

Listing and Summary of Ecstasy Medical Articles

Mood and Cognitive Effects of +/-Methylenedioxymethamphetamine (MDMA, Ecstasy): Weekend High Followed by Mid Week Low. Curan HV and Travill RA, Addiction, 1997 Jul 92(7)821-31

A comparison of 12 participants who reported having taken MDMA with 12 participants who reported having consumed only alcohol. Individuals assessed the following day and again at mid week (day 5). Acute effects of MDMA broadly replicated previous finding. MDMA users rated elevated mood on day 1 but significantly low mood on day 5, at which points some participants scored with the range for clinical depression. In contrast, the alcohol group showed less pronounced changes, with the lowest point being day 2. The MDMA group also showed significant impairments on an attention/working memory task, compared with alcohol users. Conclusions: Weekend use of MDMA may lead to depressed mood mid-week. Possible mechanisms underlying the findings are discussed in terms of temporary depletion of serotonin, serotonergic neurotoxicity, and psychological aspects of mood change.

Ecstasy-Induced Rhabdomyolysis (muscle degeneration) and its Role in the Development of Acute Renal Failure. Cunningham, Intensive Crit Care Nursing 1997, Aug 13(4) 216-23.

One of the potentially devastating side effects of Ecstasy (MDMA) is rhabdomyolysis. From consideration of the pathophysiology of rhabdomyolysis and its role in the development of acute renal failure, it becomes apparent that preventative measures and prompt treatment can prevent patients developing acute renal failure as a consequence of rhabdomyolysis. The use of drugs by young people has become prominent in the media by cases like that of Leah Betts, who died shortly after her 18th birthday following the use of ecstasy. Drug-induced rhabdomyolysis is not uncommon: heroin, methadone and temazepam have all been indicated throughout the literature as causes when a patient has been unconscious for some time allowing a crush injury to develop. The focus of this article is on the effects of ecstasy-induced rhabdomyolysis as ecstasy is a commonly used recreational drug among young people in the 16-25 age group (Brown et al 1995), with a wide variation in social class and occupations. Rhabdomyolysis is a condition seen frequently in some intensive therapy units and is one of the many side-effects of ecstasy use. It is a clinical syndrome of muscle pain, weakness and brown urine due to the breakdown of muscle. A more appropriate term, myoglobinuria, has been used following the classic description of crush syndrome in patients injured during the bombing of London in WWII. Renal failure following rhabdomyolysis is a side-effect of ecstasy use. O'Connell (1994) noted that out of nine documented deaths in Britain due to ecstasy use, five of the patients had rhabdomyolysis among their clinical symptoms; also seven out of 15 recorded cases of hyperpyrexia due to ecstasy, developed rhabdomyolysis. Drug induced rhabdomyolysis complicated by acute renal failure has a 46% mortality rate (Roth et al 1988). There are three ways in which ecstasy may induced rhabdomyolysis by causing damage to muscle cells: (1) hyperpyrexia, (2) increased energy consumption (dancing); (3) crush injury when a patient has been unconscious for some time. Ecstasy- Induced Hyperpyrexia is associated with severe metabolic acidosis, muscle rigidity, disseminated intravascular coagulation and hyperkalemia. Acute renal failure follows when the tissues have been damaged allowing myoglobin to infiltrate the extracellular fluid, eventually leading to damage of the kidney. Ecstasy-Induced Energy Consumption through exercise, for example, dancing, is an important cause of rhabdomyolysis. Exercise by itself or in the presence of any of the many metabolic disturbances that impair energy production can lead to necrosis and rhabdomyolysis (Sweny 1989). Crush Injury is possible when a patient has been unconscious for some time following the ingestion of ecstasy. Damage to compressed muscle groups of the arms, legs, and sacrum are not uncommon. Failure to appreciate the importance of muscle necrosis as the underlying problem in the crush syndrome may have disastrous consequences. Shaw et al (1994) state that there may be a delay in recognizing the signs of muscle compression and necrosis when a patient is first admitted to hospital with a drug overdose.

