CLINICAL REPORT

Collaborative Role of the Pediatrician in the Diagnosis and Management of Bipolar Disorder in Adolescents

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abstract

Despite the complexity of diagnosis and management, pediatricians have an important collaborative role in referring and partnering in the management of adolescents with bipolar disorder. This report presents the classification of bipolar disorder as well as interviewing and diagnostic guidelines. Treatment options are described, particularly focusing on medication management and rationale for the common practice of multiple, simultaneous medications. Medication adverse effects may be problematic and better managed with collaboration between mental health professionals and pediatricians. Case examples illustrate a number of common diagnostic and management issues. Pediatrics 2012;130:e1725–e1742

Pediatricians are faced with increasing numbers of patients diagnosed with bipolar disorder and taking multiple psychotropic medications. In addition, pediatricians may be seeing these patients long before they are diagnosed and treated by a child and adolescent psychiatrist or other mental health professional. Pediatric bipolar disorder, once thought to be rare in adolescents and nearly nonexistent in younger children, has been diagnosed increasingly over the past decade.1–3 In 2004, bipolar disorder accounted for 26% of primary discharge diagnoses among psychiatrically hospitalized adolescents in the United States.3 Bipolar spectrum disorders,4 encompassing the several types of bipolar disorder, have an estimated prevalence of 4% of children and adolescents in the general population.5 The diagnosis remains controversial, and there has been a shift in how the diagnosis has been defined in youth.1 Associated impairments may include severe depression, high risk of suicide, psychosis, impulsive and dangerous behaviors, social and cognitive deficits, and frequent comorbidity with other psychiatric disorders, including substance use disorders, attention-deficit/hyperactivity disorder (ADHD), anxiety disorders, oppositional defiant disorder, and conduct disorder. Insight is frequently diminished, with youth vehemently blaming others for their difficulties and having little recognition of their own disruptive symptoms.1 Management of these youth is additionally complicated by medication limitations, including troublesome adverse effects, lack of full response and the resultant common prescription of multiple medications, and incomplete prevention of relapse.1 Not surprisingly, poor adherence to prescribed dosing is common.6
This report is not expected to give general pediatricians the tools necessary to diagnose and manage these complex cases independently. Some specific techniques are described with the intent of facilitating partnerships between pediatricians and child and adolescent psychiatrists and other mental health professionals. Additional goals include improved understanding of diagnosis and treatment; earlier referral of new, suspected cases, and patients with symptom relapse or worsening; and assistance in recognizing and managing medication adverse effects.

The focus of this report is diagnosis and management of adolescents with bipolar disorder. Children are mentioned as well when the subject matter applies to them.

CLASSIFICATION

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) describes 4 types of bipolar disorders, all without age limitations: bipolar I disorder, bipolar II disorder, cyclothymic disorder, and bipolar disorder not otherwise specified. Manic symptoms are the key feature of these diagnoses; Tables 1, 2, and 3 provide criteria for mania, hypomania, and mixed episodes. A key criterion is duration: the minimum duration for mania and mixed episodes is 7 days and for hypomania is 4 days.

Bipolar I Disorder

Bipolar I disorder is the “classic” form of the disorder and requires a current or past manic or mixed episode. At any given time, the patient may be in a manic, hypomanic, mixed, or major depressive episode or may have fully or partially recovered from the last mood episode. Notably, this is a historical diagnosis because the patient may be in any current mood state and still meet this criterion. History of a depressive episode is common but not required. Other criteria are that the mood symptoms cause significant distress or impaired functioning; are not better accounted for by schizoaffective disorder or superimposed on schizophrenia, schizophreniform disorder; delusional disorder, or psychotic disorder not otherwise specified; and are not the effect of a substance (including medications) or general medical condition.

TABLE 1 Diagnostic Criteria for a Manic Episode

- A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 wk (or for any duration if hospitalization is necessary)
- During the period of mood disturbance, 3 (or more) of the following symptoms have persisted (4 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 (eg, feels rested after only 3 h)
  3. More talkative than usual or pressure to keep talking
  4. Flight of ideas or subjective experience that thoughts are racing
  5. Distractibility (ie, 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 (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

DSM-IV-TR asks for specified patterns, including longitudinal course as with or without full interepisode recovery and/or rapid cycling. Rapid cycling is defined as more than 4 mood changes in a year. Researchers have defined patterns that commonly apply to pediatric bipolar disorder, including ultrarapid cycling, episodes lasting a few days to a few weeks, and ultradian cycling, variation occurring within a 24-hour period.

