ECSTASY/MDMA

Objectives

When the reader is finished with this course he/she will be able to:

1. Identify the central molecule in the structure of ecstasy.
2. Name the neurotransmitter by which MDMA produces intoxication.
3. Identify the organ most directly affected by MDMA.
4. Identify the leading cause of death/serious morbidity from MDMA toxicity.
5. Identify the other substances known as ecstasy.
6. Briefly explain why MDMA is classified as a hallucinogenic amphetamine.
7. Identify the electrolyte abnormality seen in MDMA poisoning.
8. Name the three complications that can be caused by the hyperthermia seen in MDMA intoxication.
9. Identify the drug classification of ecstasy
10. Identify the most common serious neurological effect of MDMA poisoning.

Ecstasy is the street name for 3,4-methylenedioxymethamphetamine, also known as MDMA (this is derived from the initial letters of the major portions of the drug). This is a popular recreational drug that is also known U4EU, XTC, clarity and Adam. MDMA has been classically described as a *hallucinogenic amphetamine*. In part this is because there is structural similarity between amphetamine and mescaline (the psychoactive compound in peyote, the hallucinogenic cactus)[1] and MDMA, and also because the experience of the MDMA high has *some* similarities to the high experienced with amphetamine and mescaline use. However, although MDMA may be similar in structure to those drugs, intoxication with MDMA is a unique experience.

Merck and Company first synthesized MDMA in 1914 in Germany. The company did not specify the intended use of the drug and it was never commercially marketed. MDMA resurfaced in the 1950s; the US Army, looking for drugs to use as weapons or as interrogation tools, tried MDMA (along with LSD and many other drugs). In the 1970s MDMA began to be used as an adjunct to psychotherapy. Therapists claimed that the drug made patients more emotionally accessible, increased the level of their empathy and fostered better communication. Research in this area continues today, albeit in a very limited way.

But it was in the 1980s that MDMA began to make news. The drug became a popular "party" drug and abuse was relatively widespread. However, the Food and Drug Administration (FDA), expressing concerns over reports that MDMA could cause serious neurological damage, decided to classify MDMA as a Schedule I drug (Scheduled drugs are drugs that have abuse potential and a Schedule I drug, according to the FDA, has abuse potential and no recognized medical use, eg, heroin is a Schedule I drug).

So use and possession of MDMA became illegal in 1986, but that has not stopped its use or decreased its popularity. Exact figures are obviously impossible to come by, but in a National Institute of Drug Abuse (NIDA) report,[2] ecstasy us by school seniors increased between 1998 and 2000 from 8% to 11% for high school seniors, and increasing numbers of 8th grade students had tried the drug. The Drug Abuse Warning

Network (DAWN) reported that hospital emergency room visits due to ecstasy intoxication increased from 1143 in 1998 to 4511 in 2000, and in 2001, over 8 million people tried ecstasy.[3] Ecstasy appears to be most popular among people aged 18-25, and most users and/or potential users consider MDMA to be a very safe drug. Information about ecstasy is easily available on the internet. There are several websites (eg, www.dancesafe.org) that provide drug information and one that provides pill testing and publishes the results. Not surprisingly with an illicit drug, the actual amount of active ingredient varies widely and there is a significant percentage of tested tablets that do not have MDMA but have caffeine, amphetamine, ephedra, diphenhydramine, ketamine (another popular drug of abuse), procaine and dextromethorpham (a popular OTC antitussive) and other substances. Even tablets that have only MDMA can vary widely in the amount they contain (DanceSafe, testing results for 2005 and 2006).[4] MDMA tablets are often colorful and have fanciful logos on the tablets (eg, cartoon characters). The price varies greatly, but is usually about $25 per tablet.

Instant feedback: Although MDMA is termed a hallucinogenic amphetamine, the user does *not* experience true visual hallucinations and unless the dose taken is very large, pronounced amphetamine-like signs and symptoms are not experienced.