MDMA (Ecstasy) Use: An overview of psychiatric and medical sequelae (in German), Thomasius R, Schmolke M, and Krause D., Fortschr Neurol Psychiatr 1997 Feb; 65(2) 49-61.

Since the mid-eighties psychiatric complications and consequences of the abuse of MDMA have been reported in at least 48 cases. It is necessary to differentiate between acute psychiatric complications, which subside completely when the level of intoxication comes down, toxic psychoses and long-term psychiatric diseases as a consequence of substance abuse. The latter involve atypical and paranoid psychoses, depressions, panic disorders, depersonalization and behavioral disorders. Convulsive seizures are among the most common problems involving the central nervous system. Furthermore, there have been reports on cerebrovascular accidents and intracranial hemorrhages. Literature reports on at least 53 cases of medical complications in abusers of MDMA, 14 of which came to a lethal end. Research still blatantly lacks prospective epidemiological and clinical studies on a sufficiently large scale to identify different developments of dependency and predictors of harmful and unhealthy consumption.

MDMA - Induced Hyperthermia: A Survivor with an Initial Body Temperature of 42.9-degree C.

Mallick A., and Bodeham, J. *Accid. Emerg Med*, 1997, Sept; 14(5) 336-8.

A 19-year-old male survived hyperpyrexia (42.9 degrees C; 109 degrees F) following MDMA ingestion of three tablets four hours previously. He collapsed at a local nightclub. He developed convulsions, rhabdomyolysis, metabolic acidosis, and respiratory failure. This was successfully managed by assisted ventilation, aggressive fluid therapy and cooling measures. This is the first report of a survivor with such a severe hyperpyrexia. The use of MDMA has increased in the US, UK, and continental Europe. Severe and sometimes fatal adverse reactions are increasingly encountered in various accident and emergency (ACE) departments. These include hypothermia, metabolic derangement, seizures, hypertensive crises, cardiac dysrhythmias, disseminated intravascular coagulation, rhabdomyolysis, acute renal failure, hepatic toxicity, cerebrovascular accidents, and psychiatric disturbances. Survival with a core temperature of greater than 42 C is rare. We attribute the survival of our patient to prompt and rapid control of hyperthermia in the A&E. It would not have been possible to bring down the body temperature within an hour with cooling measures alone. Moreover, external cooling can lead to peripheral vasoconstriction and a raised core temperature. Dehydration was corrected with aggressive 0.9% isotonic fluid therapy over a period of 6 hours with pulmonary artery and central venous pressure monitoring as a guide. There have been reports of three deaths due to dilutional hyponatraemia and acute water intoxication from MDMA ingestion. This may result from drinking excessively large volumes of water throughout the event in rave parties, following the advice from drug misuse agencies, and the release of antidiuretic hormone by MDMA. Urgent estimation of serum sodium is therefore indicated in this situation.

Ecstasy and Related Substances-Serum Levels in Impaired Drivers., Moeller MR, Hartung M., J. Anal Toxicol 1997 Nov-Dec; 21(7): 591.

In 1995 and 1996, the authors were able to prove the presence of Ecstasy and related substances in impaired drivers in 30 cases. The presence of MDMA was shown in 18 cases and MDEA in 17 cases. MDEA alone was found in 5 cases. In all other cases, there was combination of these substances, sometimes with amphetamine. MDA was found in 23 cases. It can be assumed that MDA is mainly a metabolite of MDMA and MDEA. In 25 of the 30 cases, cannabis was also found indicating polydrug abuse. One subject had also consumed codeine and another one had also ingested bromazepam. Eighteen subjects had a blood alcohol concentration of less than 0.03%

3,4-Methylenedioxy Analogues of Amphetamine: Defining the Risks to Humans. Hegadoren KM, Baker GB, and Bourin M. Neurosci Biobehav Rev 1999 Mar;23(4);539-553.

