

Antidepressant Discontinuation: A Review of the Literature

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Sudden or tapered withdrawal from treatment with antidepressants, including monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), and serotonin selective reuptake inhibitors (SSRIs), can produce phenomena consisting of somatic and psychological symptoms. The literature about these discontinuation phenomena consists mainly of case reports and a limited number of controlled prospective studies. The symptoms are generally mild and transient for the TCAs and the SSRIs but may be serious for the MAOIs. They are much more common with a shorter acting SSRI, such as paroxetine, than with the longer acting agent fluoxetine. Because the symptoms of antidepressant discontinuation include changes in mood, affect, appetite, and sleep, they are sometimes mistaken for signs of a relapse into depression. Thus, it is important to directly question patients about new symptoms that occur during antidepressant discontinuation to optimally manage treatment discontinuation.

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For more than 25 years, physicians have known that abrupt or tapered withdrawal from antidepressants can produce discontinuation phenomena consisting of somatic and psychological symptoms. Flu-like symptoms; gastrointestinal distress, including nausea and vomiting; arrhythmias; anxiety; sleep disturbances; movement disorders; mania or hypomania; panic attacks; and delirium have all been reported after antidepressant withdrawal. The symptoms produced by the withdrawal of tricyclic antidepressants (TCAs) and serotonin selective reuptake inhibitors (SSRIs) are generally mild and transient but can be troubling, resulting in decreased productivity and missed work.

In addition, discontinuation symptoms may include changes in mood, affect, appetite, and sleep, which may be incorrectly interpreted as symptoms of a relapse into depression. Patients who are classified as having a relapse while they are discontinuing therapy may, in fact, be suffering from unrecognized discontinuation symptoms.

The literature about antidepressant discontinuation phenomena primarily comprises anecdotal case reports and a few controlled studies. These reports illustrate the importance of directly questioning patients about new symptoms that may emerge during discontinuation. This systematic inquiry will allow both psychiatrists and primary care physicians to reliably document withdrawal

symptoms and to optimally manage treatment discontinuation.

DISCONTINUATION SYNDROME

Malcolm Lader in 1983¹ defined a discontinuation syndrome as having a "predictable onset, duration, and offset of action containing psychological and bodily symptoms not previously complained of by the patient." The symptoms are unrelated to relapse or recurrence, and proper diagnosis requires quantitative assessment of symptoms before treatment and during antidepressant discontinuation. When patients present with these symptoms during the discontinuation phase of treatment, the physician must decide whether to temporarily increase the antidepressant dose, reinstitute the treatment, prescribe medication for symptomatic relief, switch to an alternative agent, or merely reassure the patient that the symptoms will be transient. Patients who present with these symptoms should be closely monitored by the physician.

Antidepressant discontinuation events were first reported by Andersen and Kristiansen in 1959.² The first cases of antidepressant discontinuation events were reported for imipramine. Over the past 25 years, the phenomena have been reported with MAOIs, other TCAs, and SSRIs, in particular the shorter acting SSRI paroxetine. There are several risk factors for experiencing discontinuation symptoms. Patients taking high doses of antidepressant therapy may be at increased risk, as well as those who have been treated for a long period of time. For a first episode of depression, the U.S. Depression Guideline Panel³ recommends that patients be maintained on the therapeutic antidepressant dose for 4 to 9 months. In addition, children and adolescents who are taking antidepressants could be at

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higher risk than adults for discontinuation events. The prevalence of symptoms reported after antidepressant discontinuation ranges from 0% in a study of mianserin⁴ to 100% in an investigation of imipramine interruption in 22 adolescents⁵ (Table 1).^{2,4-16} In more recent informal reports involving serotonin reuptake inhibitors, the incidence rates vary between 0% for fluoxetine,⁶ 50% for paroxetine,⁷ and 86% for fluvoxamine.¹⁷