Instant feedback: You may have heard of something called "herbal" ecstasy. This is the herb *ma huang*. It contains a sympathomimetic called ephedra and many of the herbal ecstasy preparations that have ma huang also have caffeine and other stimulants.

Instant feedback: Another drug that is occasionally sold as ecstasy is *dextromethorpham* (DM, DMX), a cough suppressant that is a common ingredient of many over-the-counter cough and cold preparations.

PHARMACOLOGY

The core structural unit of MDMA is *phenylethylamine*. This molecule is also the central structural component of amphetamine and mescaline. Chemical modifications of this molecule can produce MDMA and other designer drugs (eg, MDA, DOM, DOB, etc) and drugs such as ephedrine, mescaline, amphetamine and phenylpropanolamine (chocolate also contains a small amount of phenylethylamine but it is doubtful, in the majority of people, that it is psychoactive).[5] MDMA is well absorbed by the oral route (it is also occasionally insufflated, ie, snorted, and injected intravenously). The onset of action is approximately 30 to 45 minutes. There is little human data about the pharmacokinetics of MDMA. It appears that the peak serum concentration is achieved in 1-2 hours and the ½ life is 8.0-9.0 hours. Once it is absorbed, it passes very quickly into the tissues, and it has a very high volume of distribution.[6] It is metabolized primarily in the liver, and there is some evidence that MDMA may itself inhibit the enzyme (CYP2D6) that metabolizes MDMA and with repeated doses, serum levels could be higher.[7] It is excreted renally. (Of note, a small subset of the population is missing the liver enzyme CYP2D6, and this inability to metabolize MDMA may be the reason for idiosyncratic reactions and severe reactions after one dose).[8] Some of the metabolites are pharmacologically active, and elimination takes about 5 half-lives (approximately 40 hours); this may explain why some people may continue to feel the effects several days after taking the drug. Obviously, there is the possibility of an additive effect and the development of serotonin syndrome if MDMA is taken along with a serotonin agonist or a serotonin reuptake inhibitor (It has been postulated that all ecstasy users develop a mild serotonin syndrome).[9,10]

MDMA works by its effect on the serotonergic system. Serotonin (5-OH-tryptamine or 5 HT) is a central and peripheral neurotransmitter. Centrally, it is involved in mood, sexuality, temperature regulation, personality, appetite, sleep induction, and other functions. Peripherally, serotonin may play a role in platelet aggregation and vasoconstriction. It is synthesized from tryptophan (an amino acid) and stored in vesicles in serotonergic nerve ending. Exocytosis releases serotonin into the synapse and after uptake into the postsynaptic neuron, it is transported back into the vesicle of the presynaptic neuron or degraded by monoamine oxidase-A.[11] MDMA *stimulates the release of serotonin* and also *inhibits its reuptake* (possibly by its effect on the presyanptic serotonin transporter) so serotonin accumulates in the synaptic cleft, and there is excess stimulation of the postsynaptic serotonin receptor.[12, 13] MDMA also, to a lesser degree, stimulates the release of dopamine (this would explain some of the drug's effects on mood), norepinephrine and acetylcholine (the significance of the release of acetylcholine is not known).[14].

Instant feedback: Why is MDMA called a hallucinogenic amphetamine?
Answer: The core molecule of MDMA is the same as the core molecule of amphetamine and the hallucinogen mescaline.

Instant feedback: What is the mechanism by which MDMA produces its effects?
Answer: MDMA causes the release and inhibits the reuptake of neurotransmitters, most importantly, serotonin.

