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Ms. Sullivan and Dr. Payne Reply

TO THE EDITOR: Drs. Gupta and Sharma point out limitations with the Seasonal Pattern Assessment Questionnaire in detecting individuals experiencing seasonal affective disorder. As a self-report measure, the Seasonal Pattern Assessment Questionnaire has been used with college samples yielding high retest reliability over seasons (1). We do, however, recognize that the Seasonal Pattern Assessment Questionnaire may be overinclusive (2). Thus, for further validation of the seasonal affective disorder status, we also administered the Beck Depression Inventory–II. Seasonal affective symptoms likely exist on a continuum. Although scores on both the Seasonal Pattern Assessment Questionnaire and Beck Depression Inventory–II were correlated in our study, the majority of individuals with seasonal affective disorder based on the questionnaire did not qualify for a diagnosis of major depressive disorder. However, scores on the Beck Depression Inventory–II were still higher for subjects in the seasonal affective disorder group (excluding those subjects with seasonal affective disorder/major depressive disorder) relative to those subjects not reporting symptoms of seasonal affective disorder.

To address concerns that the Seasonal Pattern Assessment Questionnaire is overinclusive, we more closely examined the group identified as seasonal affective disorder. As Drs. Gupta and Sharma suggest, there were individuals in the seasonal affective disorder group who could be considered subsyndromal seasonal affective. Although these subjects would not be identified by the Seasonal Pattern Assessment Questionnaire as having subsyndromal seasonal affective disorder, the Beck Depression Inventory–II better describes the severity of disordered mood in these subjects. Using the major depressive disorder criterion of the Beck Depression Inventory–II as an additional indicator of seasonal affective disorder (instead of the Seasonal Pattern Assessment Questionnaire as a single indicator), we observed that the majority of subjects in the seasonal affective disorder group would be considered subsyndromal seasonal affective, while only a few met the criterion for seasonal affective disorder as illness. The few remaining participants with seasonal affective disorder/major depressive disorder were not group outliers in terms of Beck Depression Inventory scores, since there were other participants whose scores were borderline major depressive disorder. Additionally, many participants reported December as the month in which they experience the full extent of atypical seasonal changes. Taken together, these data support the hypothesis that some participants who appeared to experience subsyndromal seasonal affective disorder may have been on the verge of experiencing full seasonal affective disorder as the Winter season progressed. However, cognition may have already been impacted. Consistent with our primary finding, participants who qualified for the diagnosis of subsyndromal seasonal affective disorder based on both the Seasonal Pattern Assessment Questionnaire and Beck Depression Inventory reported cognitive difficulties equivalent to those participants with major depressive disorder. Even with an adjusted identification criterion, cognitive failures were higher in the subsyndromal seasonal affective disorder group relative to individuals with no disordered mood. It is possible that high cognitive failures early in the season are identifying characteristics of seasonal affective disorder. Cognitive failures for the subsyndromal seasonal affective disorder group could be linked to ruminative cognitive styles that may predict vulnerability to seasonal depression (3).

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Argyria as a Result of Somatic Delusions

TO THE EDITOR: With the exception of three case reports (1–3), there are no known long-term neurological or psychiatric effects of silver ingestion. Skin discoloration as a result of ingestion—referred to as argyria—is permanent, and no chelating agents effectively remove silver deposits (4–6). We report the case of an individual who used colloidal silver as an antiseptic treatment and developed argyria.

A 27-year-old man was admitted to our inpatient psychiatric service from the emergency department following a suicide attempt. During his initial evaluation, his skin was noted to be a gray-blue hue, especially on the hands and face.

The patient reported that he had been infected with a sexually transmitted disease 8 years prior. Following treatment for the sexually transmitted disease, he began to believe that he was infected with a chronic form of bacteria that was slowly killing him. He subsequently sought medical treatment from multiple emergency departments in several states. In spite of normal laboratory examinations, he became hopeless about his perceived infection and attempted to jump from a building.

During his evaluation at our inpatient psychiatric service, the patient was questioned about his unusual skin color. He reported ingesting a silver colloidal solution for 2 years prior to his admission to our service because he felt that the silver colloidal solution was the only treat-

ment that would cure the infection he was convinced was killing him. He learned about silver colloid as a possible "antiseptic" agent and instructions on how to make a silver colloid solution from the Internet.

There are two major points of interest in this case. First, as clinicians we need to be aware of the information sources our patients use and how they use them. While there is some good information on the Internet, there is also a lot of potentially harmful information. Many web sites offer easy access to products that may be harmful to patients. For example, an Internet search for "colloidal silver generators" yielded more than 100 sites. Part of our role as physicians is to provide education to our patients, not only about their illness but also about the possible misinformation that is freely available.

The second point is that seemingly innocuous "folk remedies," such as the one in our case, can lead to permanent harm. Given the fact that somatic delusions of infection or disease are not rare in psychiatrically ill patients, the use of colloidal silver might appear attractive to vulnerable patients. Clinicians are urged to be aware of the popularity and potential harm of the "remedy" presented in this case.

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Stabilization of Hypomania Following Initiation of Tamoxifen

TO THE EDITOR: Tamoxifen, an antiestrogen agent used in breast cancer treatment, inhibits protein kinase C and may have antimanic properties (1–3). We present the case of a patient with bipolar disorder who became depressed while receiving tamoxifen.

A 55-year-old Caucasian woman with bipolar disorder presented in December 2006 for evaluation of depression after starting tamoxifen for the treatment of breast cancer. While she was in her 20s, the patient's bipolar disorder was characterized primarily by hypomania. Beginning in her 30s, depressive episodes predominated. She was subjectively euthymic but at times hypomanic, and she was medication free for 3 years before starting tamoxifen. In December 2004, at age 53, she was diagnosed with stage I breast cancer and treated with lumpectomy and radiation, followed by 18 months of tamoxifen. The patient had no other conditions that present with depression. Two antidepressant trials plus stimulants had little effect until tamoxifen was discontinued by her oncologist in June 2006 when a mixed state ensued. Subsequently, lithium was started, which precipitated worsening mood. We feel that tamoxifen, then lithium, "stabilized" her mood in the depressed phase of the illness. We recommended increased dosing of lithium, antidepressant taper, avoidance of stimulants, and the addition of lamotrigine.

Mood stabilizers have been anecdotally associated with stabilization in the depressed phase of bipolar disorder. There is only indirect evidence for this phenomenon in that anticonvulsants, including valproate, are associated with risk of depression (4). Evidence for an association between tamoxifen and depression is conflicting (3, 5, 6).

One possible explanation for these clinical observations is that the pathophysiology of bipolar disorder may involve protein kinase C. Chronic administration of lithium and valproate has been shown to reduce protein kinase C isoenzymes in the frontal cortex and hippocampus in rats, and increased protein kinase C activity has been observed in postmortem brain tissue in bipolar disorder patients (7). Tamoxifen was antimanic in three small clinical studies (1–3), supporting evidence for a possible role of protein kinase C in bipolar disorder. Our case supports the need for larger studies of protein kinase C-inhibiting agents in hypomania. Because tamoxifen is widely used in the treatment of breast cancer, understanding its potential effect on mood regulation is also clinically important.

Limitations of this report include the episodic nature of bipolar disorder and unavailable follow-up data, making the association between tamoxifen use and depression tentative. We therefore advise careful consideration of risks and benefits before discontinuing tamoxifen for symptoms of depression.

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