

# Bipolar Disorder: Recent Issues in Diagnosis and Classification

Alan F. Schatzberg, M.D.

Recent findings in the diagnosis, classification, and epidemiology of bipolar disorder are reviewed. Specific bipolar subtypes are delineated. A number of key diagnostic issues that have implications for correctly establishing the diagnosis or for determining optimal treatment approaches are discussed. The epidemiology of comorbid substance abuse and bipolar disorder is reviewed as is the significance of this comorbidity vis-à-vis presenting symptoms, treatment, and outcome. The differential diagnosis between so-called *mixed states* and *agitated depressed* is reviewed, and the potential significance of comorbid bipolar disorder and attention-deficit/hyperactivity disorder is discussed.

(*J Clin Psychiatry* 1998;59[suppl 6]:5-10)

In recent years, increasing attention has been paid to the diagnosis and classification of bipolar disorders, in part because of a number of psychopharmacologic observations that specific thymoleptic agents are not equally effective in all patients with bipolar disorder. The delineation of bipolar subtypes has occurred at the same time that some investigators have argued for a widening of the bipolar concept (bipolar spectrum) to include patients whom others may view as suffering from a different type of disorder, i.e., attention-deficit/hyperactivity disorder (ADHD), borderline personality disorder, and others. This possible widening of the bipolar category has potentially great consequences on clinical practice and represents an area of considerable debate for the field. In this paper, the epidemiology and classification of bipolar disorders are reviewed. Then, a number of key issues that are tied to diagnosis and classification of bipolar disorder are discussed: comorbidity with and as a differential diagnosis from substance abuse; differential diagnosis between mixed mania and agitated depression; and the relationship between bipolar disorder and ADHD.

## EPIDEMIOLOGY

Bipolar disorders are relatively common, appearing in approximately 1.3% of the population (0.8% bipolar I and

0.5% bipolar II). Bipolar disorders represent some 50% of mood disorders seen in a psychiatric clinic.<sup>1</sup> Bipolar disorder frequently has an age at onset in the teenage years but commonly is not diagnosed until the patient's early twenties. In the elderly, bipolar disorder is often seen as a result of a medical disorder (e.g., endocrinopathy) or a neurologic disorder (e.g., cerebrovascular insult). Bipolar I disorder occurs with equal frequency in both men and women. Bipolar II disorder may be more common in women.<sup>2</sup> Suicide attempts have been reported in about 25% of bipolar patients, with suicide completion rates of about 15%.

## CLASSIFICATION

Bipolar disorder consists of phases of excitement (hypomania or mania) and often includes phases of depression. These may alternate or occur in various admixtures. As indicated in Table 1, the DSM-IV classification of bipolar illness includes four bipolar disorders that can be differentiated on the basis of degree or duration of mania/hypomania or excitement.<sup>2</sup> Key differentiating characteristics are summarized in Table 2. In addition, DSM-IV includes two excited states that are secondary to medical conditions or their treatments, or to substance abuse.

### Mania and Hypomania

Mania is characterized by elevated, expansive, or irritable mood plus a number of other signs and symptoms, including grandiosity, elation, racing thoughts, pressured speech, distractibility, decreased need for sleep, increased activity, and impulsive behavior. Mania frequently produces impaired performance or psychosis or results in hospitalization. Patients who meet criteria for mania for at least 1 week are given a diagnosis of bipolar I disorder if their disorder is not caused by drugs or a medical illness. If

---

*From the Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, Calif.*

*Presented at the symposium "Lithium in the Treatment of Manic-Depressive Illness: An Update" held May 30-31, 1997, Sea Island, Ga., and supported by an educational grant from Solvay Pharmaceuticals, Inc.*

*Reprint requests to: Alan F. Schatzberg, M.D., the Kenneth T. Norris, Jr., Professor and Chair, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Road, Stanford, CA 94305-5717.*

**Table 1. Types of DSM-IV Bipolar and Related Disorders\***

Bipolar
Bipolar I disorder
Bipolar II disorder
Bipolar disorder, not otherwise specified
Cyclothymic disorder
Related
Mood disorder due to general medical condition with manic or mixed features
Substance-induced mood disorder with manic or mixed features

\*Data from reference 2.

currently manic, the diagnosis would be termed “bipolar I disorder, currently manic.” If the patient is experiencing his or her first manic episode and has not had episodes of depression, the term “bipolar I disorder, single manic episode” is used.