ECSTASY INTOXICATION

Ecstasy users usually take a single tablet, but very experienced users may use many more. The effects of MDMA usually start within an hour of ingestion, they peak in 2-3 hours and are essentially gone in 4-5 hours

Ecstasy is a recreational drug. It is taken for the pleasurable sensations – physical and psychological – that it produces and devoteès consider it very safe. Most users report that the psychological effects predominate and these include a feeling of euphoria and well-being, heightened sensory perception, and sexual arousal. One of the most prominent psychological effects is a feeling of increased empathy. Users often report that they feel much closer emotionally towards others, they are more verbal and open, and they say that they feel that their personal defense mechanisms are no longer a barrier to communication. Because of this, the terms *empathogen* or *entactogen* have been used to describe MDMA and there are have been clinical studies that have explored the use of MDMA as an adjunct to psychotherapy.[15]

Physically, ecstasy users say they have greater endurance and a greater sense of energy, and the drug is often taken at "raves." These are very crowded, all-night parties that feature hour after hour of non-stop dancing, and the drug is taken in these situations both for its psychological effects (the drug makes it much easier to tolerate being in very close contact with others for long periods of time) and for its physical effects (increased endurance).

However, not all of the sensations of ecstasy intoxication are pleasant. Muscle tension, bruxism (teeth grinding), trismus (tight jaw muscles) headache, nausea, blurred vision and dry mouth are possible. As well, not all users report pleasurable psychological effects. Anxiety, agitation, a feeling of depersonalization, panic attacks, and even psychotic episodes have been experienced. Also, users often report a hangover effect – difficulty concentrating, depression, anxiety, drowsiness, headache – that can last for a day or two after taking the drug.[16]

Instant feedback: The physical effects produced by MDMA appear to be much stronger than the psychological effects – in most cases – but there are many clinical reports of significant psychological morbidity associated with MDMA use.

TOXICITY OF MDMA

The exact incidence of toxic reactions to MDMA is not known, and the number of fatalities can only be guessed at (as well as the number of deaths per incident of use). But given the popularity of MDMA, it appears that the risk of death is not great: During the period of July to December, 2000, there were 66 medically examined cases in the US that tested positive for phenylethylamines, and Gill (2002)[17] noted that during the period of January, 1997, and June, 2000, there were 22 MDMA-related fatalities in New York.

Toxic reactions, however, are well described in the literature and these can be understood using a systems approach. There appears to be significant individual differences in tolerance to MDMA,[18] but there are five areas of concern for the patient who is having a toxic reaction to ecstasy

Temperature regulation

Hyperthermia is probably the most dangerous complication of ecstasy use/overdose. Temperatures of 42˚C have been recorded. [19, 20] The exact mechanism for the elevated temperature has not been completely outlined, but it has been postulated that it is due to sympathetic nervous system activation, increased muscle activity, genetic susceptibility and disruption of thermoregulation mechanisms[21] The traditional explanation has been that the fever seen after MDMA use/overdose have been due to a change in the body's temperature regulation mechanism, an increase in metabolism, and the vigorous, non-stop physical activity in the situation in which ecstasy is commonly used. Raves, as mentioned earlier, feature non-stop dancing that continues for hours, often in very crowded and poorly ventilated areas. Excessive sweating and inadequate fluid intake, combined with the activity and ambience of a rave, not surprisingly cause fever. However, fever has been reported when these variables are absent. Fever and seizures were reported in two young children who ingested a single ecstasy tablet [22, 23] and laboratory experiments at room temperatures of 18˚C to 30˚C have shown that absent increased activity and high ambient temperatures, MDMA can elevate body temperature.[24] But although the exact cause of elevated body temperature associated with MDMA use is not clear, there is no doubt that it can cause serious morbidity such as [25]

Disseminated intravascular coagulation (DIC): Hyperthermia is a well-known cause of disseminated intravascular coagulation. The classic pattern of widespread clotting followed by consumption of clotting factors and bleeding has been reported (albeit infrequently) after ecstasy use,
Liver damage: Elevated temperatures can damage the liver, and MDMA itself may to have a primary toxic effect on the liver,
Renal failure: This is the end result of tissue damage, high circulating levels of myoglobin and myoglobinuria, and
Rhabdomyolysis: The pathogenesis of rhabdomyolysis in ecstasy intoxication includes hyperthermia, increased muscle activity and, occasionally, seizures.