Bipolar II Disorder

Depression typically is the major problem in bipolar II disorder. A current or at least 1 past major depressive episode is required, and the patient must have a current or past episode of hypomania with no manic or mixed episodes at any time. That is, currently or historically, a patient with bipolar I disorder has big “ups” (mania) and may or may not have “downs” (depression). A patient with bipolar II disorder has little “ups” (hypomania) plus big “downs” (major depression).

Cyclothymic Disorder

Cyclothymic disorder is characterized by relatively mild but chronic symptoms (hypomanic and depressive symptoms) that last at least 2 years (1 year with children and adolescents) before any full manic, mixed, or major depressive
episodes. These patients have little “ups” (hypomania) and little “downs” (dysthymia), but the disorder is chronic.

**Bipolar Disorder Not Otherwise Specified**

DSM-IV-TR describes the category of bipolar disorder not otherwise specified as including, “disorders with bipolar features that do not meet criteria for any specific bipolar disorder.” The American Academy of Child and Adolescent Psychiatry recommends using this diagnosis for youth with manic symptoms lasting hours to days or for those with chronic manic-like symptoms. These youth may be significantly impaired and constitute the majority of those referred to mental health professionals. Emerging evidence suggests that this disorder is on a continuum with bipolar I disorder, and 45% of patients converted to bipolar I or bipolar II disorder at follow-up an average of 5 years later, particularly patients with a family history of bipolar disorder.

**Beyond DSM-IV-TR**

Akiskal and Pinto described a bipolar spectrum in adults, ranging from bipolar I disorder to hyperthymic temperament. The disorders and conditions on the spectrum share symptom characteristics that generally responded better to mood-stabilizing medication than to antidepressant medication.

Leibenluft et al suggested research diagnostic criteria for 3 clinical phenotypes of pediatric bipolar disorder: narrow, intermediate, and broad. These criteria are included in this report to illustrate important features of diagnosis that are not present in DSM-IV-TR; they should not be construed as generally accepted by physicians or researchers. Narrow phenotype refers to a disorder in which, for at least 1 episode, full DSM-IV-TR criteria are met, including duration criteria, and elation and/or grandiosity also is present. Elation and grandiosity were argued by Geller et al to be core bipolar features. Intermediate phenotype refers to patients with episodes that met full DSM-IV-TR criteria but lacked duration criteria (episodes too short) or had mania/hypomania that was irritible rather than euphoric. This phenotype still includes mood cycling as a required feature. Broad phenotype refers to a disorder characterized by chronic irritability and hyperarousal and does not include mood cycling. Compared with their peers, children and adolescents who have the broad phenotype show markedly increased reactivity to negative emotional stimuli. The broad phenotype has been referred to as severe mood dysregulation (SMD).

SMD among children 9 to 19 years of age has a lifetime prevalence of 3.3%, with most affected children having comorbid psychiatric disorders, most frequently disruptive behavior disorders (ADHD, conduct disorder, and oppositional defiant disorder). Children with SMD were 7 times more likely to develop depression as young adults compared with those without SMD. Compared with children with narrow phenotype bipolar disorder, subjects with SMD had different psychopathological measures and were less likely to have parents with bipolar disorder, suggesting that SMD is a disorder distinct from narrow phenotype bipolar disorder.

Mood diagnoses continue to evolve. The development web site for the forthcoming Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, lists an additional proposed mood diagnosis of “disruptive mood dysregulation disorder,” characterized by severe recurrent temper outbursts in response to common stressors and similar to the broad phenotype. Characteristics for this diagnosis as well as others on the development Web site have been changing in response to public feedback. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, is expected to be published in May 2013. Because the final version may be fairly different, this report...
TABLE 6  Research Criteria for Broad Phenotype of Juvenile Mania: Severe Mood and Behavioral Dysregulation

A. Inclusion criteria
a. Age 7–17 y, with onset of symptoms before age 12
b. Abnormal mood present at least half of the day most days and of sufficient severity to be noticeable by people in the child’s environment
c. Hyperarousal, as defined by at least 3 of the following symptoms: insomnia, agitation, distractibility, racing thoughts or flight of ideas, pressured speech, intrusiveness
d. Compared with his/her peers, the child exhibits markedly increased reactivity to negative emotional stimuli that is manifest verbally or behaviorally
e. The symptoms noted in the previous 3 items are currently present and have been present for at least 12 mo without any symptom-free periods exceeding 2 mo in duration
f. The symptoms are severe in at least 1 setting and at least mild symptoms in a second setting