In 1987, Dilsaver et al.¹⁸ proposed five categories of symptoms that appear after tricyclic interruption: general somatic distress associated with anxiety (e.g., anorexia, nausea, emesis, diarrhea, diaphoresis, headache, chills, asthenia), sleep disturbances (e.g., insomnia, excessive and vivid dreams), movement disorders (e.g., akathisia, parkinsonism), behavioral activation (e.g., mania or hypomania, panic attacks, and delirium), and cardiac arrhythmia. Behavioral activation, which occurs frequently with TCAs, is especially important. These patients present with discontinuation-related manic or hypomanic episodes. Symptoms of discontinuation from MAOIs are particularly severe and include delirium, thought disorganization, depression associated with cognitive impairment, mania, hypomania, aggressiveness and irritability, agitation, insomnia, and myoclonic jerks.¹⁹ Paranoid delusions as well as visual, olfactory, gustatory, and tactile hallucinations are often observed in schizophrenic patients who are stopping MAOI treatment for depression.

SSRI discontinuation events, in contrast, are frequently transient and mild but can be very distressing. They occur more often with the shorter half-life agents (paroxetine, sertraline, and fluvoxamine) than the extended half-life agent fluoxetine.²⁰ The most common symptoms are anxiety, irritability, and flu-like symptoms (rhinorrhea, myalgia, malaise, nausea, emesis, diarrhea, shaking chills). Patients described the most frequent symptom, dizziness, as having a "swimming," "spaced-out," "drunken," or "buzzing" quality that could be markedly exacerbated by movement. Paresthesia, the next most common symptom, was reported as "burning," "tingling," or "like electric shocks."⁶ In addition, some patients noted lethargy as a new symptom of sudden onset. Others described vivid dreams or nightmares or initial or middle insomnia. While the dreaming was generally a new symptom, the insomnia often represented a deterioration in patients whose sleep had recovered during antidepressant treatment.

Discontinuation symptoms occur more frequently in patients who suddenly stop antidepressant treatment as opposed to those whose treatment is gradually tapered by their physicians. Patients may leave their medication at home when they go on vacation or forget to take their pills and experience a discontinuation event a few days later. The incidence is lower in patients who follow a tapering regimen established by their physicians than in those who suddenly stop taking the medication, but there have been several case reports where patients experienced untoward

Table 1. Incidence of Symptoms After Antidepressant Discontinuation*

Author	Drug	N	Incidence (%)
Andersen and Kristiansen ²	Imipramine	85	21.5
Kramer et al ¹¹	Imipramine	45	55.0
Law et al ⁵	Imipramine	22	100.0
Tyrer ¹³	TCA		29.4
	Phenelzine	51	32.2
Bialos et al ¹²	Amitriptyline	17	80.0
Geller et al ¹⁴	Nortriptyline	36	16.0
Diamond et al ¹⁵	Clomipramine	20	33.3
Otani et al ⁴	Mianserin	...	0
Ceccherini-Nelli et al ¹⁶	TCA	10	70.0
Mallya et al ¹⁰	Fluvoxamine	17	28.0
Barr et al ⁷	Paroxetine	6	50.0
Keuthen et al ⁸	Paroxetine	13	38.5
Coupland et al ⁶	SSRIs	158	
	Paroxetine,		
	fluvoxamine	93	17.2
	Fluoxetine	20	0
	Sertraline	45	1.5
Oehrberg et al ⁹	Paroxetine	55	34.5

*Abbreviations: SSRI = serotonin selective reuptake inhibitor; TCA = tricyclic antidepressant.