Liver damage

As mentioned previously hyperthermia can cause direct damage to the liver (hyperthermia may represent an oxidative stress [26)], but liver damage from ecstasy can be seen in the absence of hyperthermia.[27] It can be seen after acute, one-time exposures [28] and after chronic use.[29, 30] The damage can be mild, with a presentation that is similar in presentation to viral hepatitis,[31] to severe; there has been one case of transplantation following fulminant hepatic failure, and deaths have been reported.[32, 33] One cases series of 62 patients with acute liver failure noted the incidence of liver failure associated with ecstasy use to be 8%

The chronic cases appear to follow a typical clinical pattern. There is a prodromal period of a few days up to several weeks after the ingestion. Following that, the patient begins to complain of symptoms such as nausea, malaise, lethargy, vomiting, anorexia, and right upper quadrant pain.[34] Physical findings include pale-colored stools, jaundice

and dark urine. Serum bilirubin, AST and alkaline phosphatase may be elevated. In some cases, the INR can be prolonged, the patient can become hypoglycemic, and serum blood urea nitrogen and creatinine can be elevated.[35] Patients can recover quickly and uneventfully, but sepsis, encephalopathy and death from cerebral edema have been reported.[36] The acute cases appear to often involve hyperthermia or seizure activity.[37]

The mechanism for MDMA liver damage has not been clearly outlined. In some cases it may be an idiosyncratic reaction to the drug. It may be due to the drug itself, a metabolite, a contaminant introduced during illicit manufacturing, or adulteration of the MDMA with another drug. An immune-mediated mechanism has been also been proposed.[38] Impairment of heat shock proteins has also been advanced as a cause for liver damage. These proteins are produced in response to environmental stresses (eg, infection, heat). They help cells to adapt to these adverse conditions and thus prevent tissue damage that would normally be caused by the stress.[39] MDMA may impair the production of heat shock proteins. The patient is hyperthermic from the drug, but the liver is left unprotected because of the impaired production of these protective proteins.[40] It is also possible that hypotension and decreased perfusion of the liver may play a role in hepatic damage after ecstasy intoxication.

Most of the patients with liver damage after ecstasy use did not have risk factors making them susceptible hepatic injury. The clinical picture (in the chronic cases) is further confused by the lack of confirmatory evidence that documents MDMA use in the patients. Many of these patients presented for treatment days or weeks after ingestion – enough time for the MDMA to be metabolized and eliminated, so MDMA would not have been detectable in serum or urine. In addition, the amount of use and the pattern of use varies widely among these victims; liver damage has happened with one time use or after months of chronic use. This appears to negate the influence of a direct drug effect on the liver; if this were so, it seems logical that many more cases of liver damage associated with ecstasy use would have been reported.

Instant feedback: In one study, ecstasy use was the number two cause, after viral hepatitis, of liver injury in people under the age of 25.[41]

Instant feedback: Liver damage has occurred in patients with normal body temperatures and in patients with hyperthermia. It has occurred after one-time use and after chronic use and it has occurred shortly after ingestion and after a prodromal period of weeks. The bottom line: *Check liver function in all patients presenting with MDMA intoxication or a history of MDMA use.*

Hyponatremia

The intense physical activity and the elevated body temperatures that can be seen with ecstasy ingestion obviously put the patient at risk for dehydration. For most people, simple fluid replacement is sufficient to prevent fluid and electrolyte disorders, but severe fluid and electrolyte disorders have been seen, and the most common is hyponatremia.

Hyponatremia is not a common toxic effect of ecstasy intoxication (one study noted 17 cases in a three year period of reporting of all ecstasy cases, another found ten case

reported in the medical literature[42)], but it is well described in the literature[43] and sodium levels as low as 107 mEq[44] have been reported. The exact pathogenesis of this disorder has not been discovered, but there are several possible mechanisms.

