Letters to the Editor

Discontinuation Symptoms and SSRIs

Sir: I read with interest the recent supplement[1] to the *Journal* based on the meeting chaired by Dr. Schatzberg and agree that the constellation of symptoms associated with the abrupt discontinuation of selective serotonin reuptake inhibitors (SSRIs) has emerged as a topic of clinical interest. I have difficulty understanding, however, some of the conclusions drawn by the Discontinuation Consensus Panel of authors in this supplement, namely, that "discontinuation reactions are more likely to occur or to become apparent during discontinuation of SRIs [serotonin reuptake inhibitors] that have shorter half-lives than the extended half-life agent fluoxetine" and that symptoms of discontinuation are "minimized by a slow taper or by using a drug that has an extended half-life."[2(p3)]

A relatively large and growing body of anecdotal reports, open-label studies, and retrospective chart reviews describes discontinuation symptoms with the SSRIs. Clearly, each of the SSRIs, including fluoxetine,[3–9] paroxetine,[10–16] sertraline,[13,14,17,18] and fluvoxamine,[19,20] causes discontinuation symptoms. Abrupt discontinuation of SSRIs is characterized by mild and self-resolving symptoms that can include dizziness, nausea, vomiting, diarrhea, nervousness, and rhinitis.

As suggested by Schatzberg,[2] differences in elimination half-lives among the SSRIs do appear to result in distinct temporal profiles of discontinuation symptoms. Published case reports describe discontinuation symptoms for paroxetine and sertraline that generally persist for 1 to 2 weeks after cessation of treatment,[11–18] which is consistent with the approximately 24-hour elimination half-lives of these SSRIs. The longer acting fluoxetine (with an elimination half-life of 4 to 6 days for the parent compound and 4 to 16 days for the pharmacologically active metabolite, norfluoxetine) has been reported to cause discontinuation symptoms beginning up to 25 days after therapy is stopped. The case report literature describes fluoxetine-related discontinuation symptoms persisting for up to 56 days.[3,5,7–9] Thus, the longer elimination half-life of fluoxetine appears to be associated with discontinuation symptoms that occur later and last longer compared with those associated with shorter-acting SSRIs.

The preliminary findings from one direct comparative study of the SSRIs suggest that fluoxetine, unlike paroxetine or sertraline, is not associated with discontinuation symptoms.[4] However, patients in this study were assessed for only 5 to 8 days after stopping therapy, which is generally not a sufficiently long period of time for discontinuation symptoms with fluoxetine to appear. If clinical trials are to accurately study between-agent differences, they must be designed with sufficiently long follow-up to observe discontinuation symptoms that occur after long-acting agents are stopped.

Regardless of the suggestion by Rosenbaum and Zajecka[21] in the supplement that the abrupt discontinuation of SSRIs with longer elimination half-lives results in self-tapering, discontinuation symptoms nevertheless occur. Unlike agents with shorter half-lives, drugs with prolonged elimination half-lives are associated with an extended duration of adverse effects, drug accumulation, complicated titration schedules, and extended fetal exposure for women who conceive during therapy. All SSRIs should be tapered when therapy is stopped unless there is a medical reason for immediate removal of the drug. The time course of adverse effects is prolonged for SSRIs with long elimination half-lives, which, in the case of serious sequelae (e.g., serotonergic syndrome[22] or syndrome of inappropriate antidiuretic hormone secretion[23]) or a frail, elderly patient, represents a real clinical problem.

Each of the SSRIs causes discontinuation symptoms, and the time course of symptoms is directly related to the elimination half-life of the drug and the duration of therapy. The majority of published clinical data on this topic is derived from anecdotal case reports,[24] which generally rely on patients' observations of adverse effects. Clearly, patients are more likely to attribute discontinuation symptoms to a drug when symptoms occur shortly after therapy is stopped (as would occur with a shorter half-life agent) than when symptoms occur 1 week or more after discontinuing treatment (as with an agent with a longer half-life). Thus, the suggestions by some investigators that SSRIs with prolonged elimination half-lives are associated with a minimal rate of discontinuation symptoms[25,26] may be based on data that are spuriously low and not representative of actual prevalence.