Analogues of amphetamines (MDMA-Ecstasy/Adam; MDA-Love, and MDE-Eve) are drugs that produce feeling of euphoria and energy, and a desire to socialize, which go far to explain their current popularity as "rave drugs". In addition to these positive effects, the drugs are relatively inexpensive to purchase and have the reputation of being safe compared to other drugs. Yet there is mounting evidence that these drugs do not deserve this reputation of being safe. The article reviews the risks associated with analogue

drug abuse, behavioral and cognitive effects, toxicity, psychopathology, neurotoxicity, abuse potential, and the potential for drug-drug interactions associated with acute and chronic use. British newspapers abound with horror stories about young adults being hospitalized or dying after ingestion of these drugs, prompting one physician to dub the combination of MDMA and rave dancing as the "the dance of death." The most common reported after effects of MDA, MDMA, and MDEA are drowsiness, muscle aches and general fatigue, depression lasting 1-2 days, difficulty in concentration, paranoia and short-lived anxiety and irritability. The after-effects increase with successive doses, while the positive subjective effects diminish. It is difficult to collect accurate information regarding the numbers of deaths that can be ascribed directly to the ingestion of these drugs due to the presence in many of the cases of other combined drug abuse. While it is important to recognize that the number of deaths related to these drugs is relatively small when the frequency of use is considered, the lack of apparent relationship between dose and toxicity and the seriousness of the clinical presentation even when the patient survives suggests that these drugs do not deserve the "harmless" label and that educational programs are needed. Educational materials must accurately set out the risks these drugs represent to adolescents and young adults if they are to be believed. We need to move away from the scare tactics associated with some of the media coverage and provide reasoned information from which individuals make informed choices about the use of MDA, MDMA, and MDEA and can recognize warning signs that require immediate medical attention both in themselves and their follow "ravers".

Clinical and Toxicological Aspects of the Use of Ecstasy (Article in Dutch) Pennings EJ, Konijn KZ, deWolff FA., Ned Tijdschr Geneeskd 1998 Aug 29;142(35); 1942-6.

MDMA use in humans has a stimulatory effect and enhances feeling of openness and solidarity. The drug depletes serotonin stores and inhibits serotonin synthesis, and inhibits the reuptake of serotonin into the neuron. This leads to destruction of serotonergic axon terminals in animal brain. Similar events of Ecstasy damage are indicated to occur in the human brain. We strongly advise against the use of MDMA as the long term clinical consequences are not known. In man, life-threatening complications after MDMA use include hypothermia, hyponatremia, and liver failure. Psychiatric complications include psychosis, depression, panic disorder, and impulsive behavior. The chronic psychosis responds poorly to therapy.

Cognitive Performance in Recreational Users of MDMA of Ecstasy: Evidence for Memory Deficits., Parrott AC, Lees A, Garham NH, Jones M, Wesnes K. J. Psychopharmacol 1998;12(1):79-83.

Cognitive tasks performance was assessed in three groups of young people: 10 regular users of MDMA who had taken MDMA 10 times or more; 10 novice MDMA users who had taken MDMA one to nine times; and 10 control subjects who had never taken MDMA. A computerized battery of cognitive tasks was undertaken on a day when subjects were drug free. Performance on the response speed and vigilance measures (simple reaction time, choice reaction time, and number vigilance), was similar across the three subgroups. However on immediate word recall and delayed word recall, both groups of MDMA users recalled significantly fewer words than controls. Animal research has shown that MDMA can lead to serotonergic neurodegeneration, particularly in the hippocampus and frontal cortex. Although the study design was far from ideal, these data are consistent with other findings of memory decrements in recreational MDMA users, possibly caused by serotonergic neurotoxicity.

Recreational use of Ecstasy (MDMA) is Associated with Elevated Impulsivity. Morgan MJ. Neuropsychopharmacology 1998 Oct;19(4);252-64.

