

independent methods of linkage analysis may in the first instance give more accessible results than lod-score estimations.

Respiratory atopy is a disease in which the sex of the affected parent alters the risk of disease in offspring. Diseases in which imprinting takes place can be interpreted to show dominant, recessive, or polygenic inheritance, depending on the pedigrees studied.³⁰ All these patterns of inheritance have been attributed to atopy.⁴⁻⁸ Our results emphasise that when the genetics of a trait are perceived to be complex, unusual patterns of inheritance need to be considered as a cause of the complexity.

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REFERENCES

- Ishizaka K, Ishizaka T, Hombrook MM. Physico-chemical properties of reaginic antibody. IV. Presence of a unique immunoglobulin as a carrier of reaginic antibody. *J Immunol* 1966; 97: 75-85.
- Burrows B, Martinez FD, Halonen M, Barbee RA, Cline MG. Association of asthma with serum IgE levels and skin-test reactivity to allergens. *N Engl J Med* 1989; 320: 271-77.
- Bazara M, Orgel Ha, Hamburger RN. Genetics of IgE and allergy: serum IgE levels in twins. *J Allergy Clin Immunol* 1974; 54: 288-304.
- Hanson B, Kronenberg R, Johnson B, Blumenthal M. Pulmonary function, serum IgE levels and specific IgE responses in monozygotic twins reared apart. *J Allergy Clin Immunol* 1985; 75: 155.
- Marsh DG, Meyers DA, Bias WB. The epidemiology and genetics of atopic allergy. *N Engl J Med* 1981; 305: 1551-59.
- Blumenthal MN, Nambordin K, Mendell N, Gleich G, Elston RC, Yunis E. Genetic transmission of serum IgE levels. *Am J Med Genet* 1981; 10: 219.
- Boreki I, Rao DC, Lalouel JM, McGue M, Gerrard JW. Demonstration of a common major gene with pleiotropic effects on immunoglobulin E and allergy. *Genet Epidemiol* 1985; 2: 327-28.
- Cookson WOCM, Hopkin JM. Dominant inheritance of atopic immunoglobulin-E responsiveness. *Lancet* 1988; i: 86-88.
- Cookson WOCM, Sharp PA, Faux JA, Hopkin JM. Linkage between immunoglobulin E responses underlying asthma and rhinitis and chromosome 11q. *Lancet* 1989; i: 1292-95.
- Young RP, Sharp PA, Lynch JR, et al. Confirmation of genetic linkage between atopic IgE responses and chromosome 11q13. *J Med Genet* 1992; 29: 236-38.
- Shirakawa T, Morimoto K, Hashimoto T, et al. Linkage between atopic IgE responses and chromosome 11q in Japanese families. *Cytogenet Cell Genet* 1991; 58: 1970.
- Julier C, Nakamura Y, Lathrop M, et al. A detailed genetic map of the long arm of chromosome 11. *Genomics* 1990; 7: 335-45.
- Magnusson CG. Cord serum IgE in relation to family history and as predictor of atopic disease in early infancy. *Allergy* 1988; 43: 241-51.
- Ruiz RGG, Price JF, Richards D, Kemeny DM. Influence of parental atopic status on atopic disease in infancy. *Schweiz Med Wschr* 1991; 121 (suppl 40/1): 129.
- Happle R, Schnyder UW. Evidence for the Carter effect in atopy. *Int Arch Allergy Appl Immunol* 1982; 68: 90-92.
- Shirakawa T, Morimoto K, Sasaki S, et al. Prevention and prediction of allergy: maternal lifestyle effect on cord blood IgE. *Am J Epidemiol* (in press).
- Peat JK, Britton WJ, Salome CM, Woolcock AJ. Bronchial hyperresponsiveness in two populations of Australian school children III: effect of exposure to environmental allergens. *Clin Allergy* 1987; 17: 271-81.
- Cline MG, Burrows BB. Distribution of allergy in a population sample residing in Tucson, Arizona. *Thorax* 1989; 44: 425-31.
- Holford-Strevens V, Wanen P, Wong C, Manfreda J. Serum total immunoglobulin E levels in Canadian adults. *J Allergy Clin Immunol* 1984; 73: 516-22.
- Kjellman N-IM, Johansson SJO, Roth A. Serum IgE levels in healthy children quantified by a sandwich technique (PRIST). *Clin Allergy* 1976; 6: 51-59.
- Tokino T, Takahashi E, Mori M, et al. Isolation and mapping of 62 new RFLP markers on human chromosome 11. *Am J Hum Genet* 1991; 48: 258-68.
- Waye JS, Grieg GM, Willard HF. Detection of novel centromeric polymorphisms associated with alpha satellite DNA from human chromosome 11. *Hum Genet* 1987; 77: 151-56.
- Blackwelder WC, Elston RC. A comparison of sib-pair linkage tests for disease susceptibility loci. *Genet Epidemiol* 1985; 2: 85-97.
- Holt PG, McMennamin C, Nelson D. Primary sensitisation to inhalant allergens during infancy. *Pediatr Allergy Immunol* 1990; 1: 3-15.
- Jarrett EEE, Hall E. IgE suppression by maternal IgE. *Immunology* 1983; 48: 49-58.
- Seripane RA, Chafee FH, Seripane GA. Pollen immunotherapy during pregnancy: long-term follow-up of offspring. *Allergy Proc* 1989; 9: 555-61.
- Cattenach BM, Kirk M. Differential activity of maternally and paternally derived chromosome regions in mice. *nature* 1985; 315: 496-98.
- Heutnik P, van der May AGL, Sandkuijl A, et al. A gene subject to genomic imprinting and responsible for hereditary paragangliomas maps to chromosome 11q23-qter. *Hum Mol Genet* 1992; 1: 7-10.
- Solter D. Differential imprinting and expression of maternal and paternal genomes. *Annu Rev Genet* 1988; 22: 127-46.
- Hall JG. Genomic imprinting. *Arch Dis Childhood* 1990; 65: 1013-16.