The Discontinuation Consensus Panel[27] argues in the supplement that cholinergic rebound is one putative mechanism for discontinuation symptoms, particularly with paroxetine. This theory is based on in vitro findings that, among the SSRIs, paroxetine possesses the highest affinity for muscarinic receptors.[28] However, recent data from our laboratory do not support the extrapolation of these in vitro findings to the clinical setting as was done by the authors of the supplement. We compared serum anticholinergicity and anticholinergic side effects in 54 depressed, elderly patients who were being treated with therapeutic doses of paroxetine or nortriptyline. Under these clinically relevant conditions, paroxetine exhibited an 8-fold lower level of serum anticholinergicity (0.07 ± 0.19 pmol atropine equivalents) than nortriptyline (0.57 ± 0.45; $p = .0004$). In addition, nortriptyline was associated with significantly more dry mouth and tachycardia than paroxetine.[29] Paroxetine has also been shown to be devoid of adverse anticholinergic cardiovascular effects in depressed patients with ischemic heart disease as compared with nortriptyline, which, like other tricyclic antidepressants, has clinically significant cardiac effects in this population.[30] Manufacturers' prescribing information for paroxetine and sertraline describes similar rates of dry mouth for these agents[31,32] despite differences in in vitro affinities for the muscarinic receptor.[28] Thus, although paroxetine is the most anticholinergic SSRI in an in vitro setting, clinical data obtained both under rigorously controlled conditions and from clinical experience do not support the argument made in the supplement.

As stated in the supplement,[1] the available evidence demonstrates that abrupt cessation of SSRI therapy can be associated with a mild, transient constellation of somatic and psychological symptoms. Some of the conclusions drawn by the authors of the supplement warrant a closer look. Clinical experience and published reports demonstrate that, regardless of elimination half-life, all of the SSRIs cause discontinuation symptoms after abrupt withdrawal and all SSRIs should be gradually tapered

when stopping therapy. Should it be needed, management consists of restarting the SSRI and gradually tapering the dose. Alternatively, patients can be educated about the transient nature of these symptoms and encouraged to wait until the symptoms resolve. Rather than directing our efforts toward the relatively infrequent, minor, and transient discontinuation symptoms associated with SSRI therapy, clinicians may be well advised to focus their energies on the greater issues of efficacy, safety, and patient outcome.