B. Exclusion criteria
a. The individual exhibits any of the cardinal bipolar symptoms: elevated or expansive mood, grandiosity or inflated self-esteem, episodically decreased need for sleep
b. The symptoms occur in distinct periods lasting more than 4 d
c. The individual meets criteria for schizophrenia, schizoaffective illness, pervasive developmental disorder, or posttraumatic stress disorder
d. The individual has met the criteria for substance abuse disorder in the past 3 mo
    e. IQ <80
    f. The symptoms are attributable to the direct physiologic effects of a drug of abuse or to a general medical or neurologic condition

does not include additional mention of diagnoses listed on the development web site.
The balance of this report refers to DSM-IV-TR as well as proposed research diagnoses. Pediatricians should be aware, however, of the changing classification of bipolar and related disorders.

INTERVIEWING FOR MANIA

The presence or history of mania of some sort is the determining factor for a diagnosis of bipolar disorder. Typically, depressive symptoms are also present at some point in the illness and may be the major concern, but depression is not required to be present either currently or historically for a bipolar diagnosis. Depressed patients with bipolar disorder, particularly those with the narrow or intermediate phenotype, may require different medication from those with depression alone, so it is important for the pediatrician or mental health professional to attempt to make this differentiation before initiating pharmacotherapy.

Challenges in Diagnosing Mania

At a minimum, a full psychiatric evaluation should be performed to determine diagnosis.1 A significant problem is that the diagnosis of mania typically is historical. Even with a patient who demonstrates manic symptoms during the interview, the interviewer still needs to determine that the symptoms represent a change, interfere with functioning, and are associated with less evident manic symptoms. Much more often, however, the patient presents as depressed or euthymic, leaving it for the interviewer to tease out groups of symptoms that occur together in episodes and are different from “normal adolescence.” Adolescents and parents may tend to minimize these symptoms, wanting the trouble to be something less serious or, conversely, may tend to exaggerate, grasping at a bipolar diagnosis as a means of explaining a range of difficulties. Much of the public now has some education about bipolar disorder, often just enough to produce misconceptions about the diagnosis and associated symptoms, thus complicating the job of the interviewer.

Simplifications

Without specific training in this area, the general pediatrician should not attempt initiation of treatment in newly diagnosed cases. The goal for the pediatrician in identification, therefore, should be reasonable suspicion rather than diagnosis, followed by referral or seeking an appropriate mental health professional as partner. The balance of this section discusses several historical symptoms that may be considered red flags for the diagnosis. The clear presence of any of these should be considered sufficient for reasonable suspicion.

Red Flag Symptoms

Rage Outbursts or Verbal or Physical Aggression

Rage is not a bipolar symptom per se but is common with adolescents experiencing episodic irritable mania or chronic severe mood dysregulation. In both cases, the adolescent is edgy and easily frustrated and provoked. Questions the interviewer may ask include, “Do you lose your temper?” If so, the adolescent should be asked about frequency, duration, what happens, and what the triggers are (see Table 7 for a summary of examples of interview questions).

Episodes of Requiring Little Sleep

Requiring little sleep needs to be distinguished from going to bed late and getting up late and from receiving less sleep and consequently being tired the next day. Staying up late for 1 night during a sleepover or for a concert also does not count. Adolescents with this symptom have the experience of having high energy, receiving at least 2 hours less sleep per night, and remaining full of energy often after several nights of this.18 Questions include, “Do you ever have nights when you have lots of energy, do not need to sleep much, and do lots of things?” If so, “Are you tired the next day?”
Spontaneous Mood Shifts
The adolescent experiences sudden mood shifts between euthymic, giddy, depressed, or angry, with no evident circumstantial trigger. The giddy, depressed, or angry mood state should significantly interfere with functioning, such as making concentration in school or appropriate behavior with friends much more difficult. A mood shift may happen multiple times per day. Questions include, “Do you find yourself suddenly angry or extremely happy for no apparent reason?” If so, ask about frequency and duration of the moods.

Running Away, Sneaking Out at Night, Spending Money, Hypersexuality
These activities may be categorized as “excessive involvement in pleasurable activities that have a high potential for painful consequences” (Table 1). Running away also may be an example of an impulsive activity related to severe irritability. Questions include, “Have you ever run away or snuck out of the house at night?” “Do you have times when you spend a lot of money or when you feel that you cannot control your sexual urges?”