events during slow tapering^{7,21} and at low doses of these antidepressants.²²

SSRI DISCONTINUATION

Paroxetine

The SSRI discontinuation phenomena have been relatively well documented since 1993, when D'Arcy²³ reported a case of dystonia in a patient who stopped treatment with paroxetine. Since that time, other authors have noted flu-like symptoms similar to those described for TCA discontinuation in patients who are discontinuing SSRIs. Barr et al.⁷ in 1994, described flu-like symptoms in three of six patients who were being tapered from paroxetine treatment of obsessive-compulsive disorder (OCD). During the 7- to 10-day taper, the patients presented with vertigo, light-headedness, rhinorrhea, severe nausea, vomiting, diarrhea, fatigue, insomnia, and myalgia. Keuthen et al.⁸ reported on 5 of 13 patients who experienced the onset of adverse events following taper, 1 to 3 days after paroxetine discontinuation. In 1 of these patients, the symptoms remitted abruptly in 1 week after 20 mg/day of fluoxetine was added. These symptoms, particularly nausea and vomiting, are similar to those reported after TCA discontinuation. In another report,²⁴ flu-like symptoms as well as vertigo, gait instability, hypnagogic visual hallucinations, insomnia, and psychomotor agitation developed after drug discontinuation in three of five paroxetine-treated patients.

Discontinuation symptoms also emerged in 34.5% of patients after a 12-week, double-blind, placebo-controlled clinical trial (patients were taking between 20 and 60 mg of paroxetine per day) evaluating its use for panic disorder.

der.⁹ The most commonly reported adverse event was dizziness. At the end of a 6-week clinical trial for the treatment of stuttering,²⁵ two patients became manic (symptoms included shoplifting, overconfidence, and pathologic euphoria). The episodes lasted for 9 to 17 days and remitted spontaneously. Other symptoms that have been reported during paroxetine discontinuation include anorexia, nausea, diarrhea, and shaking chills,²⁶ electric shock sensations,²⁷ and headache, nausea, and vomiting 3 days after a patient was switched from paroxetine to sertraline.²⁸ Discontinuation symptoms have also been observed in patients who had been taking a relatively low dose of paroxetine. Debattista and Schatzberg²² observed flu-like symptoms in two patients 1 to 2 days after 10 mg/day of paroxetine was discontinued.

Fluvoxamine

Several reports of discontinuation symptoms after fluvoxamine treatment have been published. The half-life of a single dose of fluvoxamine—11 hours—is similar to that for the short-acting paroxetine—10 hours.²⁹ Mallya et al.¹⁰ reported that 4 of 17 patients who had been treated with fluvoxamine for OCD for 12 months presented with dizziness, nausea, headaches, confusion, memory problems, and weakness when the medication was tapered. Symptoms in all but 1 patient remitted within several weeks. Fluvoxamine was restarted in the patient whose symptoms continued, and the symptoms remitted. Twelve of 14 patients who abruptly stopped taking 300 mg/day of fluvoxamine after 8 months of therapy for panic disorder experienced dizziness, incoordination, headache, nausea, and irritability.¹⁷ The symptoms developed within 24 hours of discontinuation. These patients were probably at increased risk for discontinuation symptoms since they had been taking relatively high doses for a long period of time. In 1994, Ayd³⁰ also noted mild and transient dizziness, sweating, nausea, insomnia, tremor, and confusion in patients who stopped taking fluvoxamine.

Sertraline

Discontinuation symptoms associated with the cessation of sertraline were first reported in 1994.³¹ A 47-year-old woman suddenly ceased taking 100 mg/day of sertraline. Two days later, the patient reported fatigue, abdominal cramps, insomnia, increased dreaming, flu-like symptoms, and impairment of short-term memory. The symptoms disappeared after 25 mg/day of sertraline was reintroduced. Frost and Lal²⁷ described a patient who presented with sensations of “electrical shock” and complaints of “being electrocuted” 2 days after sertraline was discontinued following a tapering period. The symptoms continued for 13 weeks. In another report,²⁴ severe vertigo, gait instability, malaise, headache, and muscle aches developed in a patient, who had been treated with 50 mg/day of sertraline, 5 days after discontinuation.

The symptoms subsided within a week. Finally, Leiter et al.³² described two patients who presented with mood alteration, changes in cognition, headaches, paresthesia, and gastrointestinal symptoms after cessation of 8 to 9 months of sertraline treatment.