References

1. Schatzberg AF, Chair. Antidepressant Discontinuation Syndrome: Update on Serotonin Reuptake Inhibitors. J Clin Psychiatry 1997; 58(suppl 7)
2. Schatzberg AF. Introduction. Antidepressant discontinuation syndrome: an update on serotonin reuptake inhibitors. J Clin Psychiatry 1997;58(suppl 7):3–4
3. Berlin CS. Fluoxetine withdrawal symptoms [letter]. J Clin Psychiatry 1996;57: 93–94
4. Blomgren SL, Krebs W, Wilson M, et al. SSRI dose interruption study: interim data. In: New Research Program and Abstracts of the 150th Annual Meeting of the American Psychiatric Association; May 20, 1997; San Diego, Calif. Abstract NR188:118
5. Einbinder E. Fluoxetine withdrawal? [letter] Am J Psychiatry 1995; 152:1235
6. Kreider MS, Bushnell WD, Oakes R, et al. A double-blind, randomized study to provide safety information on switching fluoxetine-treated patients to paroxetine without an intervening washout period. J Clin Psychiatry 1995;56:142–145
7. Michelson D, Onawola R, Beasley C. Abrupt discontinuation of fluoxetine: a randomized, placebo-controlled study. Presented at 37th annual meeting of the New Clinical Drug Evaluation Unit; May 27–30, 1997; Boca Raton, Fla
8. Michelson D, Onawola R, Beasley C. Abrupt discontinuation of fluoxetine: a randomized, placebo-controlled study. In: New Research Program and Abstracts of the 150th Annual Meeting of the American Psychiatric Association; May 20, 1997; San Diego, Calif. Abstract NR200:122
9. Stoukides JA, Stoukides CA. Extrapyramidal symptoms upon discontinuation of fluoxetine [letter]. Am J Psychiatry 1991;148:1263
10. Barr LC, Goodman WK, Price LH. Physical symptoms associated with paroxetine discontinuation [letter]. Am J Psychiatry 1994; 151:289
11. DeBattista C, Schatzberg AF. Physical symptoms associated with paroxetine withdrawal [letter]. Am J Psychiatry 1995;152:1235–1236
12. Dominguez RA, Goodnick PJ. Adverse events after the abrupt discontinuation of paroxetine. Pharmacotherapy 1995;15:778–780
13. Fava GA, Grandi S. Withdrawal syndromes after paroxetine and sertraline discontinuation [letter]. J Clin Psychopharmacol 1995;15: 374–375
14. Frost L, Lal S. Shock-like sensations after discontinuation of selective serotonin reuptake inhibitors [letter]. Am J Psychiatry 1995;152:810
15. Phillips SD. A possible paroxetine withdrawal syndrome [letter]. Am J Psychiatry 1995;152:645–646
16. Pyke RE. Paroxetine withdrawal syndrome [letter]. Am J Psychiatry 1995;152:149–150
17. Leiter FL, Nierenberg AA, Sanders KM, et al. Discontinuation reactions following sertraline. Biol Psychiatry 1995;38:694–695
18. Louie AK, Lannon RA, Ajari LJ. Withdrawal reaction after sertraline discontinuation [letter]. Am J Psychiatry 1994;151:450–451
19. Black DW, Wesner R, Gabel J. The abrupt discontinuation of fluvoxamine in patients with panic disorder. J Clin Psychiatry 1993;54: 146–149
20. Szabadi E. Fluvoxamine withdrawal syndrome [letter]. Br J Psychiatry 1992;160:283–284
21. Rosenbaum JF, Zajecka J. Clinical management of antidepressant discontinuation. J Clin Psychiatry 1997;58(suppl 7):37–40
22. Sternbach H. The serotonin syndrome. Am J Psychiatry 1991;148: 705–713
23. Druckenbrod R, Mulsant BH. Fluoxetine-induced syndrome of inappropriate antidiuretic hormone secretion: a geriatric case report and a review of the literature. J Geriatr Psychiatry Neurol 1994;7:254–256
24. Zajecka J, Tracy KA, Mitchell S. Discontinuation symptoms after treatment with serotonin reuptake inhibitors: a literature review. J Clin Psychiatry 1997;58:291–297
25. Coupland NJ, Bell CJ, Potokar JP. Serotonin reuptake inhibitor withdrawal. J Clin Psychopharmacol 1996;16:356–362
26. Price JS, Waller PC, Wood SM, et al. A comparison of the post-marketing safety of four selective serotonin re-uptake inhibitors including the investigation of symptoms occurring on withdrawal. Br J Clin Pharmacol 1996;42:757–763
27. Schatzberg AF, Haddad P, Kaplan EM, et al, of The Discontinuation Consensus Panel. Possible biological mechanisms of the serotonin reuptake inhibitor discontinuation syndrome. J Clin Psychiatry 1997; 58(suppl 7):23–27
28. Richelson E. The pharmacology of antidepressants at the synapse: focus on the newer compounds. J Clin Psychiatry 1994;55(9, suppl A):34–41
29. Pollock BG, Mulsant BH, Nebes R, et al. Serum anticholinergicity in older patients treated with paroxetine or nortriptyline. Am J Psychiatry 1998;155:1110–1112
30. Roose S, Laghrissi-Thode F, Kennedy JS, et al. Comparison of paroxetine and nortriptyline in depressed patients with ischemic heart disease. JAMA 1998;279:287–291
31. Paxil [package insert]. Philadelphia, Pa: SmithKline Beecham Pharmaceuticals; 1997
32. Zoloft [package insert]. New York, NY: Pfizer Inc; 1997