Hypomania is characterized by milder symptoms of excitement that do not meet the criteria for mania. Subjects with hypomania are not hospitalized for their excited states and are not psychotic nor are they markedly impaired. A 4-day duration of symptoms is required for this syndrome. Patients are generally diagnosed with bipolar II disorder if they are currently hypomanic, have not been previously manic, have had previous episodes of major depression, and their disorder is not secondary to a medical disorder or substance use.

For patients with hypomanic-like symptoms that do not meet criteria for bipolar II disorder (often because they do not last for 4 days), a diagnosis of bipolar disorder, NOS (not otherwise specified) may be given. This diagnosis is also used for patients with recurrent hypomania who have not experienced an episode of major depression.

### Major Depression

Major depressive episodes may occur in the absence of hypomania or mania (in which case, the diagnosis is unipolar depression) or can be a part of a bipolar picture. Major depressive episodes can occur in either bipolar I or II subtypes. Commonly seen signs and symptoms of major depressive episodes in patients with bipolar disorder include depressed mood or interest/drive; anhedonia; psychomotoric disturbance (frequently, retardation); sleep disturbance (frequently, increased sleep); appetite disturbance (frequently, increased appetite and weight gain); diurnal variation; suicidal ideation/behavior; and decreased self-esteem. A duration of 14 days is required to establish the diagnosis of major depression.

### Mixed State

It has long been appreciated that some manic patients demonstrate considerable dysphoria or depressive symptoms—so-called *mixed states*. More recently, surveys of acutely manic patients have revealed rates of dysphoria as high as 60% or more. In the DSM-IV, to be diagnosed as having a bipolar disorder, patients must simultaneously

**Table 2. Comparisons Among DSM-IV Bipolar Subtypes\***

DSM-IV Descriptors	Bipolar I	Bipolar II	Bipolar Not Otherwise Specified	Cyclothymia
Mania (Minimum duration)	Required (1 wk)	No	No <sup>a</sup>	No <sup>b</sup>
Hypomania (Minimum duration)	Possible (4 d)	Required (4 d)	Possible (4 d)	No <sup>b</sup>
Major depression (Minimum duration)	Possible (2 wk)	Required (2 wk)	No	No <sup>b</sup>
Mixed state (Minimum duration)	Possible (1 wk)	No	No <sup>a</sup>	No <sup>b</sup>
Rapid cycling	Yes	Yes	No	No

\*Data from reference 2.

<sup>a</sup>Can occur superimposed on delusional disorder, residual schizophrenia, or psychotic disorder not otherwise specified.

<sup>b</sup>Not present in first 2 years. Can occur as superimposed condition.

meet criteria for both mania and major depression on an almost daily basis for at least 1 week. Many of the patients diagnosed clinically as having mixed mania/depression actually fall short of meeting these criteria. However, these patients still may experience considerable depressive symptomatology that may have great bearing on response to treatment. Akiskal has been critical of requiring that major depression criteria be met before making a diagnosis of mixed state.<sup>1</sup> He notes that several variations of mixed states have long been known to occur and are seen in clinical practice.

### Rapid Cycling

Bipolar patients can demonstrate frequent cycling between excited and depressive episodes. For patients who experience four or more episodes in a year, a modifier of *rapid cycling* is used. Rapid cycling can be seen in both hypomanic and manic patients. Some patients demonstrate more than four episodes per year. Rapid cycling is more common in women and may be associated with hypothyroidism.<sup>3</sup> Some investigators have argued that antidepressants may precipitate or worsen cycling,<sup>4</sup> and they advocate using antidepressants sparingly or not at all. While all antidepressants can precipitate mania or hypomania in some patients, the argument that these agents change the cyclicity of the disorder requires further study and/or evidence. In the DSM-IV, mania or hypomania precipitated by antidepressants is not necessarily diagnosed as bipolar I or II—a state of affairs that has been criticized.<sup>1</sup>

### Cyclothymia

Some patients who experience considerable fluctuations in mood do not meet the bipolar criteria for either hypomania/mania or depression because of a limited number or duration of symptoms or too brief a duration of the manic or depressive episode. Such patients are frequently diagnosed as cyclothymic. Criteria for cyclothymia include numerous manic and depressive symptoms for 2 years or more that do not meet criteria for major depres-

sion or hypomania; no 2-month or longer symptom-free interval over a 2-year period; and no major episode of mood disorder during the first 2 years of the illness.