Excess fluid intake. Due to the hours long, almost non-stop physical activity that can occur in a rave and the excessive sweating that results, participants frequently drink large amounts of water and this can cause hyponatremia (this has been called the Poland Springs™ syndrome). However, it has been pointed out that it is close to impossible for an individual to ingest sufficient water to lower serum sodium to such exceptionally low levels; excess sodium transport through the wall of a fluid-filled gut may be the cause

Excess fluid intake and muscle mass. Women have smaller muscle mass than men and as half the total body water is in skeletal muscle cells, a person with a small muscle mass would be at greater risk of hyponatremia after excess fluid intake.

Syndrome of inappropriate secretion of antidiurectic hormone (SIADH). Antidiuretic hormone (ADH, also known as vasopressin) is a hormone secreted by the posterior pituitary that is involved in the regulation of fluid balance and blood pressure control. ADH increases the re-absorption of water by the collecting duct and collecting tubule in the kidney and to some extent, increases the excretion of sodium.[45] SIADH has clearly been reported in MDMA [46] (although the number of reported cases is small) intoxication and at least in some cases, confirmed by laboratory measurements of elevated ADH secretion, both in the clinical setting and experimentally.[47, 48] In intoxication, these mechanisms are exaggerated and the patient can become profoundly hyponatremic. It is not clear why MDMA causes SAIDH. ADH release may be under serotonergic control, or acute stress may stimulate its release.

SIADH related to MDMA appears to affect women more than men, and seriousness of the pathology appears to be related to the speed at which it develops; the faster it develops, the sicker the patient will be. Signs and symptoms can be relatively mild – nausea, vomiting headache – or they can be severe: cerebral edema, respiratory arrest, seizures and cerebral hypoxia and death have been reported.

Instant feedback: If hyponatremia occurs, it cannot be predicted how far or how fast it will progress. *Patients with MDMA intoxication who are hyponatremic must have their serum sodium monitored very closely.*

Instant feedback: Patients with MDMA intoxication are often dehydrated and need water, but they also need *salt*. *Cautious* use of saline solutions is preferable for fluid replacement instead of 5% dextrose solutions. *Too much free water and not enough salt can exacerbate hyponatremia.*

Neurologic effects

Given that the central molecule of MDMA is the same as that of mescaline (a well-known hallucinogen), it is not surprising that neurologic toxicity can be a prominent part of the clinical picture of MDMA toxicity. Many of the toxic effects have already been outlined: anxiety, lethargy, depersonalization, headache, psychotic events and seizures.

Seizures are the most commonly reported neurologic event. The exact incidence of seizures as a result of ecstasy intoxication is not known, but there are *many* reports in the literature of seizures related to MDMA use and in one case series of 14 exposures leading to death, 50% of the patients suffered seizures.[49] There have also been more unusual and potentially more dangerous reactions.

Parkinsonism. Several cases of Parkinson's attributed to MDMA use have been reported: eg, a 29-year-old male developed Parkinson's after ingesting MDMA a total of 10 times in the prior year. All diagnostic tests for other causes were negative and idiopathic Parkinson's is unusual to develop in this age group.[50] Whether or not MDMA was the actual cause of Parkinson's in these cases is not clear. MDMA seems to have some effect on the dopaminergic system, non-human primate studies and several limited human studies suggest that there may be a link (damage to the dopaminergic system after MDMA use was seen), and there were several well publicized cases of Parkinson's developing after ingestion of an illicit designer meperidine analogue. However, in the three reported cases, there was no confirmatory testing of MDMA use in the patients and one author suggested that these simply represented early-onset Parkinson's.[51]

Cerebral infarction/cerebral hemorrhage. A 35-year-old male developed right hemiparesis and dysphasia due to a cerebral infarction after ingesting several tablets of ecstasy 36 hours prior to arrive.[52] Cerebral hemorrhage has also been reported after ingestion of a single ecstasy tablet, and one other case of cerebral hemorrhage and one of subarachnoid hemorrhage have been reported, and there are almost certainly other cases of infarction and hemorrhage that have not been reported. The exact cause of infarction and hemorrhage in these cases is not known. It may be that these patients had pre-existing vascular disease or congenital abnormalities. However, the central molecule of MDMA is phenylethylamine, which is the same central molecule found in amphetamine, and cerebral vascular disasters have been well described after amphetamine use. It is thought that vasculitis, cerebral artery spasm and arteritis are the cause,[53] and although it seems reasonable that the same toxic mechanisms may cause cerebral vascular events in patients intoxicated with MDMA, this has not yet been proved.

