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Ecstasy (MDMA) Deaths in New York City: A Case Series and Review of the Literature

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ABSTRACT: MDMA ("ecstasy") has gained renewed popularity as a drug of abuse. To access the epidemiology and causes of death of MDMA-positive fatalities, all deaths investigated by the OCME that tested positive for MDMA (22 deaths) between January 1997 and June 2000 were reviewed. There were three deaths in each 1997 and 1998, eleven in 1999, and five in the first part of 2000. Of these 22 deaths, 13 were due to acute drug intoxications, 7 due to mechanical injury (blunt trauma, gunshot wounds), and 2 due to a combination of natural disease and acute drug intoxication. Evidence of recent opiate and/or cocaine use was found in 7 of the acute intoxication deaths and in none of the traumatic or combination natural/intoxication deaths. The race of all decedents was White between the ages of 17–41 years, and 18 of 22 were men.

KEYWORDS: forensic science, amphetamines, forensic toxicology, MDMA, ecstasy, fatality

Ecstasy, MDMA (3,4-methylenedioxymethamphetamine), is a substituted derivative of methamphetamine that shares structural similarities with mescaline. It has sympathomimetic effects similar to methamphetamine but lacks the major hallucinogenic effects of mescaline. MDMA causes increased catecholamine (including serotonin) release and blockage of re-uptake resulting in cardiac and central nervous system effects. Despite increasing widespread use (1–3), reports of fatalities in the United States have been rare.

First synthesized in 1912, MDMA was patented in Germany by the Merck Company in 1914. The drug was "rediscovered" in the 1960s by Alexander Shulgin, who became an activist for its psychotherapeutic uses (4). In the 1980s, the drug was increasingly abused and reports of probable neurotoxicity lead in 1985 to its classification as a Schedule I drug (significant potential for abuse, no medical applications).

Its combination of euphoric and psychedelic effects led to its adoption by the underground dance scene in the late 1980s when its use at "raves" (all night electronic music dance parties) became effectively institutionalized. While the rave phenomenon started in England, the growing popularity of raves and the music of the rave scene in the United States have nurtured the use of MDMA, now most frequently known by its street name "ecstasy" (5).

Currently, in New York City, tablets sold as "ecstasy" cost users between $20 and $30. A typical oral street dose of "ecstasy" includes 75 to 150 mg of MDMA (6). The delay before onset of action is approximately 30 min, and once it has begun the effects are achieved rapidly. MDMA's effects last 4 to 6 h with an elimination half-life of approximately 8 h. The drug is primarily metabolized by the liver, where it undergoes *N*-dealkylation into MDA (3,4-methylenedioxyamphetamine), its major metabolite. MDA is also a drug of abuse (first synthesized in 1910). Approximately 65% of MDMA is excreted unchanged in the urine (7).

The primary effect of MDMA is a combination of mild euphoria and enhanced sociability: this social disinhibition led psychotherapists to dub the drug "empathy" in the 1970s. MDMA's hallucinogenic effects are slight and frank hallucinations are reported by a minority of users. With repeated use, a reduction in desired effects tends to lead to multiple dosing with a resultant increase in the incidence of concomitant unpleasant side effects. Many users experience a post-intoxication depression, which is generally brief and fairly minor but can be prolonged and profound. The effects of chronic MDMA use have not been fully elucidated but appear to include both toxic hepatitis and damage to the serotoninergic neural pathways (1,8,9).

Typical minor side effects include bruxism, trismus, muscle aches, nausea, vomiting, and irregular eye movements (hence one expression for "ecstasy" intoxication—"rolling"). Acute MDMA toxicity is similar to that noted with other amphetamines with tachycardia, hypertension, seizures, hyperthermia, rhabdomyolysis, acute renal failure, disseminated intravascular coagulation, and death (10,11). Intracranial bleeding and hyponatremia (possibly a complication both of MDMA's reported stimulation of vasopressin release (12) and of fluid overloading aimed at preventing MDMA-related dehydration) are less common (see Table 1).

