Club Drugs: MDMA, Gamma-Hydroxybutyrate (GHB), Rohypnol, and Ketamine

PAUL M. GAHLINGER, M.D., PH.D., M.P.H., University of Utah Health Sciences Center, Salt Lake City, Utah

Club drugs are substances commonly used at nightclubs, music festivals, raves, and dance parties to enhancesocial intimacy and sensory stimulation. The most widely used club drugs are 3,4-methylenedioxymethamphetamine(MDMA),alsoknownasecstasy;gamma-hydroxybutyrate(GHB);flunitrazepam (Rohypnol); and ketamine (Ketalar). These drugs are popular because of their low cost and convenient distribution as small pills, powders, or liquids. Club drugs usually are taken or ally and may be taken in combination with each other, with alcohol, or with other drugs. Club drugs often are adulterated or misrepresented. Any club drug overdoses hould therefore besuspected as polydrug use with the actual substance and dose unknown. Persons who have adverse reactions to these club drugs are likely to consulta family physician. Toxicologics creening generally is not available for club drugs. The primary management is supportive care, with symptomatic control of excess central nervous system stimulation ordepression. There are no specificantidotes except for flunitrazepam, abenzo diazepine that responds toflumazenil. Special care must be taken for immediate control of hyperthermia, hypertension, rhabdomyolysis, and seroton in syndrome. Severed rug reactions can occur even with a small dose and may requirecritical care. Club drug overdose usually resolves with full recovery within seven hours. Education of the patient and family is essential. (Am Fam Physician 2004; 69:2619-26, 2627. Copyright © 2004 American Academy of Family Physicians)

• A patient information handout on club drugs, written by the author of this article, is provided on page 2627.

Ithough alcohol remains the primary"sociallubricant,"it has been joined by many newer psychoactive drugs that are used to intensify social exeriences. Because of the prevalence of these drugs at dance parties, raves, and nightclubs, they often are referred to as "club drugs." The most prominent club drugs are MDMA (3,4-methylenedioxymethamphetamine), also known as ecstasy;gamma-hydroxybutyrate(GHB);flunitrazepam (Rohypnol); and ketamine (Ketalar). *Table 1*¹ lists the various street names for these agents.

Club drugs are favored over other recreational drugs, such as marijuana, lysergic acid diethylamide(LSD),methamphetamine,andopiates, because they are believed to enhance social interaction. They often are described as "entactogens," giving a sense of physical closeness, empathy, and euphoria. MDMA is structurally similar to amphetamine and mescaline, which is a hallucinogen. However, it is not as stimulating or addictive as amphetamine, and is considered much less likely to cause psychosis than LSD and other potent hallucinogens.² GHB

TABLE 1			
Street Names	for	"Club	Drugs"

MDMA	Ecstasy, X, M, E, XTC, rolls, beans, Clarity, Adam, lover's speed, hug drug
GHB	G, liquid ecstasy, Grievous Bodily Harm, gib, soap, scoop, nitro
GBL*	Blue Nitro, GH Revitalizer, Gamma G
BD*	Weight Belt Cleaner, Serenity, Thunder Nectar, Revitalize Plus
Flunitrazepam (Rohypnol)	Mexican valium, circles, roofies, la rocha, roche, rophies, R2, rope, forget-me pill
Ketamine (Ketalar)	K, special K, super K, vitamin K, kit-kat, keets, super acid, jet, cat valiums

MDMA=3,4-methylenedioxymethamphetamine; GHB = gamma-hydroxybutyrate; GBL = gamma butyrolactone; BD = 1,4-butanediol.

*-Chemical precursors of GHB.

Information from Gahlinger PM. Illegal drugs: a complete guide to their history, chemistry, use and abuse. New York: Plume, 2004:169-72. The most troublesome potential outcome of MDMA ingestion is hyperthermia and the associated "serotonin syndrome."

and Rohypnol are powerful sedative/hypnotic agents.Ketamine is a dissociative anesthetic that produces a dreamy tranquility and disinhibition in small doses. Unlike opiates, these sedatives encourage sociability and seldom cause nausea.

The popularity of these club drugs is due to their low cost and convenient distribution as small pills, powders, or liquids that can be taken orally. Consequently, these drugs are popular among young persons who have been educated about the hazards of drug injection and the dangers of heroin, cocaine, and methamphetamine.However,most users are unaware that MDMA is a type of methamphetamine, and incorrectly assume that substances that appear as pharmaceuticals are safe to use.