Coma: Coma *not* due to a cerebral vascular event or hyponatremia has been reported.

Amnestic syndrome. Spat et al reported a case of significant memory impairment after a psychotic episode caused by ingestion of one tablet of ecstasy. [54]

Dystonic reaction has been reported.[55]

Cardiovascular effects

As would be expected from a drug with a structural similarity to amphetamine, tachycardia and hypertension are common after ingestion of MDMA. These drugs increase the release of serotonin, but also increase the release of norepinephrine. Generally, these effects are mild and do not require specific treatment. Other, more serious effects reported are hypotension, chest pain, atrial fibrillation,[56] cardiac failure, aortic dissection[57] and cardiovascular collapse.[58]

Serotonin syndrome

Serotonin syndrome is a clinical condition that occurs when there is excess stimulation of the serotonin receptors. This can happen because certain drugs (1) directly stimulate the serotonin receptors, (2) prevent the reuptake of serotonin, (3) cause the release of serotonin from presymaptic neurons, or (4) inhibit the breakdown of serotonin. Patients exhibit autonomic, neuromuscular and cognitive effects: hyperthermia, tachycardia, hyperreflexia, myoclonus, agitation and/or confusion.[59] Some of the basic mechanisms of serotonin syndrome and many of the signs and symptoms are similar to those of MDMA toxicity, and many ecstasy users seem to display mild signs of serotonin syndrome. For some, these signs and symptoms are expected, seen as normal, and are reassurance that the MDMA they consumed was pure.

So is MDMA poisoning simply serotonin syndrome? The answer is yes – partially. There is no doubt that patients who are poisoned with MDMA experience some degree of serotonin syndrome. What it contributes to the clinical picture of toxicity can't be clearly defined and the hyponatremia, liver damage, and the degree of hyperthermia (the pathologies that make MDMA dangerous) are unique to MDMA and separate from serotonin syndrome. Also, basic treatment for the serotonin syndrome and MDMA poisoning is essentially the same, so if serotonin syndrome is contributing to the toxic effects seen in MDMA poisoning, it most likely does not increase the patient's risk of morbidity and mortality and does not change management.

Summary

It is difficult to present a *typical* picture of a patient with MDMA toxicity; the clinical presentation varies widely. However, it is more useful to simply remember that MDMA: (1) affects temperature regulation and produces hyperthermia, (2) can cause liver damage, (3) can cause hyponatremia (4) can have pronounced neurologic effects, inhibitory or excitatory, and (5) can have pronounced sympathomimetic effects.

Instant feedback: There are many clinical causes of death attributed to MDMA , *but most patients who succumb* are *hyperthermic and as a result have DIC, rhabdomyolysis* and *renal failure.*

Chronic effects of MDMA abuse

The long-term effects of MDMA use are a topic of much debate. Researchers have made vigorous efforts to determine if there is residual, permanent damage to the serotonergic system associated with chronic MDMA use. Numerous animal studies (mice, rats, non-human primates) have clearly shown lasting damage. There are decreased serotonin levels in the brain, decreased numbers of serotonin transporter molecules, decreased number of serotonin-containing neurons and degradation of serotonergic axons and axon terminals. However, although some studies have reported changes in neurocognitive function in test animals with documented brain damage from MDMA, others have not; in some cases, the test animals that had been given MDMA scored higher on certain tests than the control animals. The human studies have also provided equivocal information. Numerous studies have shown chronic neurocognitive effects in chronic MDMA users. Some of these effects are[60-63]

Impairment of verbal and visual memory,
Impairment in decision making (sometimes called executive function),
An increase in impulsivity and lack of self control,
Panic attacks,
Depression,
Phobic anxiety,
Verbal fluency, and
Complex attention.