MDMA, together with ketamine and gamma hydroxybutyric acid (GHB), have gained renewed popularity among the "club" scene and at "raves" in New York City and across the United States (13–15). In this study, all MDMA positive deaths autopsied at the New York City Office of Chief Medical Examiner (OCME) over a three-year period were examined. In addition, previous case reports of fatalities with MDMA are reviewed.

Materials and Methods

The Office of Chief Medical Examiner investigates all unexpected, violent, and suspicious deaths in New York City. Toxico-

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TABLE 1—*Adverse reactions of acute and chronic ecstasy abuse.*

Acute	Chronic
Bruxism/Trismus	Memory Impairment
Nausea/vomiting	Psychological difficulties:
Irregular eye movements	Depression
Tachydysrhythmias	Sleep Problems
Hypertension	Anxiety
Intracranial bleeding	Paranoia
Serotonin syndrome:	Liver disease
Altered mental status	
Alteration in muscle tone/activity	
Automatic instability	
Hyperthermia	
Diarrhea	
Hyponatremia	
Seizures	
Rhabdomyolysis	
Acute renal failure	
Disseminated intravascular coagulation	
Death	

logical testing is performed routinely on all autopsies and on select external examinations. All instances in which substituted amphetamines were identified by routine toxicological testing of postmortem samples from January 1997 to July 2000 were identified through the toxicology laboratory database with subsequent review of the OCME autopsy files. The OCME performed 19 366 autopsies and toxicologic analysis on 20 882 cases during the study period.

Autopsy blood specimens were collected with addition of sodium fluoride and stored at 4°C. All toxicologic testing was performed by the Forensic Toxicology Laboratory at the Office of Chief Medical Examiner with the exception of gamma hydroxybutyric acid (GHB). Specimens from cases where GHB analysis was indicated by case history were referred to National Medical Services, Inc. Ethanol concentrations were determined in blood using head space gas chromatography.

Urine specimens were routinely tested for opiates, barbiturates, benzoylecgonine (BE), cannabinoids, amphetamines, phencyclidine, and methadone by enzyme immunoassay. In cases where urine was not available, blood was tested for opiates, benzoylecgonine, and barbiturates using radioimmunoassay. The cutoff concentrations are shown below.

	Urine	Blood
Amphetamines	1000 ng/mL	NA
Opiates	300 ng/mL	100 ng/mL
Benzoylecgonine	300 ng/mL	100 ng/mL
Barbiturates	200 ng/mL	200 ng/mL
Methadone	300 ng/mL	NA
Phencyclidine	25 ng/mL	NA

NA = not available.

Results greater than or equal to the cutoff concentrations were considered positive.

Urine or blood was also screened for basic drugs (including ketamine and cocaine) by gas chromatography with a nitrogen phosphorous detector (GC/NPD). A separate analysis for sympathomimetic amines (including amphetamine, methamphetamine, MDMA, and MDA) was performed by either GC/NPD or gas chromatography/mass spectrometry (GC/MS). Of the 22 deaths, 5 did not have urine available for testing.

The conclusion that death was caused by an acute intoxication requires that three conditions be met: the toxicology results must be within the range typically encountered in such fatalities, the history and circumstances must be consistent with a fatal intoxication, and the autopsy must fail to disclose a disease or physical injury that has an extent or severity inconsistent with continued life. In deaths caused by drug intoxication with more than one drug in concentrations greater than trace amounts, it is customary to include all of the identified drugs in the cause of death.

A Medline search from 1966–2000 (August) was conducted for "MDMA" and "ecstasy" combined with "death" and "fatality" for the literature review. Case reports of deaths with MDEA (3,4-methylenedioxyethamphetamine) and not MDMA were excluded (16–18).