Club drugs often are taken together, with alcohol, or with other drugs to enhance their effect. Often, they are misrepresented, adulterated, or entirely substituted for another substance without the users' knowledge. These actions result in an extraordinarily high risk of unanticipated effects and overdose.³

In the past 10 years, there has been a generalized decrease in the use of marijuana, cocaine, and heroin in the United States, according to statistics from the Drug Enforcement Administration, the University of Michigan Monitoring the Future Study, the Columbia University National Survey of American Attitudes onSubstanceAbuse,theCommunityEpidemiology Working Group, and the Partnership for a Drug-FreeAmerica.⁴However,duringthissame period, the use of club drugs has dramatically increased.5 A 2001-2002 Chicago household survey⁶ of 18- to 40-year-old persons showed that 38 percent had attended a rave, and 49 percent of these had a taken a club drug. One Australian study⁷ showed that only 8 percent of club-goers had not consumed any psychoactive substance.

MDMA

MDMA was developed in 1914 as an appetite suppressant, but an imal tests were unimpressive, and it was never tested in humans. In 1965, psychiatrists prescribed the drug to break through psychologic defenses as an "empathy agent." By 1985, illegal laboratories were producing the drug for recreational use, and it was classified as a schedule I controlled substance.

MDMAhasbecomethemostcommonstimulant found in dance clubs and is available at 70 percent of raves.8 MDMA usually is sold as small tablets of variable colors imprinted with popular icons or words. A high proportion of MDMA pills are adulterated with substances such as caffeine,dextromethorphan,9pseudoephedrine,10or potenthallucinogenssuchasLSD, paramethoxyamphetamine(PMA),methylenedioxyamphetamine (MDA),N-ethyl-3,4-methylenedioxyamphetamine (MDEA),and4-bromo-2,5-dimethoxyamphetamine (2-CB).¹¹ Many of these substances are "designer drugs" that are illicitly manufactured variantsofpharmaceuticalsandhaveintentional and unintentional effects. For example, MDEA ("Eve"),2-CB,andPMA("death")are substituted amphetaminesbuthaveprimarilyhallucinogenic, and often unpleasant, effects.1

MDMA ingestion increases the release of serotonin,dopamine,andnorepinephrinefrom presynaptic neurons and prevents their metabolism by inhibiting monoamine oxidase. Effects of an oral dose appear within 30 to 60 minutes and last up to eight hours.12 A quicker onset of action can be achieved by snorting the powder of a crushed tablet. Users of MDMA describe initial feelings of agitation, a distorted sense of time, and diminished hunger and thirst, followed by euphoria with a sense of profound insight, intimacy, and well-being.¹³ To further enhance the sensory effects, users often wear fluorescent necklaces, bracelets, and other accessories, and apply mentholated ointment on their lips or spray menthol inhalant on a surgical mask. Unpleasant side effects of MDMA include trismusandbruxism, which can be reduced by sucking on a pacifier or lollipop.¹⁴

Adverse effects of MDMA ingestion result

from sympathetic overload and include tachycardia, mydriasis, diaphoresis, tremor, hypertension, ¹⁵ arrhythmias, ¹⁶ parkinsonism, ¹⁷ esophoria (tendency for eyes to turn inward), and urinary retention. ¹⁸ However, the most troublesome potential outcome of MDMA ingestion is hyperthermia¹⁹ and the associated "serotonin syndrome." Serotonin syndrome ismanifested by grossly elevated core body temperature, rigidity, myoclonus, and autonomic instability;²⁰ it results in end-organ damage, rhabdomyolysis and acute renal failure, hepatic failure, adult respiratory distress syndrome, and coagulopathy.²¹

MDMA ingestion directly causes a rise in antidiuretic hormone.²² Heat from the exertion of dancing in a crowded room coupled with the MDMA-induced hyperthermia can lead easily to excessive water intake and severe hyponatremia.²³ Neurologic effects include confusion, delirium,paranoia,headache,anorexia,depression,insomnia,irritability,and nystagmus,allof which may continue for several weeks.