Bruce G. Pollock, M.D., Ph.D.
Pittsburgh, Pennsylvania

Dr. Schatzberg Replies

Sir: We appreciate the comments of Dr. Pollock regarding the special supplement on SSRI discontinuation. He notes that fluoxetine can be associated with discontinuation symptoms but that these occur several weeks after discontinuation. We agree that they can occur. However, these rebound symptoms have been less frequently reported with fluoxetine than with almost all the other SSRIs and are rarely a problem. In a 6-week follow-up, double-blind study[1] of discontinuation from fluoxetine, the percentage of patients reporting any adverse events was 30% for patients continuing on fluoxetine and 40% for those switched to placebo. The incidence of dizziness at 6 weeks was 5% for those who discontinued versus 1% for those who switched to placebo. Thus, the problem does appear to be less of an issue with fluoxetine, which has a long half-life, than with other SSRIs.

The apparently higher rates of discontinuation symptoms with the shorter acting agents should not be construed as an indication that we need not be aware of the possibility of such symptoms with longer acting agents. Rather, they are more likely to occur and to be apparent with shorter acting agents where there is less time to achieve homeostasis. Of interest is the recent analysis of the World Health Organization database that noted higher rates of reporting of such symptoms in patients discontinuing from paroxetine and sertraline than in those discontinuing from fluoxetine.[2] Moreover, they noted that fluoxetine was more commonly associated with psychiatric reactions (nervousness, anxiety, depression, etc.) than with CNS manifestations (dizziness, headache, etc.) The opposite was true for paroxetine and sertraline. Thus, they concluded that these data indicated "a possible qualitative difference between the SSRIs with respect to the nature of the withdrawal syndrome."[2(p163)] This study reported mean days off drug to point of symptoms of 9.5, 24, and 6.6 days for paroxetine, fluoxetine, and sertraline, respectively. The respective medians were 2, 3, and 2 days, indicating a skewing of the data and suggesting that some patients may demonstrate earlier discontinua-

tion symptoms with fluoxetine. However, since Stahl et al. also noted that fluoxetine discontinuation was generally associated with psychiatric (rather than CNS) symptoms, the types of symptoms seen within a few days of discontinuation may have also differed among the 3 drugs.

Dr. Pollock argues for tapering all SSRIs. It is not clear whether this is necessary for the very long acting fluoxetine. While one can make this argument, to my knowledge, supporting data are not available, and the recent data from Zajecka et al.[1] suggest that it is not necessary.

Dr. Pollock presents interesting data on the low anticholinergic potential of paroxetine in vivo and in vitro. While the data certainly indicate low potential, they do not rule out a possible contribution of mild anticholinergic effects to discontinuation symptoms. Still, paroxetine's half-life and potency at the serotonin uptake site, we believe, would account for a greater risk of discontinuation symptoms.

Last, one needs to put this whole topic in a realistic clinical perspective. To my eye, the shorter acting and more potent SSRIs are more likely to give patients problems upon abrupt discontinuation. While this requires some vigilance and appropriate tapering, it does not mean that clinicians should avoid using paroxetine or venlafaxine (which have short half-lives) any more than they should avoid using longer acting agents such as fluoxetine. We, as clinicians, need to maintain a proper perspective on the utility, effectiveness, differences, and risks (albeit low) of all of these helpful agents.