Grandiosity
Grandiosity is a grossly inflated belief in oneself having special talents or abilities, such as never being in danger regardless of the activity or being the best at a certain sport, or endless talk about a real talent. This must be a change from baseline and does not include a consistent picture of boastfulness or failure to appreciate consequences. Questions include, “Do you have times when you feel that nothing can happen to you?” “Do you have times when you greatly overestimate your talents or abilities?”

Agitation or Mania with Antidepressant
Adverse effects for a patient under the influence of antidepressant medication may be edginess, agitation, or less commonly, frank mania. By definition, a cluster of manic symptoms resulting from a medication or substance is not mania. It is, however, a risk factor for mania either continuing once the medication is withdrawn or mania at another time. Questions include, “Have you ever taken medication for depression?” If so, “Did you have any side effects?” “Did you ever become very edgy or much more happy or angry than is typical for you?”

Any or all of these symptoms may be present currently, recently, or in the more distant past.

TREATMENT
Psychotherapy
Psychotherapeutic interventions are an important component of an overall treatment plan. Interventions should be targeted to the following areas.

Psychoeducation
Information is provided to patient and family on the illness, treatment options, impact on functioning, and heritability. Relapse prevention typically is an important issue. Education is provided regarding importance of treatment adherence, avoidance of precipitating factors, and early recognition of symptoms. The illness may result in a dramatic tendency to blame others and minimize one’s own symptoms and limitations, making engagement in the treatment plan difficult. For some individuals and families, education regarding relapse prevention is the key intervention.

Individual Psychotherapy
Cognitive-behavioral psychotherapy and interpersonal therapy support emotional and cognitive development, coping, and symptom monitoring.

Social and Family Functioning
Interventions aimed at communication and problem solving are needed to address disruptions in family and social relationships.

Academic and Occupational Functioning
Educational planning, specialized educational programs, and occupational training and support may be needed to address disruption of functioning in

TABLE 7 Examples of Interview Questions

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Question examples</th>
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<tr>
<td>Rage outbursts</td>
<td>“Do you lose your temper?” If so, ask about frequency, duration, what happens, what the triggers are.</td>
</tr>
<tr>
<td>Episodes of requiring little sleep</td>
<td>“Do you ever have nights when you have lots of energy, do not need to sleep much, and do lots of things?” If so, “Are you tired the next day?”</td>
</tr>
<tr>
<td>Spontaneous mood shifts</td>
<td>“Do you find yourself suddenly angry or extremely happy for no apparent reason?” If so, ask about frequency and duration of the moods.</td>
</tr>
<tr>
<td>Running away, sneaking out at night, spending money, hypersexuality</td>
<td>“Have you ever run away or snuck out of the house at night?” “Do you have time when you spend a lot of money or when you feel that you cannot control your sexual urges?”</td>
</tr>
<tr>
<td>Grandiosity</td>
<td>“Do you have times when you feel that nothing can happen to you?” “Do you have times when you greatly overestimate your talents or abilities?”</td>
</tr>
<tr>
<td>Agitation or mania with antidepressant</td>
<td>“Have you ever taken medication for depression?” If so, “Did you have any side effects?” “Did you ever become very edgy or much more happy or angry than is typical for you?”</td>
</tr>
</tbody>
</table>
school or work from ongoing or intermittent symptoms.

**Treatment of Comorbidities**

Psychosocial interventions should be aimed at treatment of pre- or coexisting substance abuse disorders, behavioral disorders, anxiety disorders, learning problems, and confounding social issues.

**Inpatient Psychiatric Hospitalization**

Inpatient care typically is aimed at preventing imminent harm to self and others as well as allowing for treatment that could not be accomplished in a less restrictive setting. A common reason for admission is suicidality, including suicidal ideation or a recent attempt. To be at high risk of suicide, the patient need not be thinking of suicide at the time of admission. Mood and behavior may have considerable day-to-day or even minute-to-minute variation; therefore, judgment as to safety should be based on recent thoughts, moods, and behaviors rather than just the current ones and on near-future projection on the basis of possible and sudden occurrence of common adolescent stressors. For example, in an adolescent with recent suicidal behavior and a history of grossly overreacting to negative circumstances, a romantic breakup could be lethal.

Other common reasons for psychiatric hospitalization for harm prevention are recent episodes of severe rage, agitation, or aggression attributable to mood symptoms or manic symptoms accompanied by severe impulsivity in areas that could inadvertently result in self-harm, such as running away or sexual activity with multiple partners. Patients with florid mania or acute psychosis typically require hospitalization even in the absence of overtly dangerous behaviors or ideation because of the high unpredictability of the behavior of afflicted individuals as well as difficulty with treatment adherence at a time when vigorous treatment is indicated.