Two days after ingestion of MDMA, users typically experience depression consistent with serotonin depletion,²⁴ which may be severe.²⁵ One study²⁶ showed that, compared with alcohol withdrawal, persons who are withdrawingfrom MDMA were more depressed, irritable, and unsociable. Repeated use of MDMA has been associated with cognitive deficits in animals andhumans, withpotentially permanent memory impairment.^{27,28}

A number of products are sold legally as "herbal ecstasy." These products, available in health food stores or on the Internet, contain stimulants such as ephedra, caffeine, and guarana, with variable additions of common herbs or vitamins.²⁹ Users of these products maybelieve they are safe alternatives to MDMA, but several cases of toxic overdose have been reported from the intense stimulation of ephedrine or excessive caffeine.³⁰

GHB

GHB is a derivative of the inhibitory neurotransmitter γ -aminobutyric acid and occurs

naturally in the central nervous system, where it is believed to mediate sleep cycles, body temperature, cerebral glucose metabolism, and memory.³¹

GHB was first synthesized in France in 1960 as an anesthetic. It later achieved popularity as a recreational drug and a nutritional supplement marketed to bodybuilders.32 Nonprescription sales in the United States were banned in 1990 because of adverse effects, including uncontrolled movements and depression of the respiratory and central nervous systems (CNS).33,34 In 2000, with 60 deaths reported from overdose and concern over its use as a "date rape" drug, GHB was reclassified as a schedule I controlled substance.35 In 2002, sodium oxybate, a formulation of GHB, was approved for the treatment of narcolepsy and classified as schedule III. Recently, sodium oxybate has been studied as a treatment for alcohol withdrawal.36,37

GHB is easily manufactured from industrial chemicals. Internet Web sites offer instructions for home production and sell kits with the requisite materials. GHB is chemically related to gamma butyrolactone and 1,4-butanediol, which are metabolized in the body to GHB.³⁸

The salty powder usually is dissolved in water and sold at \$5 to \$10 per dose. Overdose is common because the strength of the solution is often unknown. The unpleasant salty or soapy taste may be masked in flavored or alcoholic beverages.³⁹ Effects of GHB appear within 15 to 30 minutes of oral ingestion and peak at 20 to 60minutes,dependingon whether itismixed with food. Toxicity is increased if taken with alcohol or other CNS depressants.⁴⁰

GHB produces euphoria, progressing with higher dosest o dizziness, hypersalivation, hypotonia, and amnesia.⁴¹ Overdose may result in Cheyne-Stokes respiration, seizures, coma, and death. Coma may be interrupted by agitation, with flailing activity described similar to a drowning swimmer fighting for air.⁴² Bradycardia and hypothermia are reported in about one third of patients admitted to a hospital for using GHB and appear to be correlated with the level of consciousness.⁴³ Chronic use of GHB may Gamma-hydroxybutyrate (GHB) produces euphoria, progressing with higher doses to dizziness, hypersalivation, hypotonia, and amnesia.

> producedependenceandawithdrawalsyndrome that includes anxiety, insomnia, tremor, and in severe cases, treatment-resistant psychoses.⁴⁴

Rohypnol

Flunitrazepam, marketed as Rohypnol, is a potentbenzodiazepinewitharapidonset.Manufactured by Roche Laboratories, it is available in more than 60 countries in Europe and Latin America for preoperative anesthesia, sedation, and treatment of insomnia. In the United States, imported Rohypnol came to prominence in the 1990s as an inexpensive recreational sedative and a "date rape" drug.⁴⁵ The tablets are sold on the street for \$0.50 to \$5 a piece.

In a single 1- or 2-mg dose, Rohypnol reduces anxiety, inhibition, and muscular tension with a potency that is approximately 10 times that of diazepam (Valium). Higher doses produce anterograde amnesia, lack of muscular control, and loss of consciousness. Effects occur about 30 minutes after ingestion, peak at two hours, and may last up to eight to 12 hours. The effects are much greater with the concurrent ingestion of alcohol or other sedating drugs. Some users experience hypotension, dizziness, confusion, visual disturbances, urinary retention, or aggressive behavior.⁴⁶

Like other benzodiazepines, chronic use of Rohypnol can produce dependence. The withdrawal syndrome includes headache, tension, anxiety,restlessness,musclepain,photosensitivity,numbnessandtinglingoftheextremities,and increased seizure potential.⁴⁷

Ketamine

Ketamine was derived from phencyclidine (PCP) in the 1960s for use as a dissociative anesthetic.⁴⁸ It causes anesthesia without respiratory depression by inhibiting the neuronal uptake of norepinephrine, dopamine, serotonin, and glutamate activation in the *N*-methyl-*D*-aspartate receptor channel.⁴⁹ This agent can cause bizarre ideations and hallucinations—side effects that limited its medical use but appealed to recreational drug users.