The large number of controlled studies that have confirmed these effects in chronic users of MDMA, as well as similar results when volunteers are given a one-time dose, seem to leave little doubt that they are caused by MDMA. Some these effects can last for years.[64] But there is much less evidence that long-term use of MDMA causes permanent damage to the serotonergic system. It has been demonstrated that long-term, chronic MDMA users have very low levels of serotonin in the cerebrospinal fluid, reduced numbers of serotonin transporter molecules, and an upregulation of serotonin receptors. However, many of the attempts to document damage to the serotonergic system in chronic MDMA users have used screening tools that are less than perfect. Also, these studies cannot prove that MDMA caused these effects. They may have been present before MDMA (and there is some evidence that supports this[65]) use or they might simply be coincidental.

Instant feedback: Although animal studies and limited human studies suggest that long-term use of MDMA can cause permanent damage to the serotonergic system there is, as yet, no definitive proof of this.

Treatment

Without a clear history of MDMA ingestion, it can be difficult to determine if the patient is toxic from MDMA. There are many other clinical conditions that can mimic ecstasy poisoning. Some of them are

Anxiety,
Encephalitis,

Cocaine poisoning,
Amphetamine poisoning,
Anticholinergic poisoning,
Phencyclidine (PCP) poisoning,
Halucinogen (LSD, mescaline, psilocybin) poisoning,
Withdrawal syndromes,
Neuroleptic malignant syndrome, and
Serotonin syndrome.

It is also important to remember that coingestion of illicit drugs, eg, GHB, ketamine, marijuana, can confuse the clinical picture.

Assuming the patient is symptomatic due to an ecstasy ingestion, treatment should proceed using these guidelines. Most patients with ecstasy intoxication will recover uneventfully, but as mentioned earlier, serious morbidity and mortality are possible

Airway, breathing, circulation: The ABCs, for most MDMA-intoxicated patients, are not *seriously* compromised. However, patients who are comatose may need endotracheal intubation for airway protection and patients who are severely hyperthermic may need pharmacological paralysis that would necessitate intubation. Supplemental oxygen would be useful because of the increased metabolic rate, and standard measures (fluids, trendelenburg position and iv vasopressors) would be used for hypotension. Tachyarrhythmias would be expected to respond to cooling measures, benzodiazepines and rest. Hypertension is usually short-lived and given the changes in fluid status in many of these patients, it would be best to treat hypertension conservatively and with short-acting agents

Decontamination: Decontamination refers to efforts that are used to prevent the absorption of a poison or to remove it from the gut. There are four basic techniques: (1) *syrup of ipecac* acts as a local irritant and stimulates the vomiting center to produce emesis. Because of the possibility of a depressed sensorium and loss of the gag reflex from the MDMA, and the increase in intracranial pressure that accompanies forceful vomiting, syrup of ipecac should *never* be used in cases of MDMA exposure, (2) *lavage* makes intuitive sense; if the patient has swallowed something harmful put a tube into the stomach and suck it out. However, the process of lavage can increase intracranial pressure and studies have shown it is only of benefit if performed within an hour of ingestion, (3) *whole bowel irrigation* uses a large (1-2 liters per hour) oral infusion of an isotonic solution to flush out the gastrointestinal tract. Patient compliance and discomfort make this difficult to use and it is reserved for drugs that are sustained release and/or not adsorbed by activated charcoal, and (4) *Activated charcoal.* This is given orally, and adsorbs ingested drugs very effectively. It should not be given if the patient is drowsy, has a decreased/absent gag reflex or if the patient presents more than two hours after the ingestion.