References

1. Zajecka J, Fawcett J, Amsterdam J, et al. Safety of abrupt discontinuation of fluoxetine: a randomized, placebo-controlled study. J Clin Psychopharmacol. In press
2. Stahl MMS, Linquist M, Pettersson M, et al. Withdrawal reactions with selective serotonin re-uptake inhibitors as reported to the WHO System. Eur J Clin Pharmacol 1997;53:163–169

Alan F. Schatzberg, M.D.
Stanford, California

Olanzapine and Negative Symptoms

Sir: I am writing after reading the letter by Ketter et al.[1] regarding the efficacy of olanzapine in bipolar disorder patients. A 54-year-old patient of mine diagnosed with schizoaffective disorder, bipolar type and currently enrolled in a University of California-San Diego research study for her condition had a dramatic response to olanzapine, 5 mg/day. The patient had previously been maintained on risperidone, 2 mg/day, and had undergone unsuccessful trials of numerous antidepressants in an attempt to alleviate her negative symptoms. I had come to see the patient as being "chronic," as I have treated her for 3 years without seeing much gain.

Despite the lack of efficacy of the various antidepressants, the change from risperidone, 2 mg/day, to olanzapine, 5 mg/day, resulted in a marked improvement in my patient's negative symptoms. I believe that this improvement was due to a direct antidepressant effect of olanzapine rather than to response in any type of residual paranoia that was not being affected by risperidone. The patient went from being housebound and addicted to watching television to being much more active and socially engaged, taking several classes in her favorite hobby, oil painting and design. This improvement took 4 weeks to fully materialize and has been sustained over 3 months.

In light of the published case reports of bipolar patients treated with olanzapine,[1] I thought readers might be interested in an actual case of negative symptom improvement in a patient with schizoaffective disorder. I was wondering if the authors had seen such dramatic responses in chronic patients themselves.

Reference

1. Ketter TA, Winsberg ME, DeGolia SG, et al. Rapid efficacy of olanzapine augmentation in nonpsychotic bipolar mixed states [letter]. J Clin Psychiatry 1998;59:83–85

Emanuel H. Rosen, M.D.
La Jolla, California

Dr. Ketter and Colleagues Reply

Sir: We appreciate Dr. Rosen's interesting report of the efficacy of olanzapine in relieving chronic negative symptoms resistant to risperidone in a patient with schizoaffective disorder, bipolar type. His letter emphasizes several points that are in agreement with emerging data regarding the clinical utility of olanzapine.

Dr. Rosen's observation that olanzapine may directly relieve negative symptoms (rather than indirectly through relief of psychotic symptoms) agrees with clinical research findings[1] and is consistent with the possibility that olanzapine may also relieve depressive symptoms in schizophrenia and schizoaffective disorders,[2] in mixed[3] and dysphoric manic states,[4] and in nonmixed major depressive states with or without concurrent psychosis.[5,6] In addition, emerging evidence suggests that olanzapine has antimanic affects.[7,8]

The efficacy of olanzapine in Dr. Rosen's patient with risperidone-resistant illness mirrors evidence from other clinicians that this medication may benefit some patients with risperidone-resistant schizophrenia and schizoaffective disorders.[9] In our clinic as well as in several of the above-mentioned reports, some patients with chronic illness have responded to olanzapine. Emerging data from studies and case reports raise the possibility that olanzapine may have both mood-stabilizing and antipsychotic properties, perhaps based on its effects on multiple neurotransmitter systems. Controlled clinical trials appear warranted to aid in further defining the psychotropic profile of this medication.

