

increased muscle tension within 15 minutes and was transported to an emergency room. She was described as comatose and tremulous, with decorticate-like posturing and limited response to deep pain. Her pulse was 150 bpm and shallow, her temperature was 100.5 °F, and her blood pressure was 150/100 mm Hg, with a WBC count of 11,000/mm<sup>3</sup>. Blood gas analysis suggested respiratory and metabolic acidosis. Her lithium level was 1.2 meq/liter (about 8 hours after her lithium dose) and her creatine phosphokinase level was 394 U/liter. Other laboratory examinations produced unremarkable findings.

One hour after the ingestion, Ms. A was described as delirious and agitated. Five hours after the ingestion, she became fully alert and her muscle tone returned to normal, as did all other clinical and laboratory measurements. There were no obvious causes of lithium toxicity. She was discharged after a 2-day hospitalization and there were no apparent sequelae. The patient's phenelzine was initially discontinued but subsequently resumed after a relapse. She has been essentially asymptomatic since that time.

The clinical effects of MDMA typically begin within half an hour and last 4–6 hours. While chemically related to amphetamines, MDMA seems to affect serotonin neurons preferentially (3). It is believed that MDMA stimulates the release of serotonin from presynaptic nerve terminals, particularly those arising in the dorsal raphe. It is interesting to speculate that MDMA's effect on serotonin was responsible for the clinical syndrome observed. It is worth noting that lithium potentiates the effects of serotonin; however, the previously reported case of a presumed MAOI-MDMA reaction occurred in a patient who had not been exposed to lithium.

In sum, this is the second case report suggesting a toxic interaction of MDMA with an MAOI. At this point, it is prudent to be alert to the dangers of such an interaction.

#### REFERENCES

1. Sternbach H: The serotonin syndrome. *Am J Psychiatry* 1991; 148:705–713
2. Smilkstein MJ, Smolinske SC, Rumack BH: A case of MAO inhibitor/MDMA interaction: agony after ecstasy. *J Toxicol Clin Toxicol* 1987; 25:149–159
3. Barnes DM: New data intensify the agony over ecstasy. *Science* 1988; 239:864–866

GARY B. KASKEY, M.D.  
*Springfield, Mass.*

#### Bleeding, a Side Effect of Fluoxetine

SIR: The common side effects reported for fluoxetine are agitation, headache, and insomnia. During fluoxetine treatment of a patient, we encountered the hematological side effect of spontaneous bleeding, which caused bruises and menorrhagia. These symptoms improved upon discontinuation of the drug and recurred upon rechallenge, indicating that fluoxetine was related to the side effect. In this case report, we present the clinical picture of this patient.

Ms. A, a 40-year-old woman, manifested insomnia, anxiety, suicidal ideation, and loss of appetite that had lasted for a few months. The findings of pretreatment laboratory tests and a physical examination were normal. The patient enjoyed normal physical health, with no history of family

or personal bleeding disorder. She was prescribed fluoxetine, 20 mg/day, which was increased gradually to 40 and then 60 mg/day. Her response to the treatment was very good, and she resumed her daily activities. By the end of the month after she began taking fluoxetine, she noticed a heavy menstrual flow, which continued for a few days, but she did not consider it to be abnormal. Two months later, she began developing spontaneous ecchymoses; the largest, on her right thigh, was 12–15 cm in length and 3–4 cm in width. A few days later her spleen was palpable, and laboratory tests revealed that her platelet count was 195,000/mm<sup>3</sup>, WBC count was 4200/mm<sup>3</sup>, hemoglobin was 13.3 g/dl, prothrombin time was 12.5 seconds, and partial thromboplastin time was 31.3 seconds. Hence fluoxetine was discontinued. Four days later the ecchymosis was fading and the spleen was no longer palpable. The WBC count was 5,000/mm<sup>3</sup>, hemoglobin was 12.9 g/dl, platelet count was 131,000/mm<sup>3</sup>, and bleeding time was 6.5 minutes. About a month later Ms. A became so depressed that she took one 20-mg capsule of fluoxetine for 3 consecutive days. She again developed extensive ecchymosis from knee to hip, encircling from front to back. She became frightened and discontinued the fluoxetine. All her symptoms resolved again.