Toxicity and deaths from 3,4-methylenedioxymethamphetamine ("ecstasy")

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The risk of adverse reactions to 3,4-methylenedioxymethamphetamine (MDMA), more commonly known as "ecstasy", is now widely known in both the USA and UK, but the patterns of illness remain varied. We report our experience during 1990 and 1991.

There has been a recent increase in cases of severe toxicity following recreational misuse of small amounts of MDMA. Among 7 fatalities, the pattern of toxicity included fulminant hyperthermia, convulsions, disseminated intravascular coagulation, rhabdomyolysis, and acute renal failure. Until now, there have been few reports of this type of toxicity from MDMA, which may be related both to the potential of the drug to alter thermoregulation and to the circumstances of misuse. In addition, we

have monitored 7 cases of hepatotoxicity and suspect that the frequency of this complication is increasing; a history of MDMA misuse should be sought in young people presenting with unexplained jaundice or hepatomegaly. We also describe 5 subjects involved in road traffic accidents in whom MDMA was identified.

Misuse of MDMA can have severe acute toxic effects; few data are available concerning long-term morbidity, and this deserves close monitoring in future.

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Introduction

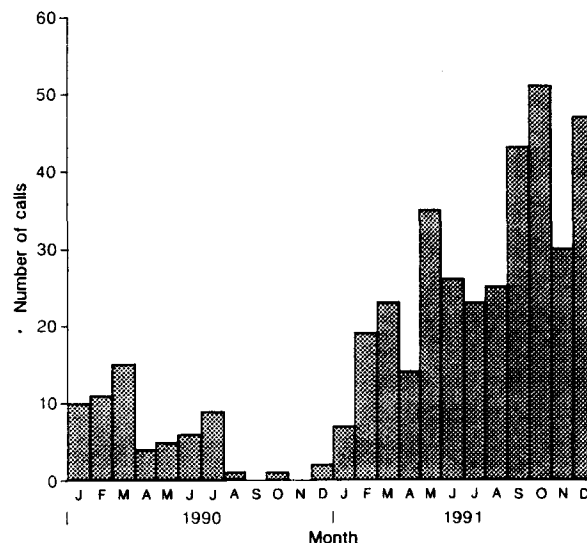
3,4-methylenedioxymethamphetamine (MDMA), commonly known as "ecstasy" or "E", was patented in 1914 as an appetite suppressant, and has been investigated as a mood-modifying drug. Its clinical use was banned in the USA in 1985 because of its neurotoxicity and its potential for misuse. In the UK, MDMA has been listed since 1977 as a class A drug under the Misuse of Drugs Act, 1971. Although misuse of MDMA in the USA has caused deaths, mainly from cardiac arrhythmias,^{1,2} there have been several cases of severe toxicity in the UK with a different clinical pattern. We report our experience.