Recent evidence suggests MDMA produces long-term reduction in serotonin. Serotonin is implicated in the regulation of mood, anxiety, aggression, impulsivity, and cognition. The combined data from two studies indicated that ecstasy users exhibited elevated impulsivity on both self-report and behavioral measures, and that those who had taken the most ecstasy had the most elevated trait impulsiveness scores. These findings are consistent with previous evidence that elevated levels of impulsivity in humans are associated with reduced levels of serotonergic function. Combined data from the study presented in this

article indicates that recreational ecstasy users committed significantly more errors in the MFF20 (Cairns and Cammock 1978) than polydrug control subjects, who had similar drug histories but had never taken illicit drugs, all of whom were of similar age, height, gender, education, and estimated premorbid IQ. By definition, some of the elevated trait impulsiveness, observed in the groups of participants who had used illicit drugs probably reflects a pre-existing predisposition that may have led to subsequent use of illicit drugs. However, it is also possible that some of the elevation of trait impulsiveness, particularly the additional elevation associated with heavy past consumption of ecstasy, may be attributable to the neurotoxic effects of ecstasy on brain 5-HT systems, because, as noted, reductions in serotonergic function have consistently been associated with elevated levels of impulsive behavior. A number of ecstasy users volunteered information indicated that their reduced ability to concentrate, impaired memory, and slowed mental processing were a direct consequence of taking ecstasy, as was their increased susceptibility to anxiety, depression, aggression, irritability, and mood swings.

Hyponatraemia and Seizures After Ecstasy Use. Holmes S B, Banerjee AK, and Alexander WD., Postgrad. Med. J., 1999 Jan; 75(879):32-3

A patient presented to our unit with seizures and profound hyponatraemia after ingestion of a single tablet of ecstasy. No other drugs were taken. Rapid elevation of serum corticosterone and prolactin levels occurs through a 5-HT receptor-mediated mechanism. 5-HT release caused increased antidiuretic hormone secretion in some controlled studies on animals. Other theories have been suggested for the pathogenesis of the hyponatremia. Hyperthermia and sweating, known consequences of ecstasy ingestion and vigorous dancing, result in sodium loss which, coupled with excessive water intake, leads to hyponatraemia. Evidence of water intoxication has been detected both in vivo and post-mortum. However, the mechanism may be more complex, and multifactorial in origin. The toxic effects of ecstasy are due directly to the parent compound and not to impurities within the tablet. The seizures proved resistant to therapy and ventilation on the intensive care unit was required. Resolution of the seizures occurred on correction of the metabolic abnormalities. The pathogenesis of seizures and hyponatraemia (low blood sodium levels) after ecstasy use is discussed. Ecstasy use should be considered in any young patient presenting with unexplained seizures and attention should be directed towards electrolyte (plasma salt) levels, particularly sodium. Learning Points: (1) Seizures following ecstasy use may not respond to therapy with anticonvulsants and benzodiazepines. (2) Ecstasy ingestion may result in hyponatraemia which is exacerbated by water intoxication. (3) Unrestricted water intake should not be recommended following ecstasy use. (4) Patients may present with seizures and hyponatraemia without other features of ecstasy toxicity.

Ecstasy, Shannon M, Pediatr Emerg Care, 2000 Oct; 16(5); 377-80.

Ecstasy in overdose has major toxicity, producing several different life-threatening manifestations. Hepatotoxicity and hyponatremia are common but poorly understood consequences of MDMA overdose. The drug can produce long-term, if not permanent, neurologic sequelae by destruction of serotonergic neurons. Chronic Ecstasy use can result in psychosis, depression, and suicidal ideation.

Human Pharmacology of 3,4-Methylenedioxymethamphetamine Psychomotor Performance and Subjective Effects. Cami J, et al., J. Clin Psychopharmacol, Aug2000 20(4): 455-66.