Fluoxetine

Fluoxetine discontinuation events are less frequent than those for the other SSRIs. In one report,³³ extrapyramidal symptoms including a tremor and diaphoresis occurred. These symptoms disappeared after 45 minutes during diphenhydramine treatment. Kasantikul³⁴ described a 68-year-old woman who became agitated and disoriented and had visual hallucinations 48 hours after discontinuing fluoxetine. The symptoms ended 1 day after fluoxetine was restarted. Finally, 9 days after 40 mg/day of fluoxetine was abruptly stopped, a patient experienced dizziness and light-headedness. The symptoms disappeared within 2 days after fluoxetine was restarted.

Venlafaxine

Venlafaxine has been studied recently, and symptoms comparable to those for paroxetine discontinuation have been reported.³⁵ A 32-year-old woman abruptly discontinued taking 300 mg/day of venlafaxine after 8 months of treatment. After 36 hours, she began to suffer from headache, nausea, abdominal distention, asthenia, and the sensation that her “sinuses were congested.” The symptoms disappeared 2 hours after a 100-mg dose of venlafaxine was administered, and they reappeared twice more when venlafaxine discontinuation was attempted. In another report,³⁶ four of nine patients who completed a 12-week trial of venlafaxine for OCD experienced troublesome discontinuation symptoms. Despite a period of taper that lasted from 4 days to 2 weeks, the patients experienced a flu-like syndrome with muscle aches, fatigue, headache, nausea, and dizziness. Symptoms were relieved after venlafaxine was resumed and then tapered more gradually. Data from a double-blind discontinuation study of venlafaxine³⁷ indicate that the rates of discontinuation-related events were significantly higher in patients who discontinued the drug compared with placebo.

The manufacturer recommends that venlafaxine treatment be tapered gradually and that the patient be monitored during drug discontinuation because a cluster of symptoms, including asthenia, dizziness, headache, insomnia, nausea, and nervousness, occurred as new symptoms during discontinuation in 5% of patients studied in a retrospective survey of premarketing studies.³⁸ Discontinuation symptoms begin earlier in patients who stop taking venlafaxine than in those who stop taking paroxetine or fluvoxamine. Patients who skip doses often report that discontinuation symptoms appear within 24 hours. Although time to onset of symptoms with paroxetine or fluvoxamine discontinua-

tion is generally 2 or 3 days, symptoms sometimes emerge during venlafaxine dose adjustments and are frequent after sudden discontinuation.

Comparative Studies

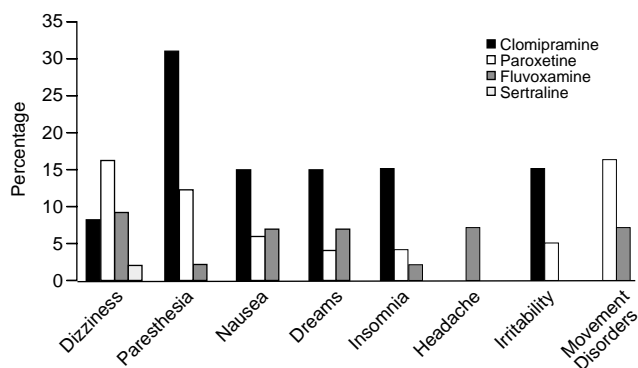
Coupland and collaborators⁶ compared discontinuation symptoms by conducting a retrospective chart review of 352 outpatients treated with a serotonin reuptake inhibitor. The patients with at least one qualitatively new symptom were defined as experiencing a discontinuation event. The authors found that symptoms occurred more frequently in patients who had been treated with one of the shorter half-life SSRIs—fluvoxamine or paroxetine—or with clomipramine than in patients taking an SSRI with an extended half-life. In this analysis, 30.8% of the clomipramine treated patients, 14.0% of the fluvoxamine-treated patients, and 20.0% of the paroxetine-treated patients experienced the discontinuation syndrome, as opposed to 2.2% of the sertraline-treated patients and 0.0% of the fluoxetine-treated patients (Figures 1 and 2).