Methods

All enquiries to the National Poisons Information Service (NPIS) in London about suspected use of "ecstasy" or MDMA were recorded and collated from January, 1990, to December, 1991. Clinical details and outcome of each case were requested from the hospital concerned and, where appropriate, from the pathologist or coroner. During the same interval, National Poisons Unit laboratory records were searched for results of samples submitted in which "ecstasy" was either mentioned or detected.

Results

There were few enquiries to the NPIS until the second half of 1991 when a striking increase in calls was noted (figure). Laboratory detection of MDMA and 3,4-methylenedioxyamphetamine (MDA) increased similarly, but MDMA was more commonly found. Although what was being sold as "ecstasy" usually contained MDMA, other substances, such as MDA or amphetamine, were also identified; mixtures were uncommon. Cases resulting in death, with analytical confirmation of MDMA ingestion, are shown in table I, and severely symptomatic cases are described in table II. Case histories already published are referenced; analytical confirmation was done in our laboratory unless otherwise stated. Since MDA is a metabolite of MDMA, coingestion of MDA with MDMA cannot be excluded by analysis of biological samples. Although the doses involved were difficult to establish with certainty, it seems that in most cases only a few tablets or



Enquiries to the National Poisons Information Service (London) about MDMA or "ecstasy".

capsules were consumed; the pattern of toxicity did not seem to be a result of overdose. One analytically documented overdose of a large amount of MDMA (allegedly 42 tablets taken at home; plasma MDMA 7.72 mg/l) was accompanied by no symptoms other than a "hangover", with tachycardia and hypertension. We have also received samples from the scene of four road traffic accidents in which MDMA was detected in samples from 5 victims (table III). The frequency of hepatotoxicity has also been monitored. Details of 7 cases are given in table IV. Liver biopsy specimens from 2 patients showed eosinophilic infiltration.

Discussion

Reports on MDMA from the USA suggest that the drug is only mildly toxic despite widespread recreational misuse.³ The main cause of severe toxicity and death is cardiac arrhythmias; rhabdomyolysis and disseminated

TABLE I—FATAL CASES OF MDMA TOXICITY

Case	Age and sex	Circumstances and amount	Clinical course	Analytical amounts (mg/l plasma)	Outcome
1	18 M	3 tablets ingested in club; collapsed, left unconscious on floor for 60 min then transferred to hospital	Cyanosed; fixed dilated pupils; temp 41.8°C; pulse 160 bpm; BP 70/60; arrhythmias and asystole	MDMA 0.36	Died 2.5 h after admission
2	17 M	2 tablets taken at party; found unconscious outside	Comatose, hypertonic, seizures; temp 41°C; tachycardia, hypertension; DIC	MDMA detected	Died 14 h after ingestion (11 h after admission)
3	18 M	5 tablets taken at party, became rigid and shaking; ejected, found collapsed	Temp 42.1°C within 4.5 h of ingestion; normotensive on admission; gastrointestinal haemorrhage	MDMA detected in blood and urine	Died 15.5 h after ingestion (11 h after admission)
4*	16 F	1 tablet taken at club; seizure	Hallucinating; temp 40°C; pulse 190 bpm; BP 80/50; DIC; metabolic acidosis	MDMA 0.424	Died 36 h after admission
5	21 F	Took tablets at party; hyperactivity, progressing to convulsions	Repeated seizures; temp 41°C; pulse 170 bpm; BP 170/100; DIC; rhabdomyolysis, ARF	MDMA 0.11	Liver transplant after 4 days; death from graft rejection after 18 days
6	20 M	Found collapsed in street after party; haemophilic	Seizures; increased muscle tone; temp 40°C; pulse 125 bpm; BP 81/40; DIC; rhabdomyolysis, ARF	MDMA 1.16; MDA 0.06; Amph 0.10	Died 60 h after admission
7*	18 M	Took 3 tablets at pop concert; collapsed	Seizures; sweating; temp 43°C; pulse 180 bpm, hypotension, DIC, rhabdomyolysis, ARF	MDMA 1.26	Died 6.5 h after admission

Analysis of samples was done in other laboratories in cases 1–4. Apart from a low concentration of amphetamine in case 5, ethanol or other drugs were not detected in any of the cases.

Temp, temperature; BP, blood pressure, mmHg; ARF, acute renal failure; bpm, beats per min; amph, amphetamine.