### Thymoleptic Treatment

Lithium, the first effective mood stabilizer introduced into practice, is particularly effective in elated/euphoric mania or hypomania. Lithium has been reported to be less effective in mixed states<sup>5-7</sup> and has been thought to be less effective in, and perhaps to be a contributor to, rapid cycling disorder.<sup>5</sup> In these subtypes, anticonvulsants may offer some advantage. In the recent multicenter comparison<sup>5</sup> of divalproex sodium, lithium carbonate, and placebo, lithium was more effective in euphoric mania, whereas divalproex appeared more effective than lithium in dysphoric mania. Divalproex was also effective in the treatment of rapid cycling, although the randomization was such that no patients with rapid cycling were treated with lithium, making direct comparisons impossible.

### Secondary Mania

In addition to antidepressants, a number of medical disorders and their treatments can cause mania or hypomania.<sup>8</sup> Glucocorticoids, such as prednisone, prescribed for various disorders (e.g., Bell's palsy, orthopedic conditions) can precipitate hypomania or mania. Drugs of abuse (i.e., stimulants) can cause hypomanic or manic symptoms. Endocrine disorders (e.g., hyperthyroidism) can be associated with excitement. Particularly in the elderly, cerebrovascular insults can be associated with excited states. Thus, clinicians need to take a careful history when assessing a manic or hypomanic subject. If a patient has a manic disorder secondary to a medical illness, the diagnosis of "mood disorder due to a general medical condition with manic features" is made. If a patient's mania occurs clearly secondary to the use or abuse of a specific substance, the term used is "substance-induced mood disorder with manic features."

## SUBSTANCE ABUSE

Substance abuse is a complicating feature in bipolar disorder. Substance abuse frequently occurs in the context of an excited state and may have great implications for treatment and outcome. In addition, substance abuse may provide some diagnostic dilemmas since stimulants can cause excitement and may make a precise diagnosis difficult.

Data from the Epidemiologic Catchment Area (ECA) study<sup>9</sup> show that more than 60% of bipolar I patients have a lifetime history of substance abuse. Of these patients, alcohol abuse alone represents 33%, and alcohol and drug abuse is 43%. Thus, alcohol abuse is found in over 70% of bipolar I patients with a history of substance abuse. Drug abuse alone represents a relatively smaller percentage of

the substance-abusing bipolar I subjects (25%). There is a sevenfold increased risk for substance abuse in bipolar I patients over the general population.<sup>9,10</sup>

Substance abuse is slightly less common in bipolar II patients. Forty-nine percent have a history of substance abuse, with alcohol abuse being present in the histories of about 80% of these patients.<sup>9,10</sup>

Substance abusers can demonstrate excited symptoms. However, the prevalence of mania in alcoholic patients is a relatively low 2% to 4%.<sup>10</sup> Further, although surveys of drug abuse treatment programs suggest that excited symptoms are much more common, the bipolar-like states are often relatively mild, with patients often having diagnoses of bipolar II, cyclothymia, or so-called hyperthymia. A recent study of depressive symptoms in alcoholic versus affective disorder patients revealed lower overall ratings of depression in primary alcoholic patients with or without affective disorder than in primary affective disorder patients with or without alcoholism.<sup>11</sup> Depressive symptoms tended to remit without medication in the primary alcoholic—but not in the affective disorder—patients over a 3- to 4-week period.

The occurrence of substance abuse in a bipolar patient may have significant implications for age at onset, course, and treatment. Bipolar disorder with comorbid substance abuse is more commonly seen in men than in women,<sup>12</sup> and in these patients, the average age at onset of the bipolar disorder is about 20 years, several years earlier than in bipolar patients without alcoholism.<sup>12,13</sup> Individuals with comorbid bipolar disorder and alcoholism generally have the onset of the primary disorder at age 20 and the secondary disorder at age 27. In an important family study, Winokur and colleagues<sup>12</sup> argued that family members with alcoholism frequently had bipolar disorder that was not diagnosed.

