Management of Bipolar Disorder

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Bipolar disorder most commonly is diagnosed in persons between 18 and 24 years of age. The clinical presentations of this disorder are broad and include mania, hypomania and psychosis. Frequently associated comorbid conditions include substance abuse and anxiety disorders. Patients with acute mania must be evaluated urgently. Effective mood stabilizers include lithium, valproic acid and carbamazepine. A comprehensive management program, including collaboration between the patient's family physician and psychiatrist, should be implemented to optimize medical care. (Am Fam Physician 2000;62:1343-53, 1357-8.)

A patient information handout on bipolar disorder, written by the authors of this article, is provided on page 1357.

ACF This article exemplifies the AAFP 2000 Annual Clinical Focus on mental health.

Bipolar disorder is characterized by variations in mood, from elation and/or irritability to depression. This disorder can cause major disruptions in family, social and occupational life. Bipolar I disorder is defined as episodes of full mania alternating with episodes of major depression. Patients with mania often exhibit disregard for danger and engage in high-risk behaviors such as promiscuous sexual activity, increased spending, violence, substance abuse and driving while intoxicated.

Bipolar II disorder is characterized by recurrent episodes of major depression and hypomania. Hypomania is manifested by an elevated and expansive mood. The behaviors characteristic of hypomania are similar to those of mania but without gross lapses of impulse and judgment. Hypomania does not cause impairment of function and may actually enhance function in the short term.

Bipolar I disorder is typically diagnosed when patients are in their early 20s. Manic symptoms can rapidly escalate over a period of days and frequently follow psychosocial stressors. Some patients initially seek treatment for depression. Other patients may appear irritable, disorganized or psychotic. Differentiating true mania from mania resulting from secondary causes can be challenging (*Table 1*).[1,2]

Bipolar II disorder typically is brought to medical attention when the patient is depressed. A careful history will usually illuminate the diagnosis. Some depressed patients exhibit hypomania when given antidepressants.[3] This variation is sometimes referred to as bipolar III disorder. The criteria for major depressive episode and manic episode, as described in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV), are summarized in *Table 2*.[4]

TABLE 1
Causes of Secondary Mania

Substance abuse	**Toxic metabolic states**
Amphetamines	Hyperthyroidism
Caffeine	Electrolyte abnormalities
Cocaine	**Central nervous system disorders**
Over-the-counter diet pills (e.g., phenylpropanolamine)	Multiple sclerosis
Methylphenidate (Ritalin)	Brain tumor
Drug withdrawal states	Sleep deprivation
Ethanol	Structural damage to right (non-dominant) hemisphere
Monoamine oxidase inhibitors	Temporal lobe (complex partial) seizures
Sympathomimetic agents	**Infections**
Tricyclic antidepressants	Encephalitis
Therapeutic agents	Syphilis of the central nervous system
Isoniazid	Sepsis
Levodopa	
Monoamine oxidase inhibitors	
Steroids	
Tricyclic antidepressants	

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TABLE 2

Criteria for Major Depressive Episode and Manic Episode

Major depressive episode

Five or more of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). Note: In children and adolescents, can be irritable mood.
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains.
4. Insomnia or hypersomnia nearly every day
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6. Fatigue or loss of energy nearly every day
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
8. Diminished ability to think or concentrate, or indeciseveness, nearly every day (either by subjective account or as observed by others)
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

Manic episode

A. A distinct period of abnormally and persistently elevated, expansive , or irritable mood, lasting at least 1 week (or any duration if hospitalization is necessary)

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

1. Inflated self-esteem or grandiosity
2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
3. More talkative than usual or pressure to keep talking
4. Flight of ideas or subjective experience that thoughts are racing
5. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
7. Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

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Epidemiology

The lifetime prevalence of bipolar disorder is 1 percent, which compares to a lifetime prevalence of 6 percent for unipolar depression.[5] The prevalence of bipolar disorder does not differ in males and females.[6] The disorder affects persons of all ages. The epidemiologic catchment area study revealed the highest prevalence in the 18-to-24-year age group.[7] In some patients, however, bipolar disorder does not become manifest until patients are older. One study reported new-onset bipolar disorder in patients older than 60 years.[8]

The incidence of bipolar disorder is increased in first-degree relatives of persons with the disorder, as is the incidence of other

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mood disorders.[9] One study revealed a 13 percent risk of bipolar disorder among offspring of persons with the disorder.[10] The risk of unipolar depression was 15 percent, and the risk of schizoaffective disorder was 1 percent.[10] The mode of inheritance remains unclear, and no algorithm exists to predict the risk of bipolar disorder.[11] Because of the familial association, genetic counseling should be offered to patients and their families as part of comprehensive educational and supportive approaches.