Of the 352 patients, 171 (48.6%) discontinued treatment under supervision, and at least one new symptom (dizziness, paresthesia, or, in one patient, nightmares) emerged in 21 patients despite slowly tapered withdrawal. In this analysis, no adverse events occurred after fluoxetine discontinuation. Dizziness and headaches were most frequently reported after paroxetine discontinuation, while paresthesia, nausea, vivid dreams, insomnia, irritability, and movement disorders occurred most often when clomipramine treatment was stopped. The symptoms persisted for up to 21 days after onset and were relieved within 24 hours by restarting the medication. Coupland et al.⁶ also described but did not include in the statistical analysis 5 patients who reported symptoms after an unplanned abrupt discontinuation—generally caused by forgetfulness—of paroxetine. Dizziness was reported by 4, paresthesia by 2, and irritability, nausea, headache, and blurring of vision on movement were each reported by 1 patient.

When they examined the United Kingdom data base of adverse drug reactions for discontinuation symptoms associated with the cessation of fluoxetine, fluvoxamine, paroxetine, and sertraline, Price et al.³⁹ found that the discontinuation syndrome was reported most frequently for paroxetine and least frequently for fluoxetine. The number of reports of adverse discontinuation events for fluvoxamine and sertraline were about equal.

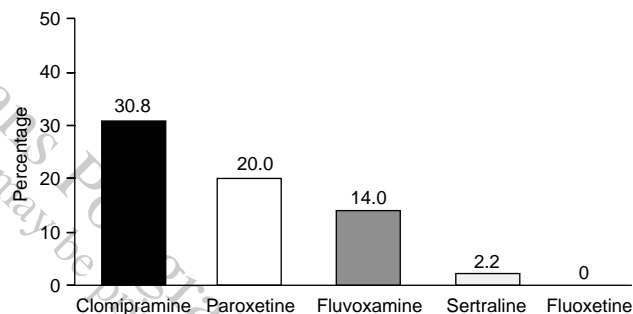
Two other prospective studies of SSRI discontinuation are under way. One multicenter study is in progress; its goal is to mimic the typical intermittent noncompliance that occurs with these drugs to evaluate whether the longer acting drug, in a well-designed prospective study, does have fewer discontinuation events. Another investigation, which was recently completed, examined discontinuation in patients who were in maintenance treatment with sertraline, paroxetine, and fluoxetine. The differences in the incidence and severity of discontinuation events for fluoxetine compared with paroxetine were significantly different.

Figure 1. Incidence of Serotonin Reuptake Inhibitor Discontinuation Symptoms*



*Data from reference 6. There were 13 clomipramine-treated patients, 50 paroxetine-treated patients, 43 fluvoxamine-treated patients, 45 sertraline-treated patients, and 20 fluoxetine-treated patients. No symptoms were reported for fluoxetine, and only dizziness was reported for sertraline. Headache was not reported with clomipramine and paroxetine, irritability was not reported with fluvoxamine, and movement disorders were not reported with clomipramine.

Figure 2. Percentage of Patients Who Experience Serotonin Reuptake Inhibitor Discontinuation Symptoms*



*Data from reference 6. No adverse events were reported for fluoxetine.

CONCLUSION

Any drug that causes adaptive changes in not only the nervous system but in any organ system is likely to be associated with symptoms of discontinuation. However, psychiatrists and other physicians who prescribe psychiatric medications must be especially watchful for the central nervous system effects that sometimes occur during antidepressant discontinuation. MAOIs and TCAs have long been associated with the discontinuation syndrome, and

recent reports have documented symptoms of SSRI discontinuation, particularly when patients are stopping treatment with shorter acting SSRIs such as paroxetine.