Ketamine is difficult to manufacture; therefore, most of the illicit supply is diverted from human and veterinary anesthesia products. As a pharmaceutical, ketamine is distributed in a liquid form that can be ingested or injected. In clubs, it usually has been dried to a powder and is smoked in a mixture of marijuana or tobacco, or is taken intranasally. A typical method uses a nasal inhaler, called a "bullet" or "bumper"; an inhalation is called a "bump". Ketamine often is taken in "trail mixes" of methamphetamine, cocaine, sildenafil citrate (Viagra), or heroin.⁵⁰

Effects of ketamine ingestion appear rapidly and last about 30 to 45 minutes, with sensations of floating outside the body, visual hallucinations, and a dream-like state.⁵¹ Along with these "desired" effects, users also commonly experience confusion, anterograde amnesia, and delirium. They also may experience tachycardia, palpitations, hypertension, and respiratory depression with apnea. "Flashbacks" or visual disturbances can be experienced days or weeks after ingestion.³² Some chronic users become addicted and exhibits evere with drawal symptoms that require detoxification.

Treatment

Because club drugs are illicitly obtained and often are adulterated or substituted, they must be considered as unknown substances. In the ever-changing world of illegal drug distribution, Internet Web sites can be helpful in identifying the rapidly changing appearances of these substances (*Table 2*).

The immediate concern with the use of club drugs is cardiorespiratory maintenance. Users often present with multiple drug ingestions, which may include stimulant and depressant drugs (e.g., MDMA combined with GHB or alcohol).When the predominant symptoms are controlled, the symptoms of a second under-



Club Drug Treatment Pathway

FIGURE 1. Algorithm for the management and treatment of ingestion of a "club drug." (MDMA=3,4-methylenedioxymethamphetamine; LSD=lysergicacid diethylamide;2-CB=4-bromo-2,5-dimethoxyamphetamine;GHB=gammahydroxybutyrate; IV = intravenous)

MDMA resulted in fatal hyperthermia. The use

of dantrolene (Dantrium) is questionable and

nolongerrecommended.54 Alkalinization of the

urine, which usually is recommended for rhab-

TABLE 2

www.aafp.org/afp

There are no specific antidotes for ingestion of club drugs, except for Rohypnol, which has the antidote flumazenil.

domyolysis, should be used cautiously because it reduces the renal clearance of amphetamine. The seroton in antagonists chlorpromazine (Thorazine) and cyproheptadine (Periactin) appear to be effective in mild to moderate cases of seroton in syndrome.⁵⁵

There are no specific antidotes for ingestion of club drugs, except for Rohypnol, which has the antidote flumazenil. With supportive care, patients usually will recover completely within seven hours.

GHB has a rapid elimination, and the drug is cleared within four to six hours after ingestion, regardless of the dose. Intubation should be avoided unlessit is absolutely necessary, because patients may be come unexpectedly combative or have protracted periods of emesis.⁵⁶ The presence of trismus suggests ingestion of stimulants and makes intubation more difficult. A benzodiazepine may be given for withdrawal symptoms.

UrineorbloodtestsforamphetamineormethamphetaminemaydetectMDMA;thesetestsalso will detect MDMA-related compounds such as 2-CB, but with decreased sensitivity.⁵⁷ A 50-mg dose of MDMA can be detected as unchanged drug in the urine up to 72 hours after ingestion. Standard toxicologic tests cannot detect GHB, but the National Forensic Laboratory (National Medical Services, 800-522-6671) will perform urinalysis for detection of GHB for a fee.

The Author

PAUL M. GAHLINGER, M.D., Ph.D., M.P.H., is an adjunct professor in the Department of Family and Preventive Medicine at the University of Utah Health Sciences Center, Salt Lake City, where he completed an occupational and environmental medicine residency. He received his medical degree from the University of California-Davis School of Medicine. Dr. Gahlinger also is in private practice at the Kaysville Clinic, Layton, Utah, and is a medical review officer for the Bioastronautics Research Division, NASA.

Address correspondence to Paul M. Gahlinger, M.D., Ph.D., M.P.H., 225 10th Ave., Salt Lake City, UT 84103 (e-mail: paulg@aros.net). Reprints are not available from the author. Rohypnol and its active metabolite 7-aminoflunitrazepam may be detected by gas chromatography/mass spectrometry testing up to 72 hours after ingestion. For assistance with assay in cases of suspected rape, contact Roche Laboratories (800-608-6540) for a free screening for Rohypnol. Tests for ingestion of ketamine are seldom available, but ketamine may be suspected if a toxicologic test is positive for PCP.⁵⁸

Providing the patient and family with educational materials about specific substances may behelpful. These materials are available on many Web sites.

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