

Letters to the Editor

Bupropion-Associated Withdrawal Symptoms Revisited: A Case Report

Sir: Previously in the *Companion*, a case of bupropion-associated withdrawal symptoms had been described.¹ That case report was followed with a reply from Dr. Johnston of Glaxo Wellcome Inc., who could not establish a relationship between bupropion cessation and withdrawal symptoms.² Since that time I have observed another case of bupropion-associated withdrawal symptoms.

Case report. Ms. A was a 27-year-old African American woman diagnosed with a major depressive episode, which was moderate in accordance with DSM-IV criteria. She also had a significant smoking history of 1 to 2 packs per day since the age of 17. Prior to initiating antidepressant therapy, she scored a 28 on the Hamilton Rating Scale for Depression (HAM-D).³ She was started on venlafaxine extended release (XR) at 37.5 mg/day without any noted side effects. Her dose was increased to 150 mg/day over the next 2 weeks. Ms. A's score on the HAM-D after 1 month on venlafaxine XR treatment was 11. Subsequently, she saw a primary care physician who started her on bupropion sustained release (SR), 150 mg b.i.d., for smoking cessation. The patient remained on bupropion treatment for 4 months but had not stopped smoking. Within a day of stopping the bupropion therapy, she began to feel irritable and anxious. She had a headache and generalized aches and pains and, in her words, felt like she "wanted to crawl out of" her skin. The bupropion treatment was restarted, and her symptoms resolved within a day.

This case highlights the possibility that as more and more patients are prescribed antidepressants for a number of reasons, clinicians must be vigilant to the possibility of withdrawal symptoms. Bupropion is recognized as an important pharmacologic intervention in the treatment of smoking cessation and is generally well tolerated.⁴ However, it may be best to taper bupropion to avoid the possibility of withdrawal symptoms.

Conclusions and opinions expressed are those of the author and do not necessarily reflect the position or policy of the U.S. Government, Department of Defense, Department of the Army, or the U.S. Army Medical Command. This case occurred while Dr. Berigan was working at William Beaumont Army Medical Center in El Paso, Texas.

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A Case Report of Drug-Induced Dermatitis With Weekly Fluoxetine

Sir: The new once-weekly formulation of fluoxetine can potentially enhance compliance with maintenance treatment. Physicians should, however, monitor the occurrence of side effects when switching patients from daily to weekly fluoxetine treatment. We present the case of a female patient with schizophrenia and depression who was switched from daily to weekly fluoxetine treatment twice and developed a full body rash on both occasions.

Case report. Ms. A, a 33-year-old white woman with DSM-IV diagnoses of chronic paranoid schizophrenia, depressive disorder not otherwise specified, and mild mental retardation, has been attending a continuing day treatment program. The patient was first hospitalized at age 18 due to auditory hallucinations and delusions of persecution. Since then, she has had multiple psychiatric admissions due to auditory hallucinations and suicide attempts. Her family history was significant for depression and alcoholism in a paternal grandparent. Her medical history was significant for obesity, cystic acne, and allergy to lithium carbonate. Ms. A remained stable until April 2001, when she developed an exacerbation of psychotic symptomatology characterized by an increase in auditory hallucinations and depression requiring inpatient treatment. She was discharged on treatment with olanzapine, 20 mg at bedtime, and fluoxetine, 20 mg daily. At entry into the day treatment program in April 2001, her Brief Psychiatric Rating Scale score was 21 and her Hamilton Rating Scale for Depression score was 5.

Eight weeks after her discharge from inpatient treatment, Ms. A was switched from daily fluoxetine treatment to fluoxetine, 90 mg weekly, and continued on treatment with olanzapine, 20 mg at bedtime. Thirteen days later, she developed a full body rash. No other medication changes had been made other than the switch to weekly fluoxetine. The weekly fluoxetine was discontinued, and she was treated with diphenhydramine, 50 mg orally. Due to lack of efficacy and the development of hives in her mouth, her family physician stopped the olanzapine treatment. Diphenhydramine was continued, and prednisone,

30 mg per day for 3 days with a subsequent tapering schedule, was added. Three days after the discontinuation of olanzapine, she developed insomnia, and zolpidem, 10 mg at bedtime, was prescribed. The patient's rash cleared, and olanzapine therapy was subsequently restarted. A dermatology consultation was sought; however, by then the rash had cleared and no new recommendations were made. Two weeks later, treatment with fluoxetine, 20 mg daily, was restarted and was well tolerated with no reappearance of a rash. Two months later, another attempt was made to restart treatment with fluoxetine, 90 mg weekly, after discontinuing daily fluoxetine therapy with the patient's consent. After 1 dose of the weekly fluoxetine, the rash recurred, leading to subsequent discontinuation of the weekly preparation and a return to daily fluoxetine treatment.