Yaryura-Tobias et al. (1) reported eight cases of bleeding after fluoxetine therapy. In our patient recurrence of bruises upon rechallenge with the drug provides substantial proof of a drug-related adverse reaction. One should be aware of the possibility of the occurrence of bleeding with fluoxetine.

#### REFERENCE

1. Yaryura-Tobias JA, Kirschen H, Ninan P, Mosberg HJ: Fluoxetine and bleeding in obsessive-compulsive disorder (letter). *Am J Psychiatry* 1991; 148:949

JAMBUR ARANTH, M.D.  
CAROL LINDBERG, M.D.  
*Torrance, Calif.*

#### Imipramine and Suicidal Thoughts

SIR: A number of case reports have been published associating fluoxetine (1–3) and desipramine (4) with the development of unexpected, possibly ego-dystonic suicidal ideation. In one (4), subsequent use of amoxapine, trazodone, and nortriptyline was associated with the return of suicidal ideation. While the issue is far from decided, especially given Fava and Rosenbaum's retrospective survey (5) that found emergent suicidal ideation not only with fluoxetine (3.5%) but with tricyclic antidepressants in general (specific drugs unspecified) (3%), I present a case of suicidal ideation which developed while a patient was taking imipramine.

Mr. A, a 59-year-old man, had been treated as an outpatient, from early 1986 to the end of 1988, with imipramine in doses of 150–200 mg/day for chronic back pain and depression. He had presented with passive suicidal thoughts ("Why go on?") and had made a self-aborted suicide attempt 16 years previously. His concurrent medications included sulindac, metoprolol, nitroglycerin, and hydrochlorothiazide. He had been treated with 150 mg/day of imipramine, with remission of his depression and better pain control, until the end of 1986, when the dose was in-

creased to 200 mg/day in an attempt to relieve what were felt to be remaining depressive symptoms (e.g., disrupted sleep). His sleep improved and his mood continued to be improved, although 5 months later he reported that he had been forgetting things and having nightmares. A repeat blood level determination at this dose was the same as at the lower dose, 221 µg/liter. He was worried that he would "have to stop the imipramine and get worse."

In December 1988, although he still reported good relief of both his depression and his back pain, Mr. A unexpectedly decided to stop his medication. A review revealed that while taking imipramine, and despite feeling less depressed and calmer, he would have "crazy impulses to walk downstairs and do things." These thoughts were dystonic, and he was fearful enough that he gave his gun collection, stored in his cellar, to a relative to hold for him. These thoughts had begun to occur sometime after the dose of imipramine had been raised to 200 mg/day. Although the thoughts came only occasionally, he decided that he would rather deal with his pain than continue to take the medicine. There were no obvious life stressors at the time, and he was ashamed to tell anyone that he was feeling these things. The dysphoric feelings and dystonic suicidal impulses passed after he stopped taking his medicine. There was no associated akathisia or anxiety and no personality disorder (although there were avoidant and dependent traits).

Other negative consequences of imipramine use, which also remitted when Mr. A stopped the drug, were excessive body movements during sleep (to a point where he once jumped from his bed into a wall and hurt himself), an increase in nightmares, thinking less clearly, and curtailing his driving because he felt slowed up in his responses. He reported some intermittent memory concerns which vacillated with the amount of pain he experienced.

Although case reports have described the association of suicidal impulses with desipramine and fluoxetine, to my knowledge this is the first report of an association with imipramine. While caution has been recommended in associating suicidal ideation with antidepressants, physicians must be alert to the possibility of suicidal impulses emerging as a drug effect not only late in a course of treatment but in the context of a positive response to an antidepressant. We must be reminded that whatever the origin of these impulses, attention to the doctor-patient relationship is essential in encouraging a patient to feel comfortable about reporting them, especially in the context of depression, where the patient is often self-effacing.