Treatment response can be affected by the presence of substance abuse. O'Connell and colleagues,<sup>14</sup> in a review of their experiences in a lithium clinic, reported that 36% of poor lithium responders had a history of alcohol abuse, in contrast with a 7% prevalence of alcohol abuse in those who largely showed a good response. Tohen and colleagues,<sup>15</sup> in a study of first episode bipolar patients treated largely with lithium, reported on follow-up extremely high rates of recurrence in a small group of alcoholic bipolar patients. In contrast, Brady and Sonne<sup>10</sup> reported that divalproex sodium was effective in alcoholic bipolar patients over a 12-week period. Both mood stabilization and a decrease in alcohol consumption were observed. One possible explanation is that over 90% of these patients demonstrated dysphoric mania, which may be more responsive to anticonvulsant therapy.<sup>5</sup> Other studies have reported that improvement of bipolar disorder in patients during the pre-anticonvulsant era was often accompanied by a decrease in alcohol abuse.<sup>12</sup> Further studies are required in this area to determine optimal treatments.

The assessment of a bipolar patient must include a review of substance abuse history. Use of a structured instrument (i.e., the substance abuse sections of the Structured Clinical Interview for DSM-III-R [SCID], CAGE, or Michigan Alcoholism Screening Test [MAST]) can assist in making a diagnosis. In a study of consecutive admissions to Massachusetts Mental Health Center, my colleagues and I reported<sup>16</sup> that urine drug screening was far less effective in establishing a diagnosis of substance abuse than was administering structured questions about substance use/abuse from the patient version of the SCID. Thus, clinicians should rely more on direct interview than on urine or blood screens. When interviewing patients, using questions from a structured interview allows for asking precise questions about agents used, how much, when, and the effects. This interview should also include questions that determine age at onset of both affective disorder and substance use/abuse to determine which is the primary disorder, which may help in assessing the need for rehabilitation treatment for the substance abuser. Commonly, stabilization of a patient with primary bipolar disorder will result in a reduction of substance use/abuse. This may occur even without direct treatment of the substance abuse, other than detoxification. Conversely, patients with primary substance abuse and dependence will generally require rehabilitation treatment.

### DIAGNOSTIC DEBATES

Before the advent of lithium carbonate as an effective treatment for bipolar disorder, many patients with psychotic manic-depressive illness were misdiagnosed as suffering from a schizophrenic disorder.<sup>1,17</sup> This was more common in the United States than in the United Kingdom.<sup>17</sup> In a major review of the literature, Pope and Lipinski<sup>18</sup> argued that previous history course, rather than cross-sectional psychotic symptoms, needed to be emphasized in establishing the correct diagnosis. Today, it is well established that many manic patients in so-called Stage III mania may exhibit disorganized thinking and behavior similar to that seen in schizophrenic patients. Increased awareness of this similarity has led to more accurate diagnoses and to the use of thymoleptic agents rather than neuroleptics.

The process of developing effective agents for a particular syndrome, however, may result in a propensity to overdiagnose that syndrome in the attempt at using a potentially effective agent or to conceptualize other disorders as being forms of the particular syndrome. These occurrences can be confusing for the field. Unfortunately, some—if not many—patients demonstrate symptoms that are suggestive of one or more disorders but that do not fit neatly into one of our standard categories. How to diagnose these patients properly can present a quandary. Improper diagnosis can lead to poor or ineffective treatment.

Without powerful diagnostic tests or genetic markers, we may not be able to answer the many diagnostic questions that commonly arise. Currently, two diagnostic questions are encountered in evaluating patients with possible bipolar disorders: the differential diagnosis between agitated depression and mixed mania, and the relationship between bipolar disorder and ADHD.

### Agitated Depression Versus Mixed Mania

Patients with major depression commonly demonstrate either psychomotor retardation or agitation or both. Agitation of at least a mild form has been reported to be present in 30% of a group of patients with major depression with a wide range of severity and in 67% of a group of patients with moderate to severe depression.<sup>19</sup> Agitated major depressive patients can sometimes appear to have bipolar-like features (e.g., decreased ability to sleep), and some clinicians may choose to conceptualize their disorders as being bipolar. However, most agitated depressives do not simultaneously meet criteria for mania and major depression, and there are a number of key differences in the seeming overlap of symptoms. For example, manic or mixed patients may demonstrate a decreased need for sleep whereas agitated depressive patients often complain of insomnia. The increased thinking in an agitated depressed patient is often seen at particular times of the day (e.g., when trying to fall asleep) and often involves ruminations about negative perceptions of self; the bipolar patient has generally increased thinking. (Increased speech is more commonly observed in bipolar disorder than in agitated depression.) Both types of patients are distractible, but in the agitated depressed patient, it may be due to preoccupation with depressive thoughts, and in the bipolar patient, it may be environmentally triggered. Too, both patients may demonstrate increased motor activity, but in the depressed patient, it is generally purposeless and unpleasant (e.g., pacing) and may be accompanied by an inability to concentrate or by psychomotor retardation. In the manic or mixed-state patient, the increased activity itself is often aimed at some grandiose or expansive goal and is seen as positive at some point in the episode.