Ms. A had been maintained for approximately 7 years on daily fluoxetine treatment, but when switched on 2 occasions to the weekly formulation of the same drug, she developed a rash. This suggests a temporal relationship between fluoxetine once-weekly and the rashes. It should be noted that this patient had tolerated daily fluoxetine well for many years, yet developed a rash on treatment with once-weekly fluoxetine.

Data from health maintenance organization formulary studies have shown that 6-month treatment completion rates for the selective serotonin reuptake inhibitors fluoxetine, paroxetine, or sertraline were only 22% to 45% in one study¹ and 35.8% in another large sample.² Enteric-coated once-weekly fluoxetine will enhance patient compliance. Once patients feel better on treatment with the antidepressant, the motivation to continue it decreases, with the patient not realizing that depression is a relapsing illness. In such instances, a long-acting preparation such as the once-weekly preparation of fluoxetine should certainly enhance compliance. Once-weekly fluoxetine should be used in patients stable on fluoxetine treatment and should not be prescribed when beginning a course of therapy for depression. Primary care physicians should keep in mind the option of using once-weekly fluoxetine, but should also note that even if patients tolerate daily fluoxetine well, they may still have allergic reactions to the weekly fluoxetine preparation, as this case illustrates. In the clinical trials, diarrhea was seen more often with once-weekly fluoxetine than with placebo ($p < .05$), and 2 events (nervousness and thinking abnormally) were seen

significantly more often ($p < .05$) with once-weekly fluoxetine compared with daily fluoxetine, 20 mg.^{3,4}

In summary, we think that primary care physicians should use enteric-coated once-weekly fluoxetine in patients who are stable on daily fluoxetine treatment; however, they should also be vigilant in watching for side effects, including allergic reactions, even if daily fluoxetine was well tolerated.

Dr. Gupta is a consultant for Eli Lilly, Pfizer, and Forest; has received grant/research support from Eli Lilly, Glaxo, and Janssen; and has received honoraria from and been a speaker/advisory board member for Eli Lilly, Pfizer, Glaxo, and Forest. Ms. Lentz and Dr. Frank report no financial affiliation or other relationship relevant to this topic.

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Book Review

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Schizophrenia Revealed: From Neurons to Social Interactions

by Michael Foster Green, Ph.D. W. W. Norton & Company, Inc., New York, N.Y., 2001, 207 pages, \$32.00.

Schizophrenia Revealed offers an impressive approach to a very difficult, misunderstood, and frustrating illness. As the author, Michael Foster Green, states in his introduction, this book serves as a forum for reviewing what he calls “exciting developments” in the diagnosis and management of schizophrenia. There is no question that this book is thorough in its review of neuroanatomy and its explanation of potential neurochemical etiologies. Much of the content would be particularly useful for someone with a strong interest in this disease. From a clinical perspective, however, it is somewhat limited.

Along those lines, 2 or 3 summary charts contain, essentially, bullet points for diagnosis and treatment. These bullets are a little different from what would be found in the DSM-IV in terms of diagnostic criteria. The advantage of this book is that it does contain clinical vignettes throughout, which help to emphasize some of the diagnostic and treatment points. These also help to personalize a disease that family physicians may not get much opportunity to treat.

Regarding diagnosis, very little is added clinically to what most of us already know about schizophrenia. There are interesting discussions regarding some of the newer imaging studies and how they might be utilized in research on schizophrenia. I found the sections on the use of positron emission tomography and magnetic resonance spectroscopy to be stimulating not only for how they might impact the evaluation of schizophrenia but also for how such investigations might alter assessments of patients with other diagnoses.

With respect to treatment interventions, a great deal of time is spent reviewing the extensive amount of cognitive and social aspects of treating this difficult disorder. Unfortunately, these approaches are very difficult for a family physician in private practice to utilize easily. The ability to coordinate such care would also depend on the resources available within the community and from the patient’s insurance. For the medical management of schizophrenia, the book has a nice review of the historical treatments, as well as some of the newer agents. Unfortunately, the book format is extremely limited in keeping current with available medications. With the pace of research and development of medications accelerating, a book is the last place a physician is likely to look for up-to-date medical management of any disease.

In summary, *Schizophrenia Revealed* is a thorough and very readable approach to the problems faced by patients and families suffering from the impacts of schizophrenia. For physicians who have either personal involvement or a large volume of patients with this diagnosis, this offering may likely help focus coordinated treatment efforts. For a family physician who does not take care of many patients with schizophrenia, this is not a particularly relevant book clinically. The important points of diagnosis and treatment are more readily found in journals or through an Internet search than through a textbook. This book’s strength lies in the compilation of a number of historical points that are particularly pertinent today, given the success of the movie *A Beautiful Mind*, which outlines the life of John Forbes Nash (a Nobel Prize-winning mathematician), who suffered from schizophrenia. I suspect there will be more readership among physicians for information purposes rather than for treatment directions, owing to the film’s popularity.

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