Results

MDMA was identified in samples from 21 medical examiner autopsies and one external examination. There were three deaths in 1997, three in 1998, eleven in 1999, and five in the first half of 2000. The circumstances, toxicology results, and causes of death are listed in Tables 2 and 3. The race of all decedents was White (including three whose next of kin described them as Hispanic) between the ages of 17–41 years (average 27) and 18 of 22 were men.

Of the 19 366 deaths that underwent autopsy, only two were caused exclusively by MDMA. The one positive death that did not undergo autopsy (due to a religious objection) also had only MDMA/MDA detected (Table 2: Case 1). There were 15 acute intoxication deaths; including one each with subarachnoid hemorrhage/hyperthermia, hyperthermia, cardiac sarcoidosis, and marked atherosclerotic coronary artery disease. Of these fifteen deaths, seven (Table 2: Cases 9–15; average MDMA concentration: 0.58 mg/L) tested positive for acute opiate (all 7) or cocaine (5) use and eight did not (Table 2: Cases 1–8; average MDMA concentration: 1.04 mg/L). The remaining seven deaths (Table 2: Cases 16–22, average MDMA concentration: 0.97 mg/L) were due to physical injuries (blunt trauma or gunshot wounds). The traumatic deaths included four falls from height, two drivers in motor vehicle collisions (BAC = 0.1 and 0.09 mg%), and one homicidal gunshot wound.

In all deaths, opiates (7 deaths), ethanol (7), ketamine (6), and cocaine (5) were the most frequent co-intoxicants. Gamma hydroxybutyric acid (GHB) was tested for in five deaths (Table 2: Cases 2, 5, 7, 8, and 9) and the respective postmortem blood concentrations were 13, 14, 7.2, 311, and 11 mcg/mL.

Discussion

There has been a recent increase in abuse of MDMA in the United States (1–3). We reviewed all MDMA-positive deaths examined at the New York City Office of Chief Medical Examiner over a three and one-half-year period. The causes of the MDMA-positive deaths may be classified into three groups: (A) co-intoxications with cocaine and/or opiates; (B) intoxications without cocaine or opiates; (C) mechanical injury deaths. The first group (A) includes acute intoxication deaths due to the combined effects of MDMA and cocaine and/or opiates. There were seven such deaths, and in all but one the person was dead when first discovered (usually at home in bed).

The second group (B) includes acute MDMA intoxications that did not involve concomitant cocaine or opiate intoxication. There

TABLE 2—*MDMA fatalities, New York City 1997-2000.*

	Age Race/Sex	Circumstances	MDMA/MDA (Blood, mg/L)	Other Toxicology Results (Blood)	Cause of Death (Other Findings)
1	30 WM	Dead at home	0.6/0.1		Intoxication
2	21 WM	Collapsed at club	3.7/0.8		Intoxication
3	29 WM	Collapsed at work	0.7/0.1		IHD*/Intoxication
4	41 WM	Collapsed following party	0.5/0.1	Ketamine	Sarcoidosis/Intoxication
5	31 WF	Collapsed at club	0.3/<0.1	BE, Ephedrine	Intoxication
6	22 WF	Collapsed at home	0.2/ND†	Cannabinoids	Intoxication (SAH‡, 42.2°C)
7	18 WM	Collapsed at club	1.7/0.1	Ketamine, Cannabinoids	Intoxication (39.4°C)
8	35 WM	Dead in bed after party	0.6/<0.1	GHB, Ketamine, BE, Methamphetamine	Intoxication
9	26 WM	Dead in bed after club	1.7/0.3	Ethanol, Cocaine, Opiates, Amphetamine	Intoxication
10	21 WM	Dead in bed	<0.1/0	Opiates	Intoxication
11	27 WM	Tourist dead after party	0.6/<0.1	Ethanol, Cocaine, Opiates	Intoxication
12	37 HM	Tourist dead in bed	0.3/0.1	Ethanol, Cocaine, Opiates	Intoxication
13	30 WM	Dead in car	0.2/0.1	Cocaine, Opiates, Diazepam	Intoxication
14	17 WF	Dead in bed after party	0.4/0.1	Opiates	Intoxication
15	20 WF	Collapsed at party	0.3/0.1	Cocaine, Opiates, Ketamine	Intoxication
16	26 WM	Shot by another	0.3/<0.1	Cannabinoids	Gunshot Wounds
17	27 HM	Driver in MVA	1.2/<0.1	Ethanol	Blunt Trauma
18	30 HM	Driver in MVA	0.2/ND†	Ethanol	Blunt Trauma
19	25 WM	Fell while escaping fire	0.3/0.1	Ethanol	Blunt Trauma
20	21 WM	Fell from bridge	2.2/0.1	Ketamine	Blunt Trauma
21	23 WM	Fell from bridge	1.3/0.1	Ethanol	Blunt Trauma
22	28 WM	Fell from roof at club	1.3/0.1	Ketamine	Blunt Trauma