Partial hospitalization or hospital day treatment is used as a less restrictive, step-down treatment from inpatient care or as step-up treatment from mental health office services. Partial hospitalization does not afford 24-hour monitoring and harm prevention provided with inpatient services but is less disruptive to the patient’s life, less expensive, and gives the patient and family more responsibility for the patient’s care while still providing intensive psychotherapeutic and medical management.

Residential treatment is longer-term, 24-hour-a-day care in a less intensive, typically nonhospital setting, and may be a month to a year or more in duration. Residential care is designed for patients who cannot be safely managed otherwise despite adequate treatment or who have symptoms that require long-term behavioral intervention to effect improvement.

**Psychopharmacology**

Medication management is an important component of treatment of youth with bipolar disorder and is the primary treatment in cases of well-defined mania. The primary medications used to treat patients with bipolar disorder are mood stabilizers, such as lithium; certain anticonvulsant medications, including divalproex, lamotrigine, carbamazepine, oxcarbazepine, gabapentin, and topiramate; and atypical antipsychotics, including aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone, paliperidone, clozapine, asenapine, and iloperidone. Adjunctive medications include antidepressant medications and “typical” antipsychotics, as well as medications for ADHD, anxiety, and insomnia; more information is available from the American Academy of Child and Adolescent practice parameters.

The American Academy of Child and Adolescent Psychiatry recommends basing the medication choice on the following: evidence of efficacy, phase of illness, type of presentation (eg, with psychotic symptoms), safety and adverse effect profile, history of medication response, and patient or family preference. Medication combinations are common, with some patients on 5 or more drugs. See Kowatch et al for a suggested prescribing algorithm.

**Efficacy Studies**

Currently, lithium, aripiprazole, risperidone, olanzapine, and quetiapine are approved by the US Food and Drug Administration (FDA) for use in adolescents with bipolar disorder (Table 8). In addition, divalproex, lamotrigine, carbamazepine, oxcarbazepine, gabapentin, and topiramate have nonmental health pediatric indications, and divalproex, lamotrigine, ziprasidone, and asenapine have indications for treatment of adults with bipolar disorder. Published studies have had mixed results (Tables 9, 10, and 11). Not all studies are available, because pharmaceutical companies are not required to publish their studies even when submitted to the FDA as part of an application for an indication. Lithium, aripiprazole, and olanzapine showed efficacy in published, double-blind, placebo-controlled studies, with open-label, chart review, and comparison studies giving support for use of divalproex, lamotrigine, clozapine, risperidone, quetiapine, and carbamazepine. Notably, divalproex and oxcarbazepine each failed to show efficacy in a double-blind, placebo-controlled study, but given the heterogeneity of this disorder, 1 negative study is not conclusive. Divalproex, lamotrigine, lithium, aripiprazole,
quetiapine, risperidone, and topiramate have shown efficacy in medication combination studies. Kowatch et al. found a medication combination response rate of 80% among patients who did not respond to monotherapy with a mood stabilizer.

**Adverse Effects**

Mood stabilizer (Table 12) and atypical antipsychotic (Table 13) medications have a variety of adverse effects, interactions, and safety concerns. Pediatricians probably need to be most aware of weight gain and metabolic effects common with the atypical antipsychotics, although weight gain is also commonly associated with valproate and, to a lesser extent, lithium. Prescription of atypical antipsychotics in youth for bipolar disorder as well as for psychosis, disruptive behavior disorders, and other mood disorders has increased drastically in recent years. Children and adolescents may be more vulnerable than adults to weight gain from these medications and, thus, likely to be at higher risk of glucose and lipid abnormalities. Weight management potentially can be addressed with suggestions of diet and exercise as well as changing the dose and/or type of medication. Use of metformin may be of some help. Stable patients should be seen by their pediatrician every 4 to 6 months, with more frequent visits when there are active adverse effects, interactions, or safety issues.