TABLE II—SEVERE COMPLICATIONS FROM MDMA INGESTION

Case	Age and sex	Circumstances and amount	Clinical course	Analytical amounts (mg/l plasma)	Outcome
1 ¹⁸	23 M	Took 3 tablets of "ecstasy" at club; convulsion; admitted to hospital 6 h after ingestion	Agitated, mydriasis, tachypnoea; pulse 120 bpm; BP 120/60; axillary temp 40°C; DIC; rhabdomyolysis, ARF	MDMA 0.2; Amph 0.1	Given veno-venous haemofiltration for 20 days; in hospital for 33 days
2	1 M	Accidental ingestion of 1 tablet of "ecstasy"; admitted to hospital after 30 min	Agitation, twitching, mydriasis; temp 38.5°C; pulse 70–170 bpm; BP 180/70; convulsions for 30 min	MDMA 0.7	Symptomatic treatment; symptom-free by 6 h after ingestion
3	19 F	Took 2 "amphetamine" tablets at club	Vomiting and watery diarrhoea after 2 h; comatose; temp 39.7°C; pulse 150 bpm; thrombocytopenia; raised aspartate transaminase	MDMA 0.97; MDA 0.05	Given forced diuresis and chlorpromazine; recovered
4	20 M	Took 3 capsules of "ecstasy" at club	Pulse 210 bpm; BP 210/70; agitated, sweating; temp 40°C; abnormal liver function tests; DIC; rhabdomyolysis, ARF	MDMA 0.24; MDA 0.02; Amph 0.02; MDEA detected in urine	Did not require haemodialysis; in hospital for 21 days
5	25 F	Took 2.5 "ecstasy" tablets over 4.5 h at home	Severe occipital headache 1 h after last tablet; BP 120/60 on presentation 5.5 h later; subarachnoid haemorrhage confirmed by computed tomographic (CT) scan	MDMA 0.21	Neurosurgery; full recovery

MDEA, methylenedioxyethylamphetamine; CT, computed tomography.

intravascular coagulation (DIC) may also take place,⁴ with 2 such fatalities reported in the UK.^{5,6}

Most cases about which we were consulted had mild symptoms, and the general pattern on presentation was that of agitation, tachycardia, hypertension, widely dilated pupils, trismus, and sweating. There was a clear pattern of toxicity in the most severe cases, which were characterised by hyperthermia, DIC, rhabdomyolysis, and acute renal failure. Death was probably due to heatstroke, in which severe hyperthermia was accompanied by DIC. This pattern of toxicity may occasionally result from amphetamine sulphate⁷ overdose, but a similar pattern with MDMA has only recently been seen in the UK; the reason for its emergence is not clear.

There is no evidence that an impurity or variation in manufacture is responsible, and we suggest that the mechanism may involve a combination of direct effects of the drug and the circumstances associated with ingestion. MDMA can cause hyperthermia in laboratory animals,⁸ which is more pronounced at high ambient temperatures.⁹ Most of the serious cases and all of the fatal cases that we have encountered were among people at crowded parties or clubs where "ecstasy" is taken as a mood enhancer and as a "dance drug". At such venues, sustained physical activity (which may itself be an effect of the drug), a high ambient

temperature, and inadequate fluid replacement could all reduce heat loss and potentiate a direct effect of the drug on thermoregulatory mechanisms, thereby leading to fulminant hyperthermia. Because of this pattern, we suggest early management with intravenous fluids and intravenous dantrolene. However, our fatal cases already had established heatstroke when first seen. Those who develop severe toxicity might also have a metabolic myopathy, as do some of those with exertional heatstroke.¹⁰

There have been no previous reports of hepatotoxicity as a complication of MDMA misuse. The 7 cases that we have reported were associated with ingestion of "ecstasy". None had a history of heavy alcohol or intravenous drug misuse, and none had evidence of infectious hepatitis. Hyperthermic liver toxicity can be excluded. Analytical confirmation of MDMA was not possible as misuse had ceased. An idiosyncratic toxic hepatitis might be responsible; whether these cases are due to MDMA or a metabolite, a contaminant in MDMA manufacture, or to an additive in tablet or capsule formulation, is not yet clear. However, hepatotoxicity seems to be increasing in frequency, and may be related to repeated exposure to MDMA as the number of long-term users increases. We suggest that a history of "ecstasy" misuse should be obtained in young people presenting with unexplained jaundice or hepatomegaly.