MDMA is of increasing use among youth because of its apparent entactogenic properties, such as euphoria, friendliness, closeness, and empathy. Experimental studies have shown MDMA to be neurotoxic. Data on pharmacologic actions of MDMA in humans are limited. A randomized, double blinded, crossover, controlled trial to assess psychomotor performance and subjective effects in eight healthy male volunteer. MDMA was given in the same range of doses used for drug purposes (75 and 125 mg). The short-term administration of MDMA produced marked euphoria, a slight impairment in the performance of psychomotor tasks, and mild changes in body perceptions without hallucinations. These data support the abuse liability of MDMA.

MDMA and MDEA Misuse: An Immunohistochemical Study on Three Fatal Cases. Fineschi V. et al., Forensic Sci Int, 1999 Sep 30; 379(378): 65-74.

Three fatal cases of MDMA/MDEA misuse were examined. These were white males, 19 and 20 years of age, in which postmortem toxicology showed the presence of MDMA in one case, MDEA in another case, and both drugs in a third case. The clinical data were analyzed and immunohistochemical investigations. A complete immunohistochemical study has made it possible to demonstrate rhabdomyolysis and myoglobinuria with alterations of the organs typical of a DIC. Clinical, histopathological and toxicological data suggests that severe or fatal complications following ecstasy ingestion could be related to idiosyncratic response. Case 1: Male, 19 years, was seen ingesting numerous tablets of ecstasy in a discotheque for the entire duration of the party until early morning. Late the following morning he began to experience respiratory difficulty, uncoordinated movements, generalized hypertonia, and hyperpyrexia (40.6C). He was diagnosed with disseminated intravascular coagulation. He suffered a cardiac arrest unresponsive to cardiopulmonary resuscitation. Toxicological analysis of body fluids showed presence of MDMA and MDA (metabolite of MDMA). Case 2: Male 20 years, went with some friends to a discotheque, where he remained for some hours and where he was seen to ingest numerous tablets of ecstasy. When he returned home around 0200, he told his mother that he felt feverish. The armpit temperature was established at 40C and he immediately went to bed. At 1200 he was found dead, his pillow soaked in blood. Toxicological analysis of body fluids showed presence of MDMA, MDA, and MDEA. Case 3: Male, 19 years was found unconscious near a discotheque and taken to ER and transferred to the ICU. Clinical course worsened, diffuse subcutaneous petechiae appeared, the patient sustained convulsion and hypotensive. Patient pronounce dead approximately 28 hours after having been found at the discotheque. Toxicological analysis of body fluids showed presence of MDEA.

New Drug of Abuse, Graeme KA, Emerg Med Clin North Am, 2000 Nov; 18(4); 625-36.

Newer club drugs of abuse are frequently used in the settings of raves and the popularity of these agents requires emergency physicians to become familiar with the clinical presentations and management of the toxicity induced by these agents.

Ecstasy - Long Term Effects on the Human Central Nervous System Revealed by Positron Emission Tomography. Obrocki J, et al, Br. J., Psychiatry; 1999 Aug; 175; 186-8.

By comparison with a control group, the glucose metabolic uptake of the ecstasy user group was altered within the amygdala, hippocampus, and Brodmann's area. The results suggest the possibility that ecstasy use has lasting effects on central neuronal activity in humans.

Toxicity of Drug Abuse - Amphetamine Designer Drugs: Mental Effects and Consequences of Single Dose Use. Morland J; Toxicol Lett; 2000 Mar 15; 112-113; 147-152

MDMA interferes with serotonin and catecholamine transporters in the central nervous system to increase monoamine synaptic levels and thereby mediate the majority of its central nervous effects. These range from wanted effects like euphoria, central nervous stimulation, and feeling of closeness to mild hallucinations, impairment of cognition and coordination and further to serious reactions like agitation, disturbed and bizarre behavior, and possibly psychosis. The full picture of the consequences of these transitory changes is not known. It has been assumed that the risk of being involved in fatalities and accidents during the state of MDMA influence is increased, but this possible risk increase has so far not been determined. Observations of the prevalence of MDMA involvement in cases of reckless driving and the MDMA blood concentrations measured indicate a risk increase comparable to that observed after use