Instant feedback: The decontamination technique of choice for an MDMA ingestion would be activated charcoal *if* the patient presents within two hours of the ingestion, is

awake and alert – and there is a reasonable expectation they will remain so – and has a normal gag reflex.

Temperature control: This is critical. Patients who die from ecstasy ingestion die because of hyperthermia, and the DIC and rhabdomyolysis (an attendant renal failure) it causes. Fans, ice lavage, cold intravenous fluids, cold baths, and packing in ice can all be tried. Antipyretics are of little value.
Hyponatremia: As mentioned earlier, patients with MDMA intoxication are often dehydrated or have a clinical history that suggests they are. Fluid replacement is then a logical therapeutic intervention, but saline is preferred over dextrose solutions to avoid aggravating the hyponatremia. Even then, fluid resuscitation should be done cautiously if serum sodium is very low, and hypertonic solutions, eg, 3.0% saline may be needed.
Seizures: Seizures would be treated with standard anticonvulsant therapy.
Basic care: The patient should be placed on a cardiac monitor and vital signs should be monitored frequently and a 12-lead electrocardiogram should be done. IV access should be obtained and blood for electrolytes, BUN, creatinine, liver functions tests and creatine phosphokinase should be obtained. Consider placing a foley catheter to help monitor intake and output.[66]

Summary

MDMA is a hallucinogenic amphetamine. It has structural similarities to mescaline and amphetamine.
MDMA works by causing a release of serotonin and inhibiting serotonin reuptake.
MDMA also interferes with the release and reuptake of norepinephrine.
There many other drugs that can cause a clinical picture similar to that of MDMA
Start treatment by stabilizing the airway, breathing and circulation.
Activated charcoal is the decontamination treatment of choice.
Hyperthermia, with the attendant complications of DIC, rhabdomyolysis and failure, is the most serious complication of MDMA intoxication and the most common cause of death.
MDMA can also cause hyponatremia, liver damage and serious cardiac and neurologic complications.
Any patient with a history of MDMA ingestion should have liver function studies.
Patients with a history of MDMA ingestion should have serum sodium monitored closely
Fluid replacement should preferably be done using saline solutions and should be done cautiously.

Post-test

1. Ecstasy is commonly classified:
   a. Benzodiazepine
   b. Imidazoline derivative
   c. Hallucinogenic amphetamine
   d. GHB derivative.

2. Ecstasy has structural similarities to:
   a. Benzodiazepines and barbituates
   b. Mescaline and amphetamine
   c. Ketamine and nicotine
   d. Cocaine and GHB

3. Name the two drugs that are also known as ecstasy.
   a. LSD and PCP
   b. Ma huang and dextromethorpham
   c. PCP and ketamine
   d. Pseudoephedrine and ma huang

4. MDMA produces pleasurable intoxication by its effect of which neurotransmitter?
   a. Epinephrine
   b. Glycine
   c. GABA
   d. Serotonin

5. The most serious effect of MDMA poisoning is:
   a. Hyperthermia
   b.Ventricular tachycardia
   c. Respiratory depression
   d. Seizures

6. MDMA poisoning can cause:
   a. DIC, rhabdomyloysis, and renal failure
   b. Hypertension, tachycardia, and congestive heart failure
   c. Metabolic acidosis, respiratory depression, and gastrointestinal bleeding
   d. Hemolytic anemia, pulmonary embolism, and angina

7. The electrolyte abnormality most commonly seen in MDMA poisoning is:
   a. Hypocalcemia
   b. Hypomagnesemia
   c. Hyperkalemia
   d. Hyponatremia

8. The decontamination technique of choice for MDMA poisoning would be:
   a. Syrup of ipecac

b. Whole bowel irrigation
c. Lavage
d. Activated charcoal

9. The organ most directly affected by MDMA poisoning is:
   a. The kidney
   b. The heart
   c. The liver
   d. The lungs

10. The central molecule of MDMA is:
   a. Benzene
   b. Phenylethylamine
   c. Indole alkaloid
   d. Lysergic acid

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