The American Diabetes Association published a protocol for use in monitoring for weight gain and metabolic changes in adults treated with atypical antipsychotics, including obtaining personal and family history of related disorders, determining weight and height, determining waist circumference, taking blood pressure, and measuring fasting plasma glucose and fasting lipid profile. Weight should
<table>
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<tr>
<th>Medication</th>
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<th>Ages</th>
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<th>Results</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Divalproex</td>
<td>Wagner et al (2002)</td>
<td>7−19; n = 40</td>
<td>Open-label trial</td>
<td>Response rate 61% with manic symptoms</td>
<td>Manic, mixed, or hypomanic</td>
</tr>
<tr>
<td>Divalproex</td>
<td>Henry et al (2003)</td>
<td>4−18; n = 15</td>
<td>Records review</td>
<td>Response rate 53% after 1 y</td>
<td>Divalproex alone and as add-on</td>
</tr>
<tr>
<td>Divalproex</td>
<td>Wagner et al (2009)</td>
<td>10−17; n = 150</td>
<td>Double-blind</td>
<td>No significant difference from placebo</td>
<td>Manic or mixed</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Chang et al (2006)</td>
<td>12−17; n = 20</td>
<td>Open-label trial</td>
<td>Significant decrease in depression, mania, and aggression</td>
<td>Lamotrigine alone and in combination with other medication</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Pavuluri et al (2009)</td>
<td>8−18; n = 46</td>
<td>Open-label trial</td>
<td>Response rate 72% with manic symptoms and 82% with depressive symptoms</td>
<td>Monotherapy</td>
</tr>
<tr>
<td>Lithium</td>
<td>Strober et al (1990)</td>
<td>13−17; n = 37</td>
<td>Naturalistic prospective follow-up</td>
<td>Relapse rate 3 times higher when lithium discontinued</td>
<td>Lithium alone and in combination with other medication</td>
</tr>
<tr>
<td>Lithium</td>
<td>Geller et al (1988)</td>
<td>12−18; n = 25</td>
<td>Double-blind</td>
<td>Significant response rate difference, 46% versus 8% of placebo group</td>
<td>Bipolar disorder with secondary substance dependence</td>
</tr>
<tr>
<td>Lithium</td>
<td>Kafantaris et al (2003)</td>
<td>12−18; n = 100</td>
<td>Open-label trial</td>
<td>Response rate 63% with manic symptoms</td>
<td>Acute mania</td>
</tr>
<tr>
<td>Lithium</td>
<td>Kafantaris, et al (2004)</td>
<td>12−18; n = 40</td>
<td>Double-blind discontinuation</td>
<td>No significant difference from placebo</td>
<td>Mania with or without psychosis or aggression</td>
</tr>
<tr>
<td>Lithium</td>
<td>Patel et al (2006)</td>
<td>12−18; n = 27</td>
<td>Open-label trial</td>
<td>Response rate 48% with depressive symptoms</td>
<td>Acute bipolar depression</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>Wagner et al (2006)</td>
<td>7−18; n = 116</td>
<td>Double-blind</td>
<td>No significant difference from placebo</td>
<td>Manic or mixed</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Del Bello et al (2002)</td>
<td>5−20; n = 26</td>
<td>Chart review</td>
<td>Response rate 73% for mania and 62% for overall illness</td>
<td>Outpatient with acute manic, mixed, or depressive episode; adjunctive or monotherapy</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Barzman et al (2005)</td>
<td>7−20; n = 25</td>
<td>Chart review</td>
<td>Response rate 64%</td>
<td>Hospitalized with acute manic, mixed, or depressive episode; adjunctive or monotherapy</td>
</tr>
<tr>
<td>Topiramate</td>
<td>DelBello, et al (2005)</td>
<td>6−17; n = 56</td>
<td>Double-blind</td>
<td>Mixed results</td>
<td>Inconclusive; study stopped early when early adult studies failed to show efficacy</td>
</tr>
</tbody>
</table>

*Includes only the most recent studies of divalproex and lithium.*
### TABLE 10
Published Studies of Efficacy of Atypical Antipsychotics for Pediatric Bipolar Disorder

