The Complications of ‘Ecstasy’ (MDMA)

To the Editor—Dr. Brown and Osterloh, in a recent letter in THE JOURNAL, reported a nearly fatal toxic reaction to 3,4-methylenedioxy-methamphetamine (MDMA). The estimated dose of MDMA administered was 100 to 150 mg and the blood levels, measured at one and two hours after hospital admission, were 6500 and 7000 ng/mL, respectively.

Before MDMA became a Schedule 1 drug on July 1, 1985, it was used in doses of 100 to 150 mg by some psychotomimetics who claimed that it was effective as a psychotomic catalyst and a sensory dissembler; at these doses, no toxic effects were reported. The experiment was performed on March 12, 1985, before the scheduling of MDMA and was carried out by one of us (J.A.) in partial requirement for the degree of Doctor of Philosophy. At that time, we carried out a controlled study of MDMA metabolism and disposition in a single patient. On the basis of that study, we believe that the dose used in the study by Dr. Brown and Osterloh would have had to have been much higher to produce the reported blood levels of MDMA of 6500 to 7000 ng/mL.

Study—A healthy 40-year-old man weighing 74 kg ingested a single 50-mg dose of MDMA. Blood samples were collected one through 24 hours after administration of the dose. Fractional urine samples were collected from zero to 72 hours. The samples were analyzed for MDMA and 3,4-methylenedioxyamphetamine (MDA) by gas chromatography/mass spectrometry. 3,4-Methylenedioxyamphetamine, the N-demethylated biotransformation product of MDMA, was also identified in the plasma and urine samples. Plasma levels and urinary excretion of MDMA and MDA are presented in the Table. In plasma, the MDMA level peaked at 105.6 ng/mL two hours after administration of the dose and declined monotonically to 6.1 ng/mL by 24 hours.

Unchanged level of MDMA was the major urinary excretion product. In 72 hours, a total of 36 mg (72%) of the
50-mg dose was recovered from the urine. The missing 25% of the dose may have been metabolized or excreted in other ways.

**Comment.**—The plasma levels of MDMA of 5600 to 7000 ng/mL reported by Drs. Brown and Osterloh were in the 20 times higher than the peak levels seen in our study and indicate that their patients must have taken a much larger dose than 150 mg, a dose only three times more than that used in our study. It is more likely that the observed severe toxic effects in the report by Drs. Brown and Osterloh represent an expected toxic reaction to an overdose rather than a hypersensitivity reaction to the subcutaneous dose of MDMA.

Since, to our knowledge, ours is the first report on blood levels of MDMA in man in which the dose is known, the blood level of MDMA found by Drs. Brown and Osterloh cannot be compared with any previously reported MDMA blood level reference values.

Recently, MDMA was identified as a neurotoxic substance that selectively destroys serotoninergic nerve terminals in rat brain.[4] The finding in our study that the biotransformation of MDMA in man results in the formation of MDMA should be a warning for the future legal or illicit use of MDMA by man.

Karl Verheyen, MD
New York State Division of Substance Abuse
Brooklyn

Jasen Alzner
Psychiatric Diagnostic Laboratory of America
Southfield, MI

Jeanne H. Jaffe, MD
National Institute on Drug Abuse
Baltimore

**Abstract.**—The plasma levels of MDMA of 5600 to 7000 ng/mL reported by Drs. Brown and Osterloh were in the 20 times higher than the peak levels seen in our study and indicate that their patients must have taken a much larger dose than 150 mg, a dose only three times more than that used in our study. It is more likely that the observed severe toxic effects in the report by Drs. Brown and Osterloh represent an expected toxic reaction to an overdose rather than a hypersensitivity reaction to the subcutaneous dose of MDMA. Since, to our knowledge, ours is the first report on blood levels of MDMA in man in which the dose is known, the blood level of MDMA found by Drs. Brown and Osterloh cannot be compared with any previously reported MDMA blood level reference values.

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**Reply.**—The data of Verheyen et al. are useful in interpreting the plasma concentrations of the MDMA measured in the patient we reported. The dose reported by the patient was certainly underestimated. The ratios of MDMA/MDMA concentrations were never more than 0.02. This also suggests an overdose when compared with the ratios in the data of Verheyen et al.

The major concern of our letter was to reinforce the warning of Dowling et al. that severe consequences have resulted from the use of MDMA. This concern is heightened by a recent report stating that 39% of students at one college campus had tried MDMA and 9% of those had Hallucinogenic-like experiences.[5] The biotransformation of MDMA in man results in the formation of MDMA should be a warning for the future legal or illicit use of MDMA by man.