of amphetamines. Parrot and Lasky (1998, *Psychopharmacology* 139, 261-8) study three groups of MDMA users, 2 days after ingestion, MDMA-users felt significantly more depressed, abnormal, unsociable, unpleasant, and less well-tempered than the controls. Cognitive performance on both vocal recall and visual scanning tasks was significantly reduced on MDMA compared to controls. Memory recall was also significantly impaired in “drug-free” MDMA users, with regular MDMA users displaying the worst memory scores at every test session. 20% of the respondent MDMA users reported difficulties in concentration, dizziness or vertigo, visual hallucinations and drowsiness. 20 psychiatrists reported high frequency of possible detrimental effects associated with previous MDMA use noted as altered time perception and cognitive changes. A series of negative effects report by subjects participating in the studies, included disorientation, blurred vision, difficulties in walking, brief short term memory loss, confusion, difficulties with multiplication and impaired judgment. “Beneficial aspects” of drug use were talkativeness, open-minded, closeness to others, and happiness. 48 MDMA cases during a 15-month period consumed between one-half to two ecstasy tablets before the adverse event brought them to a London Emergency Room. The most common clinical features were feelings of being “strange, unwell, dizzy, collapsed, loss of consciousness, nausea, vomiting and panic, anxiety, restlessness. There were six severe episodes of delirium, seizures, coma. The use of MDMA is accompanied by marked neurobiological changes in the central nervous system, particularly linked to serotonin and catecholamine transmission. A series of possible adverse acute mental and behavioral effects have been observed in people shortly after single dose use of MDMA. More serious complications of such effects have also been reported.

Death by Ecstasy: The Serotonin Syndrome? Mueller PD., et al., Annals of Emergency Medicine, 1998 Sept, Part I, 32(3), pg 377-380.

Serotonin syndrome, a condition in which there is central serotonin receptor hyperstimulation has been described since the 1950s. Classic findings of severe serotonin syndrome include hypothermia, mental status changes, autonomic instability, and altered muscle tone or rigidity. A number of medications have been implicated in the induction of serotonin syndrome, including those that reduce metabolism (ie, monoamine oxidase inhibitors), increase production (ie L-tryptophan), or inhibit uptake of serotonin (ie. Fluoxetine, clomipramine, meperidine, dextromethorphan, pentazocine, fenfluramine). MDMA has been shown in animal models to cause massive release of serotonin from pre synaptic vesicles and inhibit its uptake. The following case illustrates that MDMA can induce a toxidrome consistent with severe serotonin syndrome. A 20 year old woman was brought to the emergency department unresponsive and cyanotic. She had ingested 2 tablets of MDMA within the previous 4 hours. She had a negative past medical history, was taking no medications, and had not been previously treated with any antidepressants or other prescription medications. History of previous use of MDMA or other illicit drugs was not available. Toxicological analysis of blood and urine indicated the presence of MDMA. No other toxic substances were present except acetaminophen, barbiturate and benzodiazepine used during treatment in the hospital. Initial anxiety, nausea, tachycardia, and elevated blood pressure are followed by relaxation, euphoria, and feelings of enhanced emotional insight. Tolerance to the psychoactive properties of MDMA develops rapidly with loss of the ability to evolve the desired response with repeated doses within several hours; instead, sympathomimetic effects predominate resulting in anxiety, dysphoria and paranoia. There have been multiple case reports in the medical literature of MDMA-induced morbidity and mortality that fit the diagnostic criteria for serotonin syndrome. This is being increasingly recognized in the medical literature. The Poison Information Services in London has also summarized severe complications and fatalities associated with MDMA use, many of which fit the diagnostic criteria for severe serotonin syndrome. Most cases of toxicity appear to be idiosyncratic and are not associated with massive overdose. Since MDMA has only about one tenth the stimulant effect of amphetamine on the central nervous system, excessive sympathetic stimulation by MDMA seems unlikely in these cases.

"Saturday Night Fever": Ecstasy related problems in a London Accident and Emergency Department, Williams H., et al., J. Accid. Emerg Med 1998, 15:332, 322-326.