*IHD = Ischemic Heart Disease, †ND = Not detected, ‡SAH = Subarachnoid hemorrhage.

TABLE 3—*Postmortem concentrations.*

	MDMA		MDA	
Specimen	*n*	Range, mean	*n*	Range, mean
Blood, mg/L	21	<0.1–3.7 (0.89)	18	<0.1–0.8 (0.16)
Brain, mg/kg	2	4.0–5.7	2	0.4–0.5
Liver, mg/kg	1	9.6	1	0.6

*Results with concentrations of less than 0.1 were excluded from the mean calculation.

were eight deaths, and all but two were witnessed collapses (typically at a club or party). Of these eight deaths, only three were pure MDMA/MDA intoxications. The other co-intoxicants included: ketamine (three deaths), cannabinoids (two), ephedrine (one), GHB (one), and methamphetamine (one). Of the three pure MDMA intoxications, one had marked coronary artery disease and one did not have an autopsy. These findings support a fatal additive role of "ecstasy" with concurrent use of other "club drugs" and/or other underlying natural disease.

The third group (C) includes seven people who died from blunt injury or gunshot wounds. We invoke acute intoxications as the cause of death when it plays a pathophysiologic role in causing the death, or when the circumstances of death do not make sense without it (e.g., drowning in a bathtub). The proximate cause of death in this group of fatalities is the mechanical injury. One may postulate that drug-induced behavior or lack of judgment produced the perilous circumstances surrounding these deaths. In all instances, however, there was physical injury inconsistent with life.

Cocaine has been demonstrated in a substantial proportion of all violent deaths in New York City, suggesting that its neurobehavioral effects may increase the likelihood that a user will receive violent fatal injuries (19). Cocaine was not detected in any of the ecstasy-related-mechanical-injury deaths. Ecstasy has different neurobehavioral effects than cocaine, and what role these effects play in the ecstasy-mechanical-injury deaths is unclear (8,20,21). Ecstasy use may lead to judgment errors or be an innocent bystander, simply reflecting an overall increase in the prevalence of ecstasy use. In addition, two of these deaths involved individuals who tested positive for ketamine and four who tested positive for ethanol (blood ethanol concentrations were equal to or less than 0.10 g%).

The average concentrations of MDMA in the three groups (A, B, and C) were 0.58, 1.04, and 0.97 mg/L. The concentrations in the trauma group (C) represent the "typical" postmortem values of MDMA in people who abuse ecstasy but do not die from its direct effects. The average MDMA concentrations in Groups B (no cocaine/opiates) and C are similar. This suggests that the lethality of MDMA may not be purely dose dependent (22). People die from acute MDMA intoxications at the same concentrations as people who die from physical injury during ecstasy abuse. Group A (positive cocaine/opiates) has an average concentration of almost half of the other two groups. These findings, in addition to the distinct circumstances of these deaths, suggest that cocaine and/or opiates may have played a dominant role in these seven deaths.

