



From the editor

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Bipolar disorder Clinical questions beg for answers

A distinguished speaker at a recent national conference was describing his classification of bipolar disorder, and his slides listed subtypes I, II, II^{1/2}, III, IV, and IV^{1/2}. During the question-and-answer session, a perplexed attendee announced—with tongue in cheek—that he had 4^{1/2} questions and 2^{1/2} comments about the bipolar presentation. . . .

Let's face it, bipolar disorder is a fascinating neuropsychiatric condition that tests every clinician's diagnostic acumen and treatment skills. Many questions about its diagnosis and treatment remain unanswered.

Diagnosis. Bipolar disorder can present with many different symptoms and with phases that cycle spontaneously or in response to treatment.

And with its many mood states and multiple comorbidities, bipolar disorder is replete with red herrings. Many of its sufferers are misdiagnosed with alcoholism, anxiety, borderline personality disorder, attention-deficit/hyperactivity disorder (child or adult), or—the most frequent misdiagnosis—major depression.

Treatment. Despite a rich literature, astonishingly few large controlled clinical trials have been conducted to guide bipolar disorder pharmacotherapy.

Long-term follow-up studies indicate that depression dominates in >75% of bipolar patients' symptomatic days. Even so, (inexplicably) 8 drugs are approved in monotherapy for bipolar mania and only 1 for bipolar depression. [Quetiapine monotherapy was FDA-approved in October, joining the combination of olanzapine/fluoxetine with this labeling.]

No antidepressants are indicated for bipolar depression, yet they have been widely used despite

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their inherent risk of inducing switches to mania, hypomania, mixed states, and rapid cycling.

Winging it. Most clinicians improvise when treating rapid cycling, hypomania, cyclothymia, or bipolar II. No medications have been approved for these bipolar states, which commonly are seen in outpatient settings.

Three mood stabilizers and five atypical antipsychotics are approved for mania in bipolar I disorder, but hardly a shred of controlled evidence

exists to help you decide which drug to try first. Without controlled head-to-head trials, clinicians must choose treatment based on available data:

- Some may use quetiapine as first-line therapy because of evidence showing efficacy in both bipolar mania and bipolar depression.

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- Others may select ziprasidone or valproate ER, the only agents approved for all three types of mania (euphoric, mixed, and psychotic).
- Still others—cognizant of high nonadherence and the relapse-inducing risk of substance abuse in bipolar patients—may choose parenteral long-acting risperidone for long-term maintenance.

Combination therapy. Most bipolar disorder patients eventually receive two or more medications, but the evidence is anemic (at best) for combination therapy as well.

What is the optimal combination for mania with severe anxiety or for bipolar II disorder with mixed features or irritable depression? Dozens of iterations are possible, with nothing for prescribers to rely on except “expert consensus” guidelines

based on opinion or clinical experience. No controlled clinical trials have compared various combinations, and little is known about:

- optimal dosing of agents in combinations
- which combinations are safest in patients with coexisting medical conditions.

Much remains to be learned about diagnosis and treatment of bipolar disorder’s subtypes. Our talented and productive patients with bipolar disorder look to us to provide the safest, most effective

treatments that improve functioning without compromising quality of life. For this, we need a National Institute of Mental Health-sponsored study of bipolar disorder, similar to the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) studies of schizophrenia and Alzheimer’s disease (*see page 49*).

In the meantime, good luck managing the next bipolar II½ patient you see!



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Dear Readers,

In this issue, CURRENT PSYCHIATRY recognizes the contributions of those who have served as peer reviewers of articles published in our journal in 2006. The list of reviewers spans pages 19 and 20 and testifies to psychiatric practitioners’ strong commitment to continuing education and intellectual integrity.

We invite you to send us suggestions of topics you would like to see CURRENT PSYCHIATRY cover in 2007. If you wish to serve as a reviewer or submit an article for peer review, contact me at henry.nasrallah@currentpsychiatry.com.