Clinical Presentations

Patients with symptoms of a mood disorder often do not meet the full criteria for bipolar disorder. Many patients with bipolar disorder are diagnosed as having depression. If agitation is prominent, hypomanic symptoms may be misunderstood as representing an anxiety state. Accurate diagnosis of bipolar disorder requires obtaining a comprehensive psychiatric history.

CHILDREN

Hyperactivity is the most common behavioral manifestation of mania in children.[12] Manic children may exhibit irritability or temper tantrums.[13] The differential psychiatric diagnoses include attention-deficit/hyperactivity disorder, conduct disorder and schizophrenia.[14]

ADOLESCENTS

Manic symptoms in adolescents are similar to those in adults. Florid psychosis can be a presentation of bipolar disorder in adolescents. Included in the differential diagnosis of mania in adolescents are substance abuse and schizophrenia, which may be challenging to distinguish from bipolar disorder. The normal risk-taking behavior in some adolescents must be distinguished from the reckless nature of manic symptoms.

DURING PREGNANCY

The course of bipolar disorder during pregnancy is variable. Management requires sustained collaboration between the patient's family physician and her psychiatrist. A patient with bipolar disorder should be encouraged to plan pregnancy so that the dosage of her psychiatric medication can be slowly tapered. The risk of relapse is increased with abrupt discontinuation.[15]

If agitation is prominent in bipolar disorder, hypomanic symptoms may be misunderstood as reflecting an anxiety state.

Relapse during pregnancy must be treated aggressively with mood stabilizers. The patient should be admitted to the hospital. If lithium therapy is required, the patient should be counseled regarding the increased risk of cardiovascular malformations in fetuses exposed to lithium. Breast-feeding during lithium therapy is discouraged because lithium is excreted in breast milk.[16]

During the postpartum period, worsening of affective symptoms may occur, including rapid cycling, which is sometimes refractory to drug therapy.[17] Women who have worsening of symptoms postpartum may have an increased risk of recurrence.

Comorbid Conditions

Studies of primary care patients with major depressive disorders have demonstrated a tendency toward certain comorbid conditions. In one study,[18] more than 42 percent of patients meeting the criteria for a major depressive disorder (including bipolar disorder) had lifetime histories of substance abuse. In another study,[19] the frequency of substance abuse was 39 percent in adolescents who had symptoms of bipolar disorder. Another study[20] revealed a high prevalence of moderate to severe anxiety disorders in association with bipolar disorder, as well as a high prevalence of psychosocial morbidity.

While many patients with bipolar disorder show gradual improvement in the first several years after diagnosis, a substantial subgroup experiences poor adjustment in one or more

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Patients presenting with acute mania should be evaluated urgently; appropriate transportation of the patient from the office to the hospital must be arranged.

areas of functioning.[21] In a study of psychiatric patients who were evaluated 30 to 40 years after the index hospitalization for mania, 24 percent of the sample was considered to be occupationally incapacitated.[22]

Treatment

URGENT AND EMERGENT

If a patient with symptoms of acute mania presents to the office, a psychiatrist should be consulted, and the patient should be evaluated urgently. The family physician must know the legal requirements in the community for transferring a patient with acute mania from the office to the hospital. Often, police must be involved. It is inappropriate to expect family members to transport the patient from the office to the hospital, because family members may not appreciate the irrationality of manic thinking and the unpredictability of manic behavior.

The family physician and psychiatrist have the responsibility to inform, educate and support family members in terms of the possible need for the family to petition the court for the patient's admission to a psychiatric unit. It is important to recognize, and to try to allay, the guilt and regret family members often feel in these circumstances.

Patients with newly diagnosed bipolar disorder require a medical evaluation along with a psychiatric evaluation. *Table 3*[2,3] lists the recommended laboratory tests for patients evaluated on an inpatient or an outpatient basis. Computed tomography or magnetic resonance imaging and electroencephalography are second-line options in the evaluation of treatment-resistant patients. These studies are not routinely required without a specific clinical reason. Similarly, the need for electrocardiography in patients younger than 40 years rests with the clinician's judgment.