Drug names: amitriptyline (Elavil and others), clomipramine (Anafanil), diphenhydramine (Benadryl and others), fluoxetine (Prozac), fluvoxamine (Luvox), imipramine (Tofranil and others), nortriptyline (Pamelor and others), paroxetine (Paxil), phenelzine (Nardil), sertraline (Zoloft), venlafaxine (Effexor)

REFERENCES

- Lader M. Benzodiazepine withdrawal states. In: Trimble MR, ed. *Benzodiazepines Divided*, New York, NY: John Wiley & Sons, 1983:17–31
- Andersen H, Kristiansen ES. Tofranil treatment of endogenous depressions. *Acta Psychiatr Scand* 1959;34:387–397
- Depression Guideline Panel. *Depression in Primary Care: Detection, Diagnosis, and Treatment. Quick Reference Guide for Clinicians*. Rockville, Md: US Dept Health Human Services, Public Health Service, Agency for Health Care Policy and Research; 1993:5
- Otani K, Susa H, Kaneko S, et al. Lack of withdrawal symptoms after discontinuation of mianserin. *Lancet* 1991;337:673–674
- Law W, Petti TA, Kazdin A. Withdrawal symptoms after graduated cessation of imipramine discontinuation [letter]. *Am J Psychiatry* 1981;118:647–650
- Coupland NJ, Bell CJ, Potokar JP. Serotonin reuptake inhibitor withdrawal. *J Clin Psychopharmacol* 1996;16:356–362
- Barr LC, Goodman WK, Price LH. Physical symptoms associated with paroxetine discontinuation [letter]. *Am J Psychiatry* 1994;151:289
- Keuthen NJ, Cyr P, Ricciardi JA, et al. Medication withdrawal symptoms in obsessive-compulsive disorder patients treated with paroxetine [letter]. *J Clin Psychopharmacol* 1994;14:206–207
- Oehrberg S, Christiansen PE, Behnke K, et al. Paroxetine in the treatment of panic disorder: a randomized, double-blind, placebo-controlled study. *Br J Psychiatry* 1995;167:374–379
- Mallya G, White K, Gunderson C. Is there a serotonergic withdrawal syndrome? *Biol Psychiatry* 1993;33:851–852
- Kramer JD, Klein DF, Fink M. Withdrawal symptoms following discontinuation of imipramine therapy. *Am J Psychiatry* 1961;118:549–550
- Bialos D, Giller E, Jatlow P, et al. Recurrence of depression after discontinuation of amitriptyline. *Am J Psychiatry* 1982;139:325–329
- Tyrer P. Clinical effects of abrupt withdrawal from tricyclic antidepressants and monoamine oxidase inhibitors after long-term treatment. *J Affect Disord* 1984;6:1–7
- Geller B, Cooper TB, Carr LG. Prospective study of scheduled withdrawal from nortriptyline in children and adolescents. *J Clin Psychopharmacol* 1987;7:252–254
- Diamond BI, Borison RL, Katz R, et al. Rebound reactions due to clomipramine. *Psychopharmacol Bull* 1989; 25:209–212
- Ceccherini-Nelli A, Bordellini L, Guazzalli M, et al. Antidepressant withdrawal phenomena: prospective findings [letter]. *Am J Psychiatry* 1993;150:165
- Black DW, Wesner R, Gabel J. The abrupt discontinuation of fluvoxamine in patients with panic disorder. *J Clin Psychiatry* 1993;54:146–149
- Dilsaver SC, Greden JF, Snider RM. Antidepressant withdrawal syndromes: phenomenology and physiopathology. *Int Clin Psychopharmacol* 1987;2:1–19
- Halle MT, Dilsaver SC. Tranylcypromine withdrawal phenomena. *J Psychiatry Neurosci* 1993;18:49–50
- Lejoyeux M, Adès J, Mourad I, et al. Antidepressant withdrawal syndrome: recognition, prevention and management. *CNS Drugs* 1996;4:278–292
- Pacheco L, Malo P, Aragues E, et al. More cases of paroxetine withdrawal syndrome [letter]. *Br J Psychiatry* 1996;169:384
- Debattista C, Schatzberg AF. Physical symptoms associated with paroxetine withdrawal [letter]. *Am J Psychiatry* 1995;152:1235–1236
- D'Arcy PF. Dystonia and withdrawal symptoms with paroxetine [letter]. *Int Pharm J* 1993;7:140
- Fava GA, Grandi S. Withdrawal syndromes after paroxetine and sertraline discontinuation [letter]. *J Clin Psychopharmacol* 1995;15:374–375
- Bloch M, Stuger SV, Braun AR, et al. Severe psychiatric symptoms associated with paroxetine withdrawal [letter]. *Lancet* 1995;346:57
- Pyke RE. Paroxetine withdrawal syndrome [letter]. *Am J Psychiatry* 1995; 152:149–150
- Frost L, Lal S. Shock-like sensations after discontinuation of selective reuptake inhibitors [letter]. *Am J Psychiatry* 1995;152:810
- Phillips SD. A possible paroxetine withdrawal syndrome [letter]. *Am J Psychiatry* 1995;152:645–646
- Lane RM. Withdrawal symptoms after discontinuation of selective serotonin reuptake inhibitors (SSRIs). *Journal of Serotonin Research* 1996;3:75–83
- Ayd FJ. Fluvoxamine withdrawal symptoms. *International Drug Therapy Newsletter* 1994;11:39–30
- Louie AK, Lannon RA, Ajari LJ. Withdrawal reactions after sertraline discontinuation [letter]. *Am J Psychiatry* 1994;151:450–451
- Leiter FL, Nierenberg AA, Sanders KM, et al. Discontinuation reactions following sertraline. *Biol Psychiatry* 1995;38:694–695
- Stoukides JA, Stoukides CA. Extrapyramidal symptoms upon discontinuation of fluoxetine [letter]. *Am J Psychiatry* 1991;148:1263
- Kasantikul D. Reversible delirium after discontinuation of fluoxetine. *J Med Assoc Thailand* 1995;78:53–54
- Farah A, Laurer TE. Possible venlafaxine withdrawal syndrome [letter]. *Am J Psychiatry* 1996;153:576
- Rauch SL, O'Sullivan RL, Jenike MA. Open treatment of obsessive-compulsive disorder with venlafaxine: a series of 10 cases [letter]. *J Clin Psychopharmacol* 1996;16:81–84
- Fava M, Mulroy R, Alpert J, et al. The emergence of adverse events following venlafaxine discontinuation. In: *New Research Program and Abstracts of the Annual Meeting of the American Psychiatric Association*; May 20, 1997; San Diego, Calif. Abstract NR 255:136
- Physicians' Desk Reference. Montvale, NJ: Medical Economics; 1996
- 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