The review of the case reports (45 deaths) in the literature (Table 4) compared with the New York cases show similarities and differences. In both, the race of all decedents was White and the majority were young men. This is consistent with the current epidemiology of the abuse of ecstasy. Both sets have a group which sustains traumatic injury and a group which collapsed and died (some with the hyperthermia, rhabdomyolysis, acute renal failure, and DIC quartet) with or without intoxication with other "club drugs." A majority of deaths in both cohorts occurred during or shortly after attendance at a club, party, or rave. One major difference with the literature group is the absence of MDMA deaths with co-intoxication with cocaine and/or opiates. This may be a reflection of the substance abuse patterns in New York City versus Great Britain, where most of these literature deaths occurred.

TABLE 4—*MDMA fatalities, review of literature.*

#/Age/Sex		Circumstances	MDMA/MDA (Blood, mg/L)	Other Toxicology	Cause of Death (Other Findings)	References
1	18 M	Seizure at concert	1.26/NR*	None	Intoxication (43°C/rhabdo†/DIC)	Campkin (36)
2	19 M	Collapse, seizure	Trace/Trace	MDEA	Intoxication	Weinmann (10)
3	18 F	Collapse after ingestion	1.0/NR*	Ethanol	Intoxication	Dowling (18)
4	15 F	Collapsed after party	0.05/NR*	None	Intoxication (Rhabdo†)	Parr (28)
5	21 M	Collapsed at rave	4.2/NR*	Amphetamine	Intoxication (44°C)	Milroy (53)
6	20 M	Collapsed at disco	0.04/NR*	None	Intoxication (Hyponatremia)	Milroy (53)
7	39 M	Collapsed at club	0.06/0.12	Ethanol, Amphetamine	Intoxication/IHD	Lora-Tamayo (11)
8	18 M	Collapsed at club	0.36/NR*	None	Intoxication (41.8°C)	Henry (32)
9	17 M	Collapsed at party	Positive/NR*	None	Intoxication (41°C/DIC)	Henry (32)
10	18 M	Collapsed at party	Positive/NR*	None	Intoxication (42.1°C)	Henry (32)
11	20 M	Collapsed after party	1.16/0.06	None	Intoxication (40°C/rhabdo†/DIC)	Henry (32)
12	29 M	Collapsed after rave	0.1/NR*	None	Intoxication (Aortic Dissection)	Duflou (54)
13	22 F	Collapsed after club	0.3/NR*	PMA, Cannabinoids	Intoxication	Byard (23)
14	26 F	Collapsed at home	0.82/NR*	PMA, Methamphetamine	Intoxication (46.1°C/DIC)	Byard (23)
15	19 M	Serotonin symptoms	7.15/0.25	None	Intoxication	Fineschi (55)
16	19 M	Confused at club	Positive/NR*	Amphetamine	Intoxication	Screaton (56)