#### REFERENCES

1. Teicher MH, Glod C, Cole JO: Emergence of intense suicidal preoccupation during fluoxetine treatment. *Am J Psychiatry* 1990; 147:207-210
2. DasGupta K: Additional cases of suicidal ideation associated with fluoxetine (letter). *Am J Psychiatry* 1990; 147:1570
3. Masand P, Gupta S, Dewan M: Suicidal ideation related to fluoxetine treatment (letter). *N Engl J Med* 1991; 324:420
4. Damluji NF, Ferguson JM: Paradoxical worsening of depressive symptomatology caused by antidepressants. *J Clin Psychopharmacol* 1988; 8:347-349
5. Fava M, Rosenbaum J: Suicidality and fluoxetine: is there a relationship? *J Clin Psychiatry* 1991; 52:108-111

WILLIAM HARDOBY, M.D.  
Syracuse, N.Y.

#### Fluoxetine and Fluvoxamine in PTSD

SIR: The serotonin uptake inhibitors have now become the latest in a long line of medications touted as possibly effective in the treatment of posttraumatic stress disorder (PTSD) (1). Continuing this trend, I wish to report a patient whose PTSD symptoms responded to the serotonin uptake inhibitors fluoxetine and fluvoxamine but not to a wide variety of standard pharmacologic interventions.

Mr. A, a 41-year-old Vietnam veteran with severe PTSD, was seen regularly for supportive group psychotherapy. Despite inpatient treatment on a specialized PTSD unit and multiple trials of neuroleptics, tricyclic antidepressants, and phenelzine, Mr. A's PTSD symptoms gradually worsened after Vietnam. At the time treatment with fluoxetine was initiated, Mr. A's only medication was diazepam, 80 mg/day in divided doses. Fluoxetine was started to help Mr. A with secondary depressive symptoms, which improved somewhat at a dose of 40 mg/day. At a dose of 60 mg/day of fluoxetine, Mr. A noted moderate improvement in his PTSD symptoms, including a decrease in intrusive memories and nightmares (despite no improvement in his sleep pattern), a reduction in overall anxiety, and a lessened need to avoid cues capable of eliciting the symptoms. Unfortunately, Mr. A also developed severe anorexia. After a 30-lb weight loss over 3 months, fluoxetine was discontinued, with the return, over a matter of weeks, of PTSD and, less noticeably, depressive symptoms. A trial of fluvoxamine, 250 mg/day, was then initiated under a compassionate-use protocol for depression. This intervention resulted in a reduction in both PTSD and depressive symptoms similar to that seen with fluoxetine.

The response of this patient to treatment with two structurally different serotonin uptake inhibitors is certainly noteworthy. It is prudent to note, however, that the history of PTSD is replete with anecdotal reports of pharmacologic treatment successes, largely unconfirmed by general clinical experience or controlled trials. My patient also had depressive symptoms, took other medications, was not followed with structured rating scales or rated by blind observers, and received behavior therapy during treatment, thereby limiting the generalizability of the findings.

In any case, the intent of this communication is not to suggest that the serotonin uptake inhibitors will prove to be a panacea for patients with PTSD, particularly since the case for a noradrenergic diathesis in PTSD has been persuasively drawn. On the other hand, the seemingly robust response of PTSD patients to this class of drugs and the phenomenological similarity between PTSD and obsessive-compulsive disorder does suggest that a serotonergic connection might be profitably explored. One prediction from a serotonergic model of PTSD is that drugs useful in the treatment of obsessive-compulsive disorder may also be useful in treating PTSD. Given the marginal performance of antipanic treatments for PTSD (2), properly controlled clinical trials of serotonin reuptake blockers would seem to be in order.

#### REFERENCES

1. Davidson J, Roth S, Newman E: Fluoxetine in post-traumatic stress disorder. *J Traumatic Stress* 1991; 4:419-425
2. Friedman MJ: Toward rational pharmacotherapy for posttraumatic stress disorder: an interim report. *Am J Psychiatry* 1988; 145:281-285

JOHN S. MARCH, M.D., M.P.H.  
Durham, N.C.