Fig 2—MR performed the same day demonstrates multiple foci of high signal intensity in the periventricular white matter

small intracranial arteries, with secondary ischemia or infarction, or to focal demyelination.

This case illustrates two important points. First, though it remains uncertain whether the relationship between cocaine use and white-matter disease was more than fortuitous, if in fact cocaine use played a role, I anticipate that the incidence of this complication will increase, especially in view of the growing popularity of crack, the free-based form of cocaine. Second, since it is well documented that magnetic resonance imaging is more sensitive than computed tomography in detecting white-matter disease,[5] magnetic resonance imaging is favored over computed tomography as an imaging modality in cocaine abusers who present with neurological symptoms.

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In Reply.—We would like to thank Drs Levine, Welch, and Brust for raising the interesting possibility of subarachnoid hemorrhage as the etiology for the neurological events that occurred in our patient. Certainly, subarachnoid hemorrhage, arteriovenous malformations, cerebral ischemia, and cerebral vasculitis can all present with similar clinical manifestations.

It is unfortunate that the cerebrospinal fluid obtained from our patient was not examined for xanthochromia because it makes it difficult to know whether the blood in the cerebrospinal fluid was the result of a traumatic spinal tap. We also should note that the left-sided cerebral circulation, as mentioned in our article, was normal. The distal vessels of the right-sided cerebral circulation did not fill with dye.

Although the cerebral angiographic findings in our patient could be the result of vasospasm following a subarachnoid hemorrhage, there are several radiographic features that make this diagnosis less likely. First of all, in patients with subarachnoid hemorrhage when subarachnoid blood is not detected on a computed tomographic scan, severe vasospasm is rarely encountered.[1] Second, at angiography, spastic vessels in patients with subarachnoid hemorrhage are usually smooth in appearance.[2] Third, there are multiple areas of "beading," sequential narrowing, occlusion, and irregularity of the vessels on our patient's angiogram, findings that are much more consistent with vasculitus.[3] Finally, of the 12 reported cases of cocaine-associated subarachnoid hemorrhage that contain details of the radiological studies, seven had either aneurysms or arteriovenous malformations[4] and four had normal findings on angiograms.[1,4] One patient had occlusion of one cerebral artery and narrowing of two cerebral vessels,[4] features that may represent vasospasm. None of these patients had beading, vessel irregularity, or sequential narrowing. Our patient had no evidence of aneurysm or arteriovenous malformation.

Consequently, we believe that the case of cocaine-related stroke that we have described is due to vasculitis, although subarachnoid hemorrhage cannot be entirely eliminated as a cause. We caution clinicians to consider diagnoses other than vasculitis in patients who abuse cocaine and who present with stroke, as one case report does not imply a strong association. Furthermore, treatment of vasculitis is different from the therapy for subarachnoid hemorrhage.

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The Complications of 'Ecstasy' (MDMA)

To the Editor.—Drs Brown and Osterloh,[1] in a recent letter in THE JOURNAL, reported a nearly fatal toxic reaction to 3,4-methylenedioxymethamphetamine (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,[2] it was used in doses of 100 to 150 mg by some psychiatrists who claimed that it was effective as a psychotropic catalyst and a sensory disinhibitor; 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 Physiology.) 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 Drs 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.[3] 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, also was 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 monoexponentially to 5.1 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

Plasma Levels and Urinary Excretion of MDMA and MDA in Man After Administration of a Single 50-mg Oral Dose of MDMA*

Time of Sample, h	Plasma Level, ng/mL		Time of Sample, h	Urinary Excretion, mg	
	MDMA	MDA		MDMA	MDA
1	69.5	12.9	0-2	3.91	.06
2	105.8	14.1	2-4	10.77	.60
4	73.7	20.4	4-6	4.25	.75
6	64.6	16.5	6-8	5.84	.81
8	43.5	9.3	8-12	2.84	.39
12	38.5	2.4	12-16	1.85	.33
16	14.5	0	16-24	1.45	.22
22	11.3	0	24-48	1.35	.42
24	6.1	0	48-72	0.26	.22
Half-life, h	7.6	...	...	...	...
Total excretion (% of dose)	...	...	...	32.62 (65)	3.52 (7)

*MDMA indicates 3,4-methylenedioxymethamphetamine; MDA, 3,4-methylenedioxyamphetamine.

50-mg dose was recovered from the urine. The missing 28% of the dose may have been biotransformed into other metabolites.

Comment.—The plasma levels of MDMA of 6500 to 7000 ng/mL reported by Drs Brown and Osterloh were 60 to 70 times higher than the peak level seen in our study and indicate that their patient 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 then customary doses 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 value.

Recently, MDA was identified as a neurotoxic substance that selectively destroys serotonergic nerve terminals in rat brain.[3,4] The finding in our study that the biotransformation of MDMA in man results in the formation of MDA should be a warning for the future legal or illicit use of MDMA by man.

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In Reply.—The data of Verebey 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 MDA/MDMA concentrations were never more than 0.02. This also suggests an overdose when compared with the ratios in the data of Verebey et al.

The major concern in our letter was to reinforce the warning of Dowling et al[1] that severe consequences have resulted from the use of MDMA. This concern is heightened by (1) a recent report stating that 39% of students at one college campus had tried MDA[2] and (2) the neurotoxic effect of the metabolite MDA cited by Verebey et al.

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When Did Artificial Heart Implants Begin?

To the Editor.—In the article entitled "Artificial Heart Implants Began Five Years Ago," Ms Cowart[1] forgot to mention that the first total artificial heart was implanted in 1969 at Baylor College of Medicine. The first implantable blood pump, a left ventricular assist device (then called a "left ventricular bypass pump"), also was implanted at Baylor College of Medicine six years previously (1963). The latter device has been on display at the Smithsonian Institution since being donated in 1964. This places the use of artificial pumping devices in humans at least four years ahead of the first human heart transplant. It also makes the total artificial heart implant 19 years old rather than five years old, as described in the article.

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1. Cowart VS: Artificial heart implants began five years ago. *JAMA* 1987;258:3085.

In Reply.—Early attempts to devise an artificial heart focused on the device as a bridge to transplantation and not as a permanent replacement. In 1969, Denton Cooley, MD, implanted an artificial heart in a 47-year-old patient who survived for 65 hours.[1] There were critics who said that the heart had been inadequately tested in animals and that the quality of life that the device could provide did not merit trial in a human.[2] In 1981, Cooley attempted a second implant. That patient was maintained for 54 hours before receiving a heart transplant; he died eight days later. In both instances, the question was whether the device was capable of sustaining life so that it could actually be considered an artificial heart. However, interest in developing a total artificial heart seems to date from about 1963[3] and, in that sense, Dr Hall is correct in saying that there is a background prior to the Clark implant of 1982.

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2. *New Options, New Dilemmas: An Interprofessional Approach to Life or Death Decisions.* Lexington, Mass, Lexington Books, 1986, p 63.
3. Jarvik RK: The artificial heart: A study in myopia. *MD*, September 1984, pp 69-74.

CORRECTION

Incorrect Numbers.—Two incorrect numbers appeared in the SPECIAL COMMUNICATION entitled "Generic Drugs and the Prescribing Physician," published in the Sept 4 issue of THE JOURNAL (1987;258:1200-1204). In the second paragraph of the acknowledgment section on page 1204, the correct Government Printing Office order number for *Approved Drug Products With Therapeutic Equivalence Evaluations* is 917 061 00000-6 and the correct telephone number for placing orders is (202) 783-3238.