vial containing two or three "rocks" ranging from only \$5 to \$15. Each rock yields two to three inhalations.(1)

### PHARMACOLOGY

Cocaine is a sympathomimetic drug. Its psychoactive effects result from the blocking of norepinephrine, serotonin and dopamine reuptake at the presynaptic nerve endings. Clinically, this produces a "fight or flight" response consisting of pupil dilatation, peripheral vasoconstriction, increased heart rate and increased muscle contractility.

The nature and severity of cocaine's effects are determined by its purity, the dose and the route of administration. The degree of euphoria is related to the drug's speed of absorption and not necessarily to the amount used. Furthermore, toxicity is more a result of a rise in blood concentration level than the amount of drug in the body.

Although smoking is not an efficient way of delivering cocaine, it produces the most rapid onset of the drug's psychoactive effects.(1,11-14) the euphoric "rush" of crack begins seven to eight seconds after inhalation and subsides within five to ten minutes. Regardless of the route of administration, the intense cocaine high is always followed by an extreme low, or "crash."(1,11,12,14)

Cocaine affects every system of the body. Acute cocaine toxicity, like amphetamine toxicity, is characterized by nervousness, increased excitement, dizziness, blurred vision and tremors. Within a few minutes of administration, the user may experience hallucinations of visual "snow lights" or tactile "cocaine bugs." Paranoia and acute psychosis are not uncommon.

Because of its marked stimulatory effects, cocaine is often used in combination with other drugs, particularly sedatives and depressants. To diminish the crash following a cocaine high, heroin is sometimes used in a practice called "speedballing."(12,13)

Crack smokers have an increased incidence of psychiatric problems, psychosis and associated violence as compared with users of other forms of cocaine.(15) One survey of 144 adult crack users(16) found that 31 percent exhibited violent behavior and 65 percent experienced extreme paranoia. The psychosis associated with cocaine use is very difficult to distinguish from that seen in true schizophrenia, especially in chronic users. (1,12,17)

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Acute cocaine toxicity may result in convulsions, cardiac arrhythmias and respiratory arrest. Malignant hyperthermia is common, because the drug stimulates the temperature regulatory center and causes increased skeletal muscle activity. (1,11-13,17,18) Sudden surges in blood pressure can cause spontaneous intracerebral bleeding, cerebrovascular accidents and aneurysmal ruptures. (13,17) Tachycardia, multiple premature ventricular contractions, acute left ventricular failure, pulmonary edema and ventricular tachycardia can occur. Death may occur as a result of cardiovascular and respiratory collapse. (17) Obviously, any cocaine user with a predisposing cardiac condition is at increased risk. (12,13,17,18)

Chronic toxicity occurs with continued use of high doses of cocaine. Chronic use is associated with weight loss, insomnia and depression. Pulmonary complications are more likely to occur in crack smokers than in users of other forms of cocaine. Crack users may have chest congestion and chronic cough. (1,13,19,20) Increased bronchial hyperactivity in asthmatic users has also been reported. (21) More serious respiratory complications include pneumomediastinum, pneumothorax and pneumopericardium. (13,15,19,20) Cornstarch or talc, often used as an adulterant, can contribute to severe pulmonary parenchymal disease. (22)

### TREATMENT

Treatment of cocaine intoxication is supportive. Although anxiety, depression and irritability are withdrawal signs, antidepressants and anxiolytic agents should be avoided if possible, since their use may mask other significant symptoms. Verbal reassurance is important. Frequent monitoring of vital signs is essential to alert the physician to the presence of hyperthermia, a hypertensive crisis or cardiac arrhythmias.

Rectal temperature should be monitored, and hyperthermia should be treated aggressively with a cooling blanket, ice packs and fans. Sodium nitroprusside (Nipride, Nitropress), nifedipine (Adalat, Procardia) or phentolamine (Regitine) is recommended for the treatment of hypertensive crisis. (19) Propranolol has also been effective in treating hypertension; however, this drug should be used with caution or should be reserved for the treatment of cocaine-induced tachycardia. (13,19) Ventricular ectopy should be treated with beta blockers or lidocaine (Xylocaine). (19)

Diazepam is the drug of choice for the management of seizures, while haloperidol is effective in the treatment of acute psychosis. (11-13,19) Any metabolic derangement, such as acidosis, should be corrected as quickly as possible. (19)

Cocaine intoxication is generally self-limited, and detoxification can take place in less than 24 hours. (13) However, the craving for the drug can be severe. Since the withdrawal symptoms experienced with cocaine are related to dopamine depletion, use of dopamine agonists may lessen the severity of these symptoms. Amantadine (Symmetrel), bromocriptine (Parlodel) and carbidopa with levodopa (Sinemet) have been used in some treatment centers. Study results vary as to the efficacy of these agents in the management of cocaine withdrawal. (1,12,23-27)

Tricyclic antidepressants, such as desipramine (Norpramin, Pertofrane), imipramine (Janimine, Tofranil) and trazodone (Desyrel), also have a role in the treatment of cocaine dependence. Like cocaine, the tricyclics block reuptake of norepinephrine; therefore, these agents are useful in treating the depression associated with cocaine use. (26,27) The principal disadvantage of tricyclic antidepressants is that their effects do not become apparent until they have been taken for at least ten days. (26,27)

Bromocriptine may emerge as the treatment of choice for acute cocaine craving during the first two weeks of withdrawal. Desipramine may become the drug of choice for managing persistent depressive syndromes associated with cocaine withdrawal. (26)

### Diagnosis of Drug Abuse

Drug abuse may be defined as the use of a chemical in an inappropriate way or in an inappropriate amount to achieve a desired pharmacologic effect. The diagnostic criteria for substance abuse, as given in the revised third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R), include a pattern of pathologic use, impairment of behavioral, social or occupational functioning as a result of substance abuse, and a minimum duration of disturbance of one month. (28,29) The DSM-III-R criteria for diagnosing designer drug intoxication are given in Table 2. (29)

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Ideally, the diagnosis of drug abuse should be made before the user suffers serious mental or physical harm. General warning signs of drug abuse are listed in Table 3. Although not meant to be all-inclusive, the table lists signs related to changes in a drug user's personal appearance, habits and social adjustment.

Families and close friends of a drug user may notice changes in behavior that suggest a problem. In some cases, however, these changes are gradual, and the physician may have a better vantage point from which to suspect drug abuse. In the family physician's office, the first step in the diagnosis of drug abuse is awareness that a problem may exist. A detailed history can provide the initial clues.

### Treatment Considerations

The immediate treatment for all designer drug intoxications is supportive. Pharmacologic intervention is reserved for symptomatic treatment of adverse drug reactions. In mixed-substance intoxications, patients may present with a complex combination of signs and symptoms.

In addition to the basic treatments discussed in this article, counseling and rehabilitation are essential to the long-term treatment of a drug abuser. Many detoxification units and chemical dependency centers are available for physician referral. Both outpatient and inpatient facilities exist. A list of treatment programs and their locations can be found in the U. S. Journal's 1989 National Treatment Directory for Alcoholism, Drug Abuse and Other Addiction Problems.(30)

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TABULAR DATA OMITTED