Forty eight consecutive MDMA related cases were identified. All were in the 15-30 year age group with the majority presenting in the early hours at weekends and having consumed the drug MDMA at a nightclub. The mean number of tablets consumed was two and almost 40% had taken MDMA before. Poly drug use was common with half of the samples having concurrently taken another illicit substance - most commonly other stimulants (amphetamines and cocaine). A wide range of adverse clinical features was found. The most common symptoms were vague and nonspecific such as feeling strange or unwell, however many patients had collapsed or lost consciousness. The most common signs elicited were related to sympathetic over activity, agitation/disturbed behavior, and increased temperature. The more serious complications of delirium, seizures, and profound unconsciousness (coma) were commoner when MDMA was used in combination with other substances. In a review of 48 cases, in 33% of the cases, MDMA was the only substance used. In nearly 17% of the cases alcohol was also consumed; while, other illicit drugs were used with MDMA in 31% of the cases (12 instances amphetamine, 2 instances cocaine, 3 instances LSD, 5 instances THC, two instances GHB, and 2 instances of other illicit drugs). A combination of MDMA, alcohol, and another drug were reported in nearly 19% of the cases. Another illicit substance was therefore used in combination with MDMA in half the 48 episodes reviewed. Of those case in which the patient used MDMA alone, 81% had high pulse rates, 43% felt unwell, dizzy, weak, or strange; between 30-40% reported one or more of the following - loss of consciousness or collapse, nausea or vomiting, panic, anxiety, restlessness, palpitations dilated pupils, hyperventilation, high blood pressure. Between 10-25% of the individuals reported thirst, visual disturbances, abdominal pain, difficulty breathing, headache, shaking sweating, feeling hot/cold, hypothermia, hallucinating, or other complaints. Similar but slightly higher percentages were recorded in those who were polydrug abusers - used MDMA in addition to another drug.

Pathology of Deaths Associated with "Ecstasy" and "Eve" Misuse, Milroy CM., et al., Fr.Jor.Path., 1996, 49, pg 149-153.

The postmortum findings in deaths associated with MDMA and MDEA were studied in seven young while men aged between 20-25 years of age. Sticking changes were identified in the liver, which varied from foci of individual cell necrosis to centrilobular necrosis. In one case, there was massive hepatic necrosis. Changes consistent with catecholamine induced myocardial damage were seen in five cases. In the brain, perivascular haemorrhagic and hypoxic changes were identified in four cases. Overall, the changes in four cases were the same as those reported in heat stroke, although only two cases had a documented history of hyperthermia. Of these four cases, all had changes in their liver, three had changes in their brains, and three in their heart. Of the other three cases, one man died of fulminant liver failure, one of water intoxication and one probably from a cardiac arrhythmia associated with myocardial fibrosis. These data suggest that there is more than one mechanism of damage in ring substitute amphetamine misuse, injury being caused by hyperthermia in some cases, but with ring substituted amphetamines also possibly having a toxic effect on the liver and other organs in the absence of hyperthermia.

Toxicity and Deaths from 3,4-methylenedioxymethamphetamine (Ecstasy), Henry JA., et al., Lancet, 15 Aug 1992, 340, pg 384-387.

The risk of adverse reactions to MDMA is now widely know in both the US and UK, but the patterns of illness remain varied. The article relates experiences encountered during 1990 and 1991, during which time there were an increase in cases of severe toxicity following the ingestion of small quantities of MDMA. Among 7 fatalities, the pattern of toxicity included fulminant hypothermia, convulsions, disseminated intravascular coagulation, rhabdomyolysis, and acute renal failure. In addition, 7 cases of hepatotoxicity were monitored and suspect that the frequency of this complication is increasing. Also described were 5 subjects involved in road traffic accidents in whom MDMA was identified. The article

detailed the level of MDMA and other drugs encountered along with information on circumstances surrounding the ingestion, clinical course of events and outcomes - half of which were fatal.