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TO THE EDITOR: We read with interest the report by Dr. Onyike et al. involving a patient who developed mania while being treated with pegylated IFN-α and ribavirin. This is important since pegylated IFN-α is used in the treatment of chronic hepatitis C and other viral illnesses and has been associated with a significantly lower incidence of depression in comparison to unmodified IFN-α (1). While pegylated IFN-α may also be associated with a reduced incidence of mania, it is important for clinicians to be aware of this potential side effect. Neuropsychiatric disturbances usually occur after repeated IFN-α exposure (days or months) or upon treatment discontinuation. The latter may have been an important factor in the reported case since the patient missed many doses of IFN-α before starting the new course of pegylated IFN-α. Since preclinical studies have shown that IFN-α decreases dopamine in the brain (2), a sudden withdrawal from IFN-α may have induced a surge of this neurotransmitter, which has been hypothesized to be important in mania.

The authors minimized the likelihood that the selective serotonin reuptake inhibitor (SSRI) fluoxetine may have been implicated in the switching process since it was initiated years earlier and the dose was doubled over 4 months before this mood alteration. We take the opposite view, suggesting that fluoxetine may have contributed to the switching process. This opinion is partially based upon recent work by Ramasubbu (3), who described two depressed patients—one with unipolar depression and the other with dysthymia. In both instances, the patient became hypomanic when the SSRI (sertraline and paroxetine, respectively) dose was significantly increased, and the hypomania resolved with subsequent dose reduction. In these cases, the switching occurred approximately 1 month after the dose increase, similar to the case by Dr. Onyike et al., in which mania developed 4 months after the SSRI dose increase.

In addition to less serious side effects (e.g., gastrointestinal symptoms), antidepressants, including SSRIs, are capable of inducing hypomanic/manic episodes (4). This is a particular concern in patients with a history of bipolar disorder but has also been described in nonbipolar depressives (3), including the patient presented by Dr. Onyike et al. Patients with a previous history of IFN-α-induced depression may also prove to be especially vulnerable.

Gastroenterologists frequently treat patients with chronic hepatitis C with a history of bipolar or major depressive disorder. These physicians should consider consultation with a psychiatrist since many of these patients are already taking antidepressants and/or necessitate prescriptions of antidepressants to prevent and/or treat IFN-α-induced depression. A psychiatrist would more effectively be able to monitor and/or intervene if a hypomanic/manic episode occurred.

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TO THE EDITOR: The article by Dr. Onyike et al. detailing the case of mania caused by pegylated IFN-α with ribavirin was a thorough review. It will be particularly useful for those who have not yet treated a patient experiencing these adverse psychiatric consequences from IFN-α.

However, I saw one recommendation in the review that I disagree with. In the appendix of the article, there was a table with treatment recommendations for a patient experiencing manic symptoms from IFN-α treatment. I noticed that gabapentin was one of the agents. Although there have been numerous case reports and open-label studies citing the usefulness of gabapentin for mania, a double-blind, placebo-controlled trial is the gold standard and the ultimate "litmus test." In 2000, Pande and colleagues (1) observed no difference between gabapentin and placebo for the adjunctive treatment of mania. If this trial failed to show an effect as an adjunct, I don't see how gabapentin could be used as monotherapy either.

When considering that the National Public Radio network has broadcast to the general public four times in 2003 alone regarding a lawsuit involving gabapentin for bipolar disorder (2), I believe it is inadvisable to use this agent for mania—medication-induced or not.

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Dr. Onyike and Colleagues Reply

TO THE EDITOR: We agree with Dr. Rifai et al. that a decision to prescribe pegylated IFN-α 2a with ribavirin to patients with a history of psychiatric disorder requires a comprehensive risk-benefit assessment. However, exactly which data should go