References

1. Tollefson GD, Sanger TM. Negative symptoms: a path analytic approach to a double-blind, placebo- and haloperidol-controlled clinical trial with olanzapine. Am J Psychiatry 1997;154:466–474
2. Tollefson GD, Sanger TM, Lu Y, et al. Depressive signs and symptoms in schizophrenia: a prospective blinded trial of olanzapine and haloperidol. Arch Gen Psychiatry 1998;55:250–258
3. Ketter TA, Winsberg ME, DeGolia SG, et al. Rapid efficacy of olanzapine augmentation in nonpsychotic bipolar mixed states [letter]. J Clin Psychiatry 1998;59:83–85
4. Sharma V, Pistor L, Kueneman K. Treatment of dysphoric mania with olanzapine. In: New Research Program and Abstracts of the 151st Annual Meeting of the American Psychiatric Association; May 30–June 4, 1998; Toronto, Ontario. Abstract NR670:249
5. Rothschild AJ, Bates KS, Boehringer KL, et al. Olanzapine response in psychotic depression. In: New Research Program and Abstracts of the 151st Annual Meeting of the American Psychiatric Association; May 30–June 4, 1998; Toronto, Ontario. Abstract NR679:251–252
6. Weisler RH, Ahearn EP, Davidson JR, et al. Adjunctive use of olanzapine in mood disorders: five case reports. Ann Clin Psychiatry 1997; 9:259–262

7. Soutullo CA, Sorter MT, Foster KD, et al. Olanzapine in the treatment of adolescent acute mania: preliminary report of seven cases. In: New Research Program and Abstracts of the 151st Annual Meeting of the American Psychiatric Association; May 30–June 4, 1998; Toronto, Ontario. Abstract NR163:11
8. Tohen M, Sanger T, Tollefson GD, et al. Olanzapine versus placebo in the treatment of acute mania. In: Syllabus and Proceedings Summary of the 151st Annual Meeting of the American Psychiatric Association; May 30–June 4, 1998; Toronto, Ontario. No. 53:22–23
9. Karki SD, Bellnier TJ, Burliss H. Evaluation of olanzapine therapy in schizophrenic and schizoaffective patients resistant to risperidone. In: New Research Program and Abstracts of the 151st Annual Meeting of the American Psychiatric Association; May 30–June 4, 1998; Toronto, Ontario. Abstract NR531:210–211

Terence A. Ketter, M.D.
Mirène E. Winsberg, M.D.
Sallie G. DeGolia, M.D.
Magdolna Dunai, M.D.
Debbie L. Tate
Connie M. Strong, M.S.
Stanford, California

Priapism in a Patient Taking Sertraline

Sir: Most discussion of male sexual dysfunction secondary to selective serotonin reuptake inhibitors (SSRIs) centers on decreased function.[1] We report here on a case of priapism in a patient taking sertraline, 200 mg/day.

Case report. Mr. A, a 47-year-old married white man, presented to the emergency room with a 4-day history of intermittent priapism with moderate pain. He reported several brief episodes (usually less than 1 hour) over the previous month for which he had not sought evaluation. Treatment with intracorporeal methoxamine in the emergency room led to temporary detumescence, but erection occurred at home several hours later. Upon a return visit the next day, Mr. A received repeat treatments with methoxamine that were ineffective, a urologist was called for consultation, and Mr. A was admitted.

Mr. A had a history of depression and attention deficit disorder for which he was taking sertraline, 200 mg/day, and dextroamphetamine, 10 mg/day, respectively. He was also taking lisinopril, 20 mg/day, and ketoprofen, 200 mg/day, for hypertension and arthritis. He had no other known medical problems or history of trauma, and he denied use of illicit drugs or excess alcohol. Laboratory studies revealed a complete blood cell count, electrolyte and creatinine levels, and urinalysis results within normal limits.

Both dilute epinephrine injected in the corpora cavernosa and Winter's shunt procedure yielded incomplete detumescence. The aspirated blood was noted to be dark and oily, consistent with low-flow priapism. Mr. A was advised to wait for spontaneous resolution and that he would most likely experience impotence. Follow-up several weeks later revealed that the priapism had fully resolved and that Mr. A was not impotent. After resolution, he had been started on nefazodone treatment with no further abnormal erectile function.