TABLE III—ROAD TRAFFIC ACCIDENT VICTIMS IN WHOM MDMA WAS IDENTIFIED

Case	Age and sex	Circumstances and amount	Clinical course	Analytical amounts (mg/l plasma)	Outcome
1	21 M	Driver of car in head-on collision	Multiple fractures	MDMA 0.1	Death
2	23 M	Passenger of same car as case 1	Multiple skull fractures	MDMA 0.13	Death
3	21 M	Involved in accident after taking "ecstasy" and alcohol	Superficial chest injuries	MDMA 0.05	Self-discharge from accident department
4	23 F	History of accident, but not witnessed; denied drug use	Superficial lacerations; drowsy	MDMA 0.34; MDA 0.03; Amph 0.02; ephedrine and triprolidine in urine	Full recovery
5	18 M	Pedestrian hit by car whilst staggering across road (amyl nitrite bottle found in pocket)	Aggressive, agitated; temp 38°C; left extensor plantar reflex, nystagmus, left cerebellar signs, normal CT scan, blood in CSF	MDMA 0.15; MDA 0.02; Amph and ephedrine in urine	Discharged after 11 days with minor residual deficit

Ethanol was not detected in any case; CSF, cerebrospinal fluid.

TABLE IV—MDMA HEPATOTOXICITY

Case	Age and sex	Dose and duration of MDMA ingestion and other drug use	Clinical presentation	Hepatitis antigens	Progress and outcome
1	29 M	Took MDMA on 7 occasions. Also user of psilocybe, cocaine, and cannabis	Cholestatic jaundice, peripheral oedema, ascites	HA total Ag + HA IgM – HBsAg – HBsAb + weak HCAb – HA IgM – HBsAg –	Slow recovery (over 3 months)
2	19 M	Admitted to taking one MDMA tablet 3 weeks previously	2 week history of flu-like diarrhoeal illness with jaundice. AST 1509 IU/l, GGT 103 IU/l, bilirubin 170 mmol/l, AP 369 IU/l	HA IgM – HBsAg – HCAb – HA IgM – HBsAg –	Slow recovery. At 2 weeks, AST 350 IU/l, GGT 68 IU/l, bilirubin 91 mmol/l, AP 220 IU/l
3	19 M	History of MDMA misuse. No history of other drug intake	1 week after last dose of MDMA, increasing jaundice, vomiting, confusion. Bilirubin 400 mmol/l	HA IgM – HBsAg – HCAb – HA IgM – HBsAg – HCAb –	Fulminant hepatic failure, required liver transplant. Successful
4	27 F	MDMA taken on 3 occasions. No IV drug misuse for over 5 years	3 severe episodes of relapsing hepatitis, each following MDMA. Bilirubin 400 mmol/l	HA IgM – HBsAg – HCAb – HA IgM – HBsAg –	Full recovery
5	20 M	Regular MDMA use for 3 months until 2 weeks before admission, plus LSD and cannabis for 2 years	Jaundice, bilirubin 530 mmol/l, AST 2600 IU/l. Encephalopathy, coagulopathy, ARDS	HA IgM – HBsAg – HCAb – HA IgM – HBsAg –	Death
6	20 M	Regular weekly use of MDMA for 10 months	Jaundice, tender hepatomegaly. Bilirubin 40 mmol/l	HA IgM – HBsAg – HCAb – HA IgM – HBsAg –	Resolution
7	19 M	History of escalating doses over 3 months to 4 tablets weekly	Pruritus, jaundice. AST 659 IU/l, AP 276 IU/l, bilirubin 181 mmol/l	HA IgM – HBsAg – HCAb – HA IgM – HBsAg –	Slow resolution

There was no history of regular alcohol or intravenous drug use, and there was no evidence of paracetamol overdose. Case 1 had taken cocaine occasionally.

AP, alkaline phosphatase; ARDS, adult respiratory distress syndrome; AST, aspartate transaminase; GGT, γ -glutamyl transferase; IV, intravenous; HA, hepatitis A; HBsAg, hepatitis B surface antigen; HBsAb, hepatitis B surface antibody; HCAb, hepatitis C antibody.

The recent increase in cases of toxicity due to MDMA and drugs sold as "ecstasy" deserves to be publicised widely for several reasons. First, in a culture in which multi-drug misuse is increasingly accepted, there is a general impression that "recreational" drug use is unlikely to have serious adverse effects. "Ecstasy" is widely misrepresented as being safe. Second, clinicians should be aware of the pattern of toxicity so as to permit correct diagnosis and management. The differential diagnosis of severe hyperthermia should include misuse of MDMA as well as severe infections, stroke, heatstroke, neuroleptic malignant syndrome, malignant hyperthermia, and monoamine oxidase inhibitor overdose, together with the adverse effects of amphetamine, methamphetamine, and cocaine. Third, young people with behavioural disturbances and victims of motor vehicle or other accidents may be under the influence of MDMA. Misuse should be suspected, and analytical confirmation may be needed, when the circumstances suggest that MDMA is involved. Finally, hepatotoxicity should be included as a complication of MDMA misuse, and this may account for unexplained jaundice or hepatomegaly.