Discussion

Dr. Lejoyeux: The literature includes case reports of patients who, for example, forget to take their medication for a weekend. They go on vacation without the pills and experience a discontinuation event a few days later. Although my colleagues and I generally tell patients to taper antidepressants, the patients often choose to simply stop taking the medication when the prescription runs out.

Dr. Schatzberg: Intermittent noncompliance frequently causes discontinuation phenomena. For example, I once gave a patient instructions for tapering venlafaxine. About 10 days later, he called and said, "I haven't been able to get out of bed for about a week because I have terrible vertigo and dizziness." I asked, "How much venlafaxine are you taking?" He responded,

"I'm not taking any. I know you told me to taper the medication, but I just stopped taking it."

Dr. Kaplan: In clinical practice, I have seen more incidences of discontinuation symptoms from sertraline than are indicated by the literature. I don't see discontinuation symptoms as often for sertraline as for paroxetine, but I certainly see it more frequently than with fluoxetine.

Dr. Zajecka: At least one case report exists about a woman who took sertraline throughout her pregnancy and was breast feeding [Kent LSW and Laidlaw JDD. Suspected congenital sertraline dependence. *Br J Psychiatry* 1995;167:412-413]. She stopped breast feeding when the infant was 3 weeks old, and the infant experienced agitation, restlessness, poor feeding, broken sleep patterns, constant crying, and an enhanced startle reaction.

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