The distinction between pediatric bipolar disorder (P-BP) and attention-deficit/hyperactivity disorder (ADHD) is a crucial one that can have serious acute and long-term ramifications and consequences. This issue of *Psychiatric Annals* presents three articles on the diagnosis and course of these illnesses, and a future issue will present three articles on the psychiatric and medical comorbidities, neurobiological risk factors, and differential treatment.

The differential diagnosis is of great importance because the treatment of the two disorders is distinctly different. Moreover, ADHD is more than three times as prevalent (10.8% in 2011) than P-BP and has more than 20 preparations for approved for treatment by the US Food and Drug Administration (FDA), including the psychomotor stimulants, alpha-2 adrenergic agonists, and the nor-epinephrine reuptake inhibitor atomoxetine. In stark contrast, there are no FDA-approved medications for P-BP in children younger than age 10 years, and expert consensus guidelines are based on an inadequate clinical trial literature for older children with bipolar I disorder (BP-I). Medications for P-BP include a number of atypical antipsychotics; anticonvulsants such as valproate, lamotrigine, and carbamazepine; and lithium; with many suggestions about treatment in children being indirectly inferred from efficacy data in adults.

A further complicating factor is that there is a high incidence of comorbidity of ADHD with P-BP, so it becomes especially important to recognize and first treat and stabilize mood in P-BP and then secondarily treat residual (persistent) ADHD symptoms with low-dose stimulants.

However, all too often the opposite occurs. The P-BP is not recognized early and children with comorbid presentations are often treated with high-dose stimulants and antidepressants without a concomitant mood stabilizer or atypical antipsychotic. This usually leads to inadequate behavioral stabilization and delay in the onset of appropriate treatment, with adverse consequences for a child’s social, psychological, and educational development.

P-BP, including the spectrum of bipolar disorder not otherwise specified (BP-NOS), bipolar II disorder (BP-II), and BP-I, can emerge with very considerable dysfunction and disability that is often difficult to treat and achieve remission, even when it is recognized early.

Nevertheless early recognition may help ward off many of the difficult long-term consequences of P-BP, and a substantial percentage of children may show a course toward illness resolution upon long-term follow-up. However, most prospective data in those with P-BP show a considerable burden of illness in a high percentage of patients, and these observations converge with those from adults with BP that onset of illness in childhood carries a more difficult prognosis than those with adult onset.

Compounding this difficulty is the finding that independent of the early onset, the duration of the delay to first treatment for either mania or depression is a separate and additional predictor of more time and severity of depression in adulthood. Even when the illness in children is carefully diagnosed by experts, 8-year follow-up of naturalistic treatment in the community left children symptomatic two-thirds of the time, and regrettably 37% of the children never
received any of the recommended treatments for P-BP. Parenthetically, those who did receive treatment with lithium had the highest rate of remission.

Mitchell and Goldstein emphasize the high comorbidity of both P-BP and ADHD with substance abuse and anxiety disorder, as well as with medical problems. This article lays out the need to treat these comorbid conditions concurrently, but notes the absence of a treatment literature to guide therapeutics in this highly underserved population. The articles in this and the next issue of *Psychiatric Annals*, thus, emphasize the critical need for treatment-related studies to better guide clinical therapeutics in these children who are at high risk for a poor outcome if inadequately treated.

Although there are currently no FDA-approved (or even well-studied) drugs for treating the high incidence of substance abuse and anxiety disorder comorbidity in children with bipolar disorder, when the need is great one might consider extrapolating data from other patient populations and illnesses in evaluating potential treatment options.

For example, N-acetylcysteine (NAC) has a record of safety in children, improves mood and anxiety in bipolar patients, and has a robust efficacy profile in primary substance abuse disorders, including cocaine, heroin, and alcohol in adults, and marijuana in adolescents. Thus in the absence of controlled data in children with P-BP, one might still consider an individual clinical trial of NAC when the patient has a comorbid anxiety or substance abuse disorder that requires pharmacological as well as psychological therapy.

The articles in these two issues of *Psychiatric Annals* emphasize the importance of early recognition and appropriate treatment of P-BP, particularly in the United States, where more than one-quarter of the illness in adults begins before age 13 years and two-thirds begins prior to age 19 years (as opposed to only about one-third in European countries such as the Netherlands and Germany). Chang discusses the neurobiological markers of high risk and it is hoped that these in conjunction already known clinical risk variables will help in early recognition and treatment of children in the very earliest prodromes and stages of illness.

Even before neurobiological markers become well defined and validated, the currently known clinical risk factors can be utilized in considering early intervention. These include 1) a positive family history of bipolar and mood disorders, especially if the parents are ill and have other comorbidities; 2) a history of psychosocial stressors, such as verbal, physical, or sexual abuse in childhood; and 3) the presence of early prodromal anxiety, mood, or bipolar symptoms. In contrast to childhood bipolar disorder, investigators in schizophrenia are decades ahead in the study of high risk and prodromal states, and it is further hoped that a secondary benefit of these two issues will be to help foster a new generation of treatment research. Much needed is the design, conduct, and implementation of early intervention and secondary prevention studies in childhood onset bipolar disorder, as well as the development of a robust treatment literature for those already with the full-blown illness (tertiary prevention).

**REFERENCES**


Robert M. Post, MD, is Clinical Professor of Psychiatry, George Washington University, Washington, DC; and Head, Bipolar Collaborative Network, Bethesda, MD; and a member of the Editorial Board of *Psychiatric Annals*.

He worked at the National Institute of Mental Health (NIMH) for 36 years studying and treating patients with refractory bipolar disorders. He and his group have won multiple national and international awards and published more than 1,000 manuscripts. He wrote a book entitled *Treatment of Bipolar Disorder: A Casebook for Clinicians and Patients* and now edits a newsletter available at: www.bipolarnews.org. He founded the Stanley Foundation Bipolar Network, which now continues as the Bipolar Collaborative Network and includes nine well-known US and European co-investigators.

He is starting a new network for children (ages 2-12 years) with or at risk for mood and bipolar disorders where parents rate their children on a weekly basis on a secure website. This will soon become active and available as advertised on www.bipolarnews.org. With this Child Network initiative he hopes to describe how the youngest children with anxiety, depression, and bipolar illness and its prodromes are being treated and how well the treatments are working and tolerated.

Address correspondence to Robert M. Post, MD, Bipolar Collaborative Network, 5415 W. Cedar Lane, Suite 201B, Bethesda, MD 20814; email: robert.post@speakeasy.net.


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