If necessary, and if the patient has been in good general health, mood stabilizers, as well as other drugs used in the treatment of bipolar disorder, can be started before the test results are available. If the need to begin treatment is urgent, medication can be given even before laboratory specimens are obtained.

COLLABORATIVE ONGOING CARE

Given the chronic nature of bipolar disorder and its impact on the entire family, it is

TABLE 3

Laboratory Evaluation of Patients Presenting with Bipolar Disorder

Inpatient

- Complete physical examination
- Serum levels of lithium, valproic acid (Depakene), carbamazepine (Tegretol) and selected tricyclic antidepressants (if relevant)
- Thyroid function tests
- Complete blood count and general chemistry screening
- Urinalysis if lithium therapy is initiated
- Electrocardiography in patients older than 40 years
- Urine toxicology for substance abuse
- Pregnancy test (if relevant)

Outpatient

- Complete physical examination
- Serum levels of lithium, valproic acid, carbamazepine and selected tricyclic antidepressants (if relevant)
- Thyroid function tests
- Complete blood count and general chemistry screening
- Urinalysis if lithium therapy is initiated
- Pregnancy test (if relevant)
- Second-line tests: urine toxicology for substance abuse and electrocardiography in patients older than 40 years

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important for the patient's family physician and psychiatrist to develop an effective and collaborative relationship. Informed collaboration depends on an agreed method of communication in a frequency that meets the needs of each physician.[24] A Canadian model brings psychiatrists and counselors into family practice offices for shared care.[25]

At the onset of bipolar disorder, the family physician might seek psychiatric consultation for differential diagnosis and treatment recommendations. Often, the psychiatrist assumes responsibility for initial management until the patient's clinical pattern is determined. During follow-up, both physicians should monitor the patient for signs of psychosis, mood swings, violence and self-harmful behaviors. As the patient's illness stabilizes and management becomes routine, the physicians can renegotiate, with each other and with the patient, responsibility for ongoing care.

When the patient's condition has become stable, the psychiatrist may not need to see the patient as often, although the frequency of follow-up psychiatric visits depends on the course of the illness, the patient's adherence to treatment, medication requirements, the need for ongoing psychotherapy and patterns of care in a particular geographic area. It is important for the patient's family physician and psychiatrist to coordinate medication prescriptions and follow-up laboratory tests such as determination of serum drug levels. In addition, counseling and family therapy are important components of management and may be rendered by the family physician, psychiatrist and/or psychologist.

MEDICATION

Recommendations for drug therapy in patients with bipolar disorder are summarized in *Table 4*.[23]

Medication is the key to stabilizing bipolar disorder. Initial treatment of mania consists of lithium or valproic acid (Depakene). If the patient is psychotic, a neuroleptic medication

Tricyclic antidepressants may induce rapid cycling of symptoms.

is also given. Long-acting benzodiazepines may be used for treating agitation. However, in patients with a substance-abuse history, benzodiazepines should be used with caution

TABLE 4

Recommendations for Drug Therapy in Patients with Bipolar Disorder

Considerations for prescribing mood stabilizers

Lithium: For classic, euphoric mania; for mixed manic episode; when a mood stabilizer alone is used to treat depression; when the mood stabilizer must be given in a single evening dose; in patients with liver disease, excessive alcohol use or cocaine use; and in patients older than 65 years

Valproic acid (Depakene): For classic, euphoric mania; for mixed manic episode; for mania with rapid cycling; for long-term maintenance therapy in patients who do not tolerate lithium because of the "flat" feeling lithium causes; in patients with structural central nervous system disease, renal disease and cocaine use; and in patients older than 65 years

Carbamazepine (Tegretol): For mixed manic episode; for mania with rapid cycling; in patients with structural central nervous system disease or renal disease

An antipsychotic agent

High- or medium-potency antipsychotic agents are used as adjunctive treatment for mania with psychosis or psychotic depression.

A benzodiazepine

Sleep and sedation in mania or hypomania; insomnia in depression

The combination of a mood stabilizer, an antidepressant and an antipsychotic

Psychotic depression

The combination of a mood stabilizer and an antidepressant

Nonpsychotic depression

A mood stabilizer alone

Milder depression in bipolar I disorder

Bupropion (Wellbutrin)

Bipolar depression

Patient with high risk of manic switch or rapid cycling

A selective serotonin reuptake inhibitor

Bipolar depression

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