<table>
<thead>
<tr>
<th>Medication</th>
<th>Study</th>
<th>Ages</th>
<th>Type</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>Barzman et al (2004)</td>
<td>5–19; n = 30</td>
<td>Chart review</td>
<td>Response rate 67%</td>
<td>Bipolar or schizoaffective, adjunctive or monotherapy</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Biederman et al (2005)</td>
<td>6–17; n = 41</td>
<td>Records review</td>
<td>71% improvement of manic symptoms</td>
<td>Aripiprazole alone and as add-on</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Biederman et al (2007)</td>
<td>6–17; n = 19</td>
<td>Open-label trial</td>
<td>Significant improvement</td>
<td>Mania</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Tramontina et al (2007)</td>
<td>8–17; n = 10</td>
<td>Open-label trial</td>
<td>Significant improvement</td>
<td>Comorbid bipolar and ADHD, improved both mania and ADHD symptoms</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Tramontina et al (2007)</td>
<td>10–17; n = 29</td>
<td>Double-blind</td>
<td>Significant response rate difference, 44% (10 mg), 64% (30 mg), 26% (placebo)</td>
<td>Manic or mixed</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Biederman et al (2005)</td>
<td>5–6</td>
<td>Open-label trial</td>
<td>Significant improvement</td>
<td>Severe treatment-resistant manic or mixed</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Biederman et al (2007)</td>
<td>5–6</td>
<td>Open-label trial</td>
<td>Significant improvement</td>
<td>Acute mania</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Tramontina et al (2009)</td>
<td>5–6</td>
<td>Double-blind</td>
<td>Significant response rate difference, 89% vs 52% of placebo group</td>
<td>Acute mania or mixed</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Frazier et al (2001)</td>
<td>12–17; n = 14</td>
<td>Double-blind</td>
<td>Significant response rate difference, 45% vs 19% of placebo group</td>
<td>Bipolar disorder</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Tohen et al (2007)</td>
<td>17–16; n = 161</td>
<td>Double-blind</td>
<td>45% vs 19% of placebo group</td>
<td>Acute mania or mixed</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Del Bello et al (2007)</td>
<td>12–18; n = 32</td>
<td>Double-blind</td>
<td>Response rate 87% with mood symptoms</td>
<td>Patients at high risk for bipolar I</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Scheffer et al (2010)</td>
<td>6–16; n = 75</td>
<td>Open-label trial</td>
<td>94% much improved at 8 wk; rapid loading tolerated</td>
<td>Bipolar depression</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Frazier et al (1999)</td>
<td>4–17; n = 28</td>
<td>Records review</td>
<td>Response rate 82% with manic and aggressive symptoms</td>
<td>Bipolar disorder</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Biederman et al (2005)</td>
<td>6–17; n = 30</td>
<td>Open-label trial</td>
<td>Response rate 70% with manic symptoms</td>
<td>Mixed or hypomanic</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Haas et al (2009)</td>
<td>10–17; n = 189</td>
<td>Double-blind</td>
<td>Response rate 70% with manic symptoms</td>
<td>Manic, mixed, or hypomanic</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Carlson et al (2010)</td>
<td>5–12; n = 151</td>
<td>Chart review</td>
<td>Significant response rate difference, 59% (0.5–2.5 mg), 63% (3–6 mg), 26% (placebo)</td>
<td>Acute mania or mixed</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Krieger et al (2011)</td>
<td>7–17; n = 21</td>
<td>Open-label trial</td>
<td>Reduced duration of rages</td>
<td>Hospitalized children with possible bipolar disorder</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Del Bello et al (2009)</td>
<td>12–18; n = 32</td>
<td>Double-blind</td>
<td>No significant difference from placebo</td>
<td>Severe mood dysregulation</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>Biederman et al (2007)</td>
<td>6–17; n = 21</td>
<td>Open-label trial</td>
<td>Response rate 71% with manic symptoms</td>
<td>Mania</td>
</tr>
</tbody>
</table>
have shown efficacy in open-label trials (Table 9) and quetiapine was not significantly better than placebo (Table 10).

Medication Combinations

Adolescents with bipolar disorder may have a range of symptoms within the disorder, including symptoms of mania or hypomania, depression, and psychosis. They may also have a variety of other psychiatric disorders, including anxiety, obsessive-compulsive disorder, post-traumatic stress disorder, and attention-deficit/hyperactivity disorder. These comorbidities can lead to a complexity of symptoms and often difficult choices for medication management.

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TABLE 12. Adverse Effects and Possible Monitoring of Mood Stabilizers