In patients treated with antidepressants, priapism has most often been recognized as a side effect of trazodone, with postmarketing reports suggesting an estimated incidence of 1 in 1000 to 1 in 10,000 cases.[2,3] It is thought to result from α_1-adrenergic blockade, which causes increased parasympathetic tone relative to sympathetic tone, resulting in obstruction of venous drainage from the corpora cavernosa through smooth muscle relaxation.[2] The incidence appears to be unrelated to age, but priapism is more likely to occur at lower doses and early in treatment than otherwise.[2,3]

Among the SSRIs (fluoxetine, fluvoxamine, paroxetine, and sertraline), no cases of priapism have been reported in clinical trials. A review of the United States literature identified only 1 report of priapism in a patient taking sertraline[4] and 2 reports in patients taking paroxetine.[5,6] The largest number of cases is found in voluntary reports received by the Adverse Events Reporting System (AERS) in the Center for Drug Evaluation of the Food and Drug Administration. As of December 1997, there had been reports of priapism in 46 patients taking sertraline, 24 taking paroxetine, 4 taking fluvoxamine, and 51 taking fluoxetine.[7] Compared with the total number of reports of any adverse event, these figures yield rates of 0.46%, 0.34%, 0.24%, and < 0.12%, respectively. These cases indicate only an association with the drug, not necessarily causality.

Because no reports have been made of associated priapism during premarketing or postmarketing or in the literature for the other medications this patient was taking, it seems most likely that sertraline was the cause of the priapism. If α_1 blockade is indeed the mechanism of action, then among the SSRIs sertraline might be most likely to cause priapism, since the α_1 blocking ability of sertraline is nearly 10-fold that of paroxetine, 16-fold that of fluoxetine, and 21-fold that of fluvoxamine.[8] Murray and Hooberman[9] have suggested a different mechanism, namely through 5-HT_{1B} agonist and reuptake blockade activity. Mulhall and Honig[10] note that reuptake inhibition at the peripheral 5-HT_{1C} receptor could also facilitate erection. To our knowledge, comparative data are not available for the SSRIs on these measures.

The mechanism for low-flow priapism remains a mystery in some cases. Impotence as a sequela is reported at 35% for those with 5 days of priapism to 60% for those with 10 days.[10] Studies of nocturnal tumescence with sertraline might be helpful in further delineating the risk. In the meantime, prescribers should be aware that not all sexual dysfunction with SSRIs is in the form of diminished activity. We must take a careful history of sexual side effects throughout treatment.

References

1. Gitlin MJ. Psychotropic medications and their effects on sexual function: diagnosis, biology, and treatment approaches. J Clin Psychiatry 1994;55:406–413
2. Thompson JW Jr, Ware MR, Blashfield RK. Psychotropic medication and priapism: a comprehensive review. J Clin Psychiatry 1990;51: 430–433
3. Warner MD, Peabody CA, Whiteford HA, et al. Trazodone and priapism. J Clin Psychiatry 1987;48:244–245
4. Mendelson WB, Franko T. Priapism with sertraline and lithium. J Clin Psychopharmacol 1994;14:434–435
5. Ahmad S. Paroxetine-induced priapism [letter]. Arch Intern Med 1995;155:645
6. Bertholon F, Krajewski Y, el Allali A. Effet detonant: prapisme sous paroxetine. Ann Med Psychol 1996;154:145–146
7. Adverse Events Reporting System (AERS) [database online]. Rockville, Md: US Public Health Service, Food and Drug Administration, Center for Drug Evaluation; December 1997
8. Richelson E. Synaptic effects of antidepressants. J Clin Psychopharmacol 1996;16 (suppl 2):1S–9S
9. Murray MJ, Hooberman D. Fluoxetine and prolonged erection. Am J Psychiatry 1993;150:167–168
10. Mulhall JP, Honig SC. Priapism: etiology and management. Academic Emerg Med 1996;3:810–816

Elizabeth H. Rand, M.D.
Tuscaloosa, Alabama