17	18 F	Psychotic at club	ND*/0.246	None	Intoxication (43°C/rhabdo†/DIC)	Coore (41)
18	17 M	Agitated outside club	0.23/NR*	Ethanol	Intoxication (42°C/rhabdo†/DIC)	Dar (31)
19	21 F	Seizures at party	0.11/NR*	Amphetamine	Intoxication	Henry (32)
20	16 F	Seizure, psychosis	0.42/NR*	None	Intoxication (42°C/DIC)	Chadwick (35)
21	34 M	Unresponsive in bed	0.2/ND*	None	Intoxication (WPW Syndrome)	Suarez (34)
22	20 F	Unresponsive (home)	2.3/0.095	None	Intoxication (serotonin)	Mueller (33)
23	27 F	Collapsed at club	0.18/NR*	Ethanol	Intoxication (Hyponatremia)	O'Connor (27)
24	21 M	Dead in bed after party	2.1/8.5	MDEA, Amphetamine	Intoxication	Milroy (53)
25	20 M	Dead after party	0.18/0.12	MDEA	Intoxication (40°C/rhabdo†/DIC)	Fineschi (55, 57)
26	20 M	Unresponsive in bed	0.09/0.13	None	Intoxication	Milroy (53)
27	17 M	Unresponsive in bed	NR*/0.1	Secobarbital	Intoxication	Reed (58)
28	32 M	Found unresponsive	ND*/Positive	None	Intoxication (41°C/rhabdo†/DIC)	Simpson (59)
29	26 M	Found dead in car	ND*/0.8	Ethanol	ASCVD/Intoxication	Nichols (60)
30	32 M	Found dead in car	1.1/NR*	None	Acute Asthma	Dowling (18)
31	24 M	Found dead in bed	NR*/10.0	Methaqualone	Intoxication	Poklis (44)
32	19 M	Found dead	0.49/0.29	Amphet, MDEA, Dipyrone	Intoxication	Lora-Tamayo (11)
33	21 M	Dead in bed	2.1/8.5	MDEA, Amphetamine	Intoxication	Forrest (16)
34	53 M	Suicidal overdose	3.05/NR*	None	Intoxication	Walubo (39)
35	30 M	Found dead, syringe	0.98/ND*	Ethanol, Opiates, Amphet	Intoxication	Lora-Tamayo (11)
36	29 M	Found dead outdoors	4.07/0.49	Ethanol, Opiates, Alprazolam	Intoxication	Lora-Tamayo (11)
37	30 M	Found unresponsive	NR*	NR	Intoxication (38.58C/rhabdo†)	Squier (62)
38	21 M	Driver in MV‡	0.1/NR*	None	Blunt Injury	Henry (32)
39	23 M	Passenger in MV‡	0.13/NR*	None	Blunt Injury	Henry (32)
40	22 M	Fell from utility tower	Positive/NR*	None	Electrocution	Dowling (18)
41	23 M	Stabbed	0.23/0.05	MDEA	Stab Wound	Lora-Tamayo (11)
42	17 M	Jump from window	0.23/0.04	Methamphetamine/ Amphet	Blunt Injuries	Lora-Tamayo (11)
43	32 M	Pedestrian MV‡	0.27/0.0	Ethanol	Blunt Injuries	Lora-Tamayo (11)
44	21 M	Driver in MV‡	0.17/0.18	Ethanol, Amphet, MDEA	Blunt Injury	Lora-Tamayo (11)
45	26 M	MV (unspecified)‡	0.03/0.15	Ethanol, BE, MDEA	Blunt Injury	Lora-Tamayo (11)