<table>
<thead>
<tr>
<th>Medication</th>
<th>Summary of adverse effects</th>
<th>Suggested monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>Reduced renal function, hypothyroidism, nausea, diarrhea, abdominal distress, sedation,</td>
<td>Baseline: serum electrolytes, creatinine, BUN, calcium, CBC count, TFTs, EKG, pregnancy test (sexually active female patients)</td>
</tr>
<tr>
<td></td>
<td>tremor, polyuria, wt gain, acne, cardiac conduction problems, hypoparathyroidism</td>
<td>Ongoing: lithium level, renal function, thyroid function, calcium</td>
</tr>
<tr>
<td></td>
<td>Wt gain may be additive when combined with an atypical antipsychotic26</td>
<td>Every 6 mo: divalproex level, liver function tests, CBC</td>
</tr>
<tr>
<td></td>
<td>Toxic levels may produce confusion, ataxia, dysarthria, seizures, coma, death</td>
<td>Baseline: CBC</td>
</tr>
<tr>
<td>Divalproex</td>
<td>Polycystic ovaries, nausea, increased appetite, wt gain, sedation, thrombocytopenia, hair</td>
<td>Every 6 mo: carbamazepine level, CBC</td>
</tr>
<tr>
<td></td>
<td>loss, tremor, vomiting, rare pancreatitis or liver failure</td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Multiple medication interactions (decrease or increase the other medication levels including oral contraceptive failure), sedation, ataxia, dizziness, blurred vision, nausea, vomiting, aplastic anemia, hyponatremia, Stevens-Johnson</td>
<td></td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Severe cutaneous reactions (risk ≥3 times greater than 1 in 100), dizziness, tremor, sedation, asthenia, headache, interactions with oral contraceptives, case reports of leucopenia, agranulocytosis, hepatic failure, multiorgan failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Baseline: CBC and liver function tests</td>
<td></td>
</tr>
<tr>
<td>Oxicarbamazepine</td>
<td>Hypothyroidism, oral contraceptive failure, cutaneous reactions, cognitive symptoms, sedation, coordination difficulties, nausea, vomiting, asthenia, headache, dizziness26</td>
<td>Baseline and periodic: serum sodium</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Mostly benign; most common are sedation, dizziness, tremor, headache, ataxia, fatigue, wt gain</td>
<td>None</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Oral contraceptive failure, sedation, fatigue, impaired concentration, psychomotor slowing, word-finding difficulties, nephrolithiasis</td>
<td>Baseline and periodic: serum bicarbonate</td>
</tr>
</tbody>
</table>

BUN, blood urea nitrogen; CBC, complete blood cell (count); EKG, electrocardiogram; TFT, thyroid function test.

pital. The way to decrease the likelihood of relapse and treat current symptoms more quickly is to “cross-taper,” for example, starting the second medication with the full dose of the first medication, and then, if the second medication is tolerated and appears to be adding incremental benefit, the second medication gradually is increased while the first medication is decreased.

- Treat comorbid disorders. Additional medications may be used to treat symptoms of comorbid disorders, such as inattention with ADHD or worrying with an anxiety disorder.

**PRESCRIBING GUIDELINES**

The process of medicating is stepwise, with few patients having a full, lasting response to all symptoms with the first dose of the first medication. Each step is the opportunity for the physician to make a change (add or stop a medication or change a dose) or continue the current regimen as is (eg, the patient is stable or improving or needs a longer amount of time for a medication to work or for an adverse effect to resolve). Each patient becomes an individual study, with the result sometimes being good efficacy with odd-appearing or counterintuitive medication combinations. A number of issues may guide the decision at each step:

- **One Change at a Time.** With multiple medications, knowing which medication is causing positive effects or adverse effects may be difficult. Making 1 change at a time and then observing the effect can help deal with this problem, although this guideline may be discontinued at times for the sake of urgency or when there is little expected overlap in effects and

insomnia, that is treated with a medication just for that symptom.

- **Cross-taper.** When a medication is thought to be working poorly or not at all, a decision may be to replace it with another medication. The cleanest way to do so is to taper down the dose of the first medication, wait for a period of time for medication “wash out,” and then start the second medication at a low dose with subsequent appropriate increases. This approach may be problematic at times if, in retrospect, the first medication is discovered to have been more effective than previously thought, but regardless, the patient goes longer without an effective medication. The likelihood of a relapse is higher, and depending on the patient’s history, relapse may be debilitating or life-threatening or may interfere with a planned transition, such as starting school or leaving the hospital.
adverse effects of medications in a particular combination.

- **Important Cluster of Symptoms.** When a group of symptoms is causing severe impairment and distress, such as full-fledged mania or acute psychosis, it must be addressed first.

- **Treat the Most Troublesome Symptoms First.** A more common situation is that there is no group of symptoms that is overwhelming. In that case, first treat the group of symptoms that is causing the most distress or impairment. For example, moderate depression is treated before mild to moderate inattentiveness.

- **Opportunity to Reduce the Number of Medications That Eventually Will Be Needed.** A medication may be used that may not be the best for any particular group of symptoms but has the potential to treat ≥2 groups of symptoms.

- **Manage an Adverse Effect.** Depending on the urgency of the