This July 2011 issue of Psychiatric Annals, guest edited by me, brings up one of the most interesting clinical conundrums that has been simmering over the past 5 years: An increasing realization that bipolar depression may not respond as well as unipolar depression to antidepressant medications.

It seems the field was content with the notion that bipolar depression responded to antidepressants, especially (not so) “new” generation antidepressants, just as unipolar major depression does. To some practitioners, a major depressive episode is a major depressive episode — whether it occurs in bipolar disorder or in major depression.

Then data from the STEP-BD study — questioning the efficacy of antidepressants in bipolar depression was published. Several follow-up samples of convenience from this large study raise doubt,1,2 but the study by Dr. Gary Sachs and colleagues, published in the New England Journal of Medicine,3 showed that randomly assigned bupropion or paroxetine did not do as well as placebo over 6 months (23% vs. 27% response). This was followed by a recently published meta-analysis finding the same.4 Yes, there are studies suggesting some effect with bipolar depression over time, but the data seems to be increasingly questioning the sustained effect of antidepressants in many bipolar patients.5,6

If this is the case, where does that leave us?

Well, quetiapine probably shows the most robust evidence of antidepressant effect in bipolar depression7,8 (check out those effect sizes), and there is data supporting the use of lamotrigine in bipolar depression9 — and what else? Thanks to Dr. Mark Frye and associates, we have some evidence that modafinil has antidepressant effects that help bipolar patients10 and thanks to Dr. Chris Aiken, a review of some evidence for the therapeutic effect of pramipexole11 provided small numbers but notable effect sizes. Both of these have been a vast help to my patients when I was stuck for answers.

And don’t forget MAOI inhibitors. Dr. Mallinger and colleagues have recently provided us with some additional encouraging data in treating bipolar depression.12

Very little of this is gold-standard level data — large, randomized, double blind placebo-controlled studies such as those we get when there is a commercial interest — but hey, where is there any gold-standard data to guide us regarding treatment-resistant depression, which is now suspected increasingly to be predominantly bipolar depression?13

So, until we find the gene or brain circuit that will lead to the silver bullet, we have to rely on whatever data, or even clinical experience, we can find. The conundrum continues.

In this issue, in addition to treatment resistance, there are other serious problems we have to contend with in treating bipolar patients.

Two cases present the occurrence of side effects of treatment with the newer generation of antipsychotic medications: akathisia, presenting in a somewhat unusual form; and sialorrhea. Another case reviews lamotrigine treatment, shown to be helpful in treating...
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and preventing bipolar depression, and the association of emerging suicidal ideation that often accompanies it. Managing psychosis is yet another common clinical problem in bipolar patients; here, it is reviewed in the context of a case presentation that involved delusional filicidal impulses.

Finally, the journal’s publishers and I invite you to enjoy an expanded front section of this issue, in which we chronicle the many developing clinical news items on the subject of bipolar disorder. This includes, among other articles, an update on the valuable studies recently presented at the Ninth International Conference on Bipolar Disorder in Pittsburgh, as well the importance of monitoring our patients on second-generation antipsychotics for metabolic disorders. Don’t miss the opportunity to read the timeline on the history of bipolar disorder on page 346. Looking at the issues we’ve faced since the second century in this disorder — from compliance problems to the economic limitations that our patients face in affording medications they need to the issues we as clinicians face in trying to help them sustain and improve their lives — it is at times frustrating to see how far we have to go in finding effective treatments. At the same time, just 150 years or so from the time that bipolar disorder was called “circular insanity,” it’s also incredibly humbling to see how far we have come.

Jan Fawcett, MD, a graduate of Yale University School of Medicine, joined the Department of Psychiatry at the University of New Mexico School of Medicine after 30 years of service as the Stanley Harris Sr. Chairman of the Department of Psychiatry at Rush Medical College in Chicago. He has pursued a career of research in the treatment of affective disorders and the prevention of suicide since completing his fellowship at the National Institute of Mental Health (NIMH) Clinical Center in 1964. Dr. Fawcett has been awarded the Dr. Jan Fawcett Humanitarian Award by the National Depressive and Manic Depressive Association (now the Depression and Bipolar Support Alliance) and has been given lifetime research awards by the American Association of Suicidology and the American Foundation for Suicide Prevention. He was also presented the Menninger Award in 2000 by the American College of Physicians for his research in mental health. In 2005, Dr. Fawcett shared the Falcone Prize for affective disorders research from the National Alliance for Research in Schizophrenia and Depression (NARSAD).

He is currently a principal investigator of the Recurrent Depression Prevention with Medication and Cognitive Behavioral Therapy project, a five-year study funded by the NIMH at Rush Medical Center in collaboration with investigators at Vanderbilt University and the University of Pennsylvania. He is a co-author of the American Psychiatric Association’s Practice Guidelines Committee on the assessment and management of suicidal patients and is chairperson of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition, (DSM-V) Mood Disorders Task Force.

Dr. Fawcett has always maintained an active clinical practice focusing on patients with treatment-resistant major affective disorders and continues to do so in his work as a Professor in the Department of Psychiatry at the University of New Mexico School of Medicine.
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doi: 10.3928/00485713-20110627-01