*NR/ND = Not reported/Not detected, †Rhabdo = Rhabdomyolysis, ‡MV = Motor Vehicle Collision.

Hyperthermia frequently has been described with substituted amphetamine use and is a dominant finding in the United Kingdom deaths (18,23). Only two New York deaths (both witnessed collapses) had documented hyperthermia, and one of these included subarachnoid hemorrhage (23–26). This regional difference between the United States and the United Kingdom may be related to different patterns of usage. For example, abuse in the United States often involves small groups in quiet settings while the United Kingdom circumstances favor raves with marathon dancing in hot environments with scarce water supply (27,28). In addition, improvement in hospital management of these intoxications may have resulted in fewer deaths by this mechanism. In New York City, hyperthermia due to acute cocaine intoxication, heat stroke without drug use, and delerium tremens are commonly seen and treated during the summer months in local emergency departments (29). The lack of these types of deaths also may be a reflection of how these deaths were selected. Usually, however, bloods from the day of the hospital admission on the delayed acute intoxication deaths are requested and analyzed.

Clinically, acute ecstasy poisoning has symptoms similar to other stimulant intoxications. Patients usually present with clinical signs and symptoms collectively known as the "sympathomimetic toxidrome" (30). This includes stimulation of the central and peripheral nervous system with tachydysrhythmias, hypertension, hy-

perthermia, diaphoresis, delirium, agitation, and even acute psychosis (14,31,32). If untreated, this condition can progress to unstable ventricular tachydysrhythmias, intracranial hemorrhage, and status epilepticus with ensuing life-threatening hyperthermia, rhabdomyolysis with acute renal failure, disseminated intravascular coagulation, and death (18,23,24,32–36). Patients may also be diagnosed with serotonin syndrome (described later) and hyponatremia as complications of ecstasy poisoning. Hyponatremia, which can cause altered mental status and cerebral edema, is treated with fluid restriction (12,14,28,37,38).

The drug-induced release of serotonin in the central nervous system and increased heat production from muscle activity may lead to life-threatening hyperthermia (33,39,40). The duration of hyperthermia and the peak temperature are likely predictors of morbidity and mortality in these patients (31,41). There have been several case reports of MDMA-induced morbidity and mortality attributed to the serotonin syndrome (33,42). This syndrome includes three of the following symptoms: altered mental status, alteration in muscle tone or activity, autonomic instability, hyperthermia, and diarrhea (33,43). Status epilepticus may lead to extreme hyperthermia. Rhabdomyolysis may also result from seizures and increased motor activity. If this muscle breakdown progresses, it may result in acute renal failure. Disseminated intravascular coagulation is an extremely late complication usually preceding death.

Routine hospital urine toxicology screening will detect the general class of amphetamines, however, specific detection of MDMA requires gas chromatography or gas chromatography/mass spectrometry (GC/MS) (44,45). Once amphetamines are detected by urine or blood screening, a separate blood analysis is performed for quantitation. If urine is not available for postmortem examination, amphetamine screening, confirmation, and quantitation is done in blood. Five cases in the current study were detected in this manner. Since it is not feasible to routinely screen blood for amphetamines in all cases, the number of MDMA positive deaths may be underestimated. One must be aware of the case circumstances and have a low threshold for further testing. In the absence of urine, blood should be screened for amphetamines in the following cases: (1) other drugs of abuse are detected; (2) there is no efficient anatomic cause of death; or (3) there are compelling case circumstances.

The purity of a typical oral street dose of "ecstasy" is variable, with harm-reduction organizations reporting approximately 50% of the tablets containing only MDMA and as many as 10% containing none at all (46). Frequent contaminants and adulterants include caffeine, ephedrine, dextromethorphan, methylendioxyamphetamine (MDA), amphetamine, and paramethoxyamphetamine (4-methoxyamphetamine, PMA), all of which may have similar central nervous system effects (23,47–49). This lack of standardization of "ecstasy" tablets makes analysis of much of the clinical medical literature pertaining to the effects of "ecstasy" difficult, since the exact composition of the tablets taken are frequently unknown, and hospitals are not equipped to do rigorous forensic toxicologic analysis. Harm-reduction organizations that provide (or sell) simple screening color tests (Marquis or Mandelin reagents) to allow abusers to "test" the purity of their drug provide a false sense of security and miss harmful adulterants. Methorphan, which is routinely screened for in our laboratory, was not detected in any of the ecstasy deaths. Ephedrine, however, was detected in one death.

In addition to adulterants and other illicit drugs, adverse interactions with prescribed medications have been reported. These include tricyclic antidepressants and anti-retroviral drugs used in the treatment of acquired immune deficiency syndrome (51,52). Human immunodeficiency virus 1 (HIV-1) protease inhibitors affect the cytochrome P450 system by inhibition of one or more of the various isoforms. Specifically, Ritonavir (one of four commercially available protease inhibitors) inhibits the CYP2D6 isoform which is also involved in MDMA metabolism. The duration of the stimulation effect of MDMA may be prolonged.

We expect that physicians practicing in the United States, both in the clinical and death investigation settings, will see an increasing number of patients who use MDMA. Physicians should be aware of the presentation and natural history of these conditions, the various management strategies (53), and the high likelihood of co-intoxications including the possibility of life-threatening interactions with a wide range of medications.

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