We conclude that MDMA is capable of causing severe toxicity, and that its pattern of acute toxicity as seen in this series may be due mainly to the circumstances in which it is misused. Apart from those effects described, experimental data indicate that MDMA is a neurotoxin,^{11,12} and cases have been reported of psychosis,¹³⁻¹⁵ panic,¹⁶ and depression.¹⁷ The frequency and degree of long-term adverse effects on the human brain and mental function remain unknown, but in view of widespread and continuing illegal distribution, both acute and chronic effects of this drug deserve further study. We are establishing a database on adverse effects of recreational drug misuse and we would be pleased to hear of hepatic or other unusual acute or chronic effects related to the ingestion of MDMA.

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REFERENCES

1. Dowling GP, McDonough ET, Bost RO. "Eve" and "Ecstasy". A report on five deaths associated with the use of MDEA and MDMA. *JAMA* 1987; 257: 1615-17.
2. Suarez RV, Reimersma R. "Ecstasy" and sudden cardiac death. *Am J Forensic Med Pathol* 1985; 9: 339-41.
3. Peroutka SJ. Incidence of recreational abuse of 3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy") on an undergraduate campus. *N Engl J Med* 1987; 317: 1542-43.
4. Brown C, Osterloh J. Multiple severe complications from recreational ingestion of MDMA ("Ecstasy"). *JAMA* 1987; 258: 780-81.
5. Chadwick IS, Linsley A, Freemont AJ, Doran B, Curry PD. Ecstasy 3,4-methylenedioxymethamphetamine (MDMA), a fatality associated with coagulopathy and hyperthermia. *J R Soc Med* 1991; 84: 371.
6. Campkin NTA, Davies UM. Another death from Ecstasy. *J R Soc Med* 1992; 85: 61.
7. Ginsberg MD, Herzman M, Schmidt-Nowara W. Amphetamine intoxication with coagulopathy, hyperthermia, and reversible renal failure. *Ann Intern Med* 1970; 73: 81-85.
8. Schmidt CJ, Black CK, Abbate GM, Taylor VL. MDMA-induced hyperthermia and neurotoxicity are independently mediated by 5-HT₂ receptors. *Brain Res* 1990; 529: 85-90.
9. Gordon CJ, Watkinson WP, O'Callaghan JP, Miller DB. Effects of 3,4-methylenedioxymethamphetamine on autonomic thermoregulatory responses of the rat. *Pharmacol Biochem Behav* 1991; 38: 339-44.
10. Hopkins PM, Ellis FR, Halsall PJ. Evidence for related myopathies in exertional heat stroke and malignant hyperthermia. *Lancet* 1991; 338: 1491-92.
11. Ricaurte G, Bryan G, Strauss L, Seiden L, Schuster C. Hallucinogenic amphetamine selectively destroys brain serotonin nerve terminals. *Science* 1985; 229: 986-88.
12. O'Hearn E, Battaglia G, De Souza EB, Kuhar MJ, Molliver ME. Methylenedioxymethamphetamine (MDA) and methylenedioxymethamphetamine (MDMA) cause ablation of serotonergic axon terminals in forebrain: immunocytochemical evidence. *J Neurosci* 1988; 8: 2788-903.
13. McGuire P, Fahy T. Chronic paranoid psychosis after misuse of MDMA ("ecstasy"). *BMJ* 1991; 302: 697.
14. Schifano F. Chronic atypical psychosis associated with MDMA ("ecstasy") abuse. *Lancet* 1991; 338: 1335.
15. Creighton FJ, Black DL, Hyde CE. "Ecstasy" psychosis and flash-backs. *Br J Psychiatry* 1991; 159: 713-15.
16. Whitaker-Azmitia PM, Aronson TA. "Ecstasy" (MDMA)-induced panic. *Am J Psychiatry* 1989; 146: 119.
17. Benazzi F, Mazzoli M. Psychiatric illness associated with "ecstasy". *Lancet* 1991; 338: 1520.
18. Fahal IM, Sallomi DF, Yaqoob M, Bell GM. Acute renal failure after ecstasy. *BMJ* 1992; 305: 29.