Whether increased activity in agitated depressive patients is due to a similarly altered biology of a specific brain system or pathway as in bipolar disorder remains to be determined. Carroll<sup>20</sup> has elegantly articulated three neurobiological systems or functions that can help separate depressed and manic patients: reinforcement/reward, central pain, and psychomotor regulation. This type of approach may help us to understand how a patient may show excited features (i.e., increased activity) while still appearing otherwise to be depressed. More specifically, such patients may demonstrate typical depressive characteristics of the reinforcement/reward dimension (e.g., inhibition and anhedonia) and the central pain dimension (e.g., distress to usually nonaversive events) but not in the psycho-

motor dimension where they are, in a sense, more active. Dimensional approaches to classification may help clear up some of the confusion inherent in applying strict categorical criteria.

### ADHD Versus Bipolar Disorder

The past decade has witnessed a growing increased awareness regarding ADHD in both children and adults. The relationship between ADHD and bipolar disorder has become an area of increasing research. A number of investigators have observed relatively high current or lifetime rates of ADHD or symptoms of the disorder in bipolar youths and adults. Winokur et al.<sup>21</sup> noted that bipolar adults reported higher rates (> 20%) of ADHD symptoms in their childhood than did their unipolar depressed (about 9%) counterparts. Similarly high rates of a history of ADHD symptoms have also been reported in a study by Strober and colleagues<sup>22</sup> in adolescents with bipolar I disorder. More recently, West and colleagues<sup>23</sup> reported that 57% of a small group of adolescent manic patients met criteria for comorbid ADHD. In a longitudinal study, Biederman and colleagues<sup>24</sup> noted that bipolar disorder was present at baseline in 11% of ADHD children, but an additional 12% met criteria for bipolar disorder at 4-year follow-up. Healthy controls demonstrated significantly lower rates of bipolar disorder at both baseline (0%) and follow-up (1.8%). The increased risk of bipolar disorder did not appear to be due to an overlap in symptom criteria. These data suggest that ADHD may be a risk factor for bipolar disorder, or alternatively that bipolar disorder may start with attentional problems in childhood or adolescence.

The presence of this comorbidity has implications for the presentation and outcome. Adolescent manic patients with ADHD frequently demonstrate mixed states and have higher mania ratings than do bipolar disorder patients without ADHD.<sup>24</sup> Conversely, children with primary ADHD and secondary bipolar disorder more commonly demonstrate other psychiatric comorbidity and are more impaired than are their ADHD-only counterparts. Manias tend to be marked by irritability and mixed symptoms.

In adults, the possibly overlapping picture can be quite confusing to clinicians. Whereas some 20% of adult bipolar patients may report attentional problems in childhood, it is not always clear whether these symptoms were (or are) clinically significant, or moreover whether they truly represented a syndrome separate from the early manifestations of the bipolar disorder itself. This may be particularly true in milder forms of bipolar illness where there can be questions regarding the affective disorder diagnosis. An accurate diagnosis is of practical importance since stimulants could provoke excitement in bipolar patients, particularly in the absence of thymoleptic treatment. The development of a sensitive rating instrument for measuring adult ADHD has been reported<sup>25</sup>; however, in

that study, adult ADHD subjects were not compared with bipolar patients. Thus, today we do not have an easy method for distinguishing ADHD from bipolar disorder, particularly in adults. In children, Weller and colleagues<sup>26</sup> have argued that bipolar manic or hypomanic patients demonstrate a decrease in their need for sleep and difficulty falling asleep that are different from their baseline, whereas in ADHD patients such symptoms are chronic and represent the usual pattern. This diagnostic dilemma is likely to continue for some time, particularly in view of the growing use of the ADHD diagnosis. Ultimately, the solutions rest with identifying genetic markers and specific neuropsychological test profiles for both disorders.

*Drug names:* divalproex sodium (Depakote), prednisone (Delta-Dome and others).

### REFERENCES

1. Akiskal HS. The prevalent clinical spectrum of bipolar disorders: beyond DSM-IV. *J Clin Psychopharmacol* 1996;16(suppl 1):4S-14S
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
3. Bauer MS, Whybrow PC, Winokur A. Rapid cycling bipolar affective disorder I: association with grade I hypothyroidism. *Arch Gen Psychiatry* 1990;47:427-432
4. Wehr TA, Goodwin FK. Can antidepressants cause mania and worsen the course of affective illness? *Am J Psychiatry* 1987;144:1403-1411
5. Bowden CL, Brugger AM, Swann AC, et al. Efficacy of divalproex vs lithium and placebo in the treatment of mania. *JAMA* 1994;271:918-924
6. Secunda SK, Katz MM, Swann A, et al. Mania: diagnosis, state measurement and prediction of treatment response. *J Affect Disord* 1985;8: 113-121
7. Himmelhoch JM, Malla D, Neul JF, et al. Incidence and significance of mixed affective states in a bipolar population. *Arch Gen Psychiatry* 1976; 33:1062-1066
8. Krauthammer C, Klerman GL. Secondary mania: manic syndromes associated with antecedent physical illness or drugs. *Arch Gen Psychiatry* 1978; 35:1333-1339
9. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) study. *JAMA* 1990;26:2511-2518
10. Brady KT, Sonne SC. The relationship between substance abuse and bipolar disorder. *J Clin Psychiatry* 1995;56(suppl 3):19-24
11. Brown SA, Inaba BA, Gillin JC, et al. Alcoholism and affective disorder: Clinical course of depressive symptoms. *Am J Psychiatry* 1995;152:45-52
12. Winokur G, Coryell W, Akiskal HS, et al. Alcoholism in manic-depressive (bipolar) illness: familial illness, course of illness, and the primary-secondary distinction. *Am J Psychiatry* 1995;152:365-372
13. Sonne SC, Brady KT, Morton WA. Substance abuse and bipolar affective disorder. *J Nerv Ment Dis* 1994;182:349-352
14. O'Connell RA, Mayo JA, Flatow L, et al. Outcome of bipolar disorder in long-term treatment with lithium. *Br J Psychiatry* 1991;159:123-129
15. Tohen M, Wateraux CM, Tsuang MT, et al. Four-year follow-up of twenty-four first-episode manic patients. *J Affect Disord* 1990;19:79-86
16. Albanese M, Bartel R, Bruno R, et al. Comparison of measures used to determine substance abuse in an inpatient psychiatric population. *Am J Psychiatry* 1994;151:1077-1078
17. Cooper JE, Kendell RE, Gurland BJ, et al. *Psychiatric diagnosis in New York and London: a comparative study of mental hospital admissions*. London, England: Oxford University Press; 1972
18. Pope HG Jr, Lipinski J. Diagnosis in schizophrenia and manic-depressive illness: a reassessment of the specificity of "schizophrenic" symptoms in the light of current research. *Arch Gen Psychiatry* 1978;35:811-828
19. Schatzberg AF, DeBattista C, DeGolia S. Valproate in the treatment of agitation associated with depression. *Psychiatric Annals* 1996;26(suppl):

- S470-S473
20. Carroll BJ. Brain mechanism in manic depression. *Clin Chem* 1994;30: 303-308
  21. Winokur G, Coryell W, Endicott J, et al. Further distinctions between manic-depressive illness (bipolar disorder) and primary depressive disorder (unipolar depression). *Am J Psychiatry* 1993;150:1176-1181
  22. Strober M, Morrell W, Burrough J, et al. A family study of bipolar I disorder in adolescence: early onset of symptoms linked to increased familial loading and lithium resistance. *J Affect Disord* 1988;15:255-268
  23. West SA, McElroy SL, Strakowski SM, et al. Attention deficit hyperactivity disorder in adolescent mania. *Am J Psychiatry* 1995;152:271-273
  24. Biederman J, Faraone S, Mick E, et al. Attention-deficit hyperactivity disorder and juvenile mania: an overlooked comorbidity? *J Am Acad Child Adolesc Psychiatry* 1996;35:997-1008
  25. Ward MF, Wender PH, Reinherr FW. The Wender Utah Rating Scale: an aid in the retrospective diagnosis of childhood attention deficit hyperactivity disorder. *Am J Psychiatry* 1993;150: 885-890
  26. Weller EB, Weller RA, Fristad MA. Bipolar disorder in children: misdiagnosis, underdiagnosis, and future directions. *J Am Acad Child Adolesc Psychiatry* 1995;34:709-714

© Copyright 1998 Physicians Postgraduate Press, Inc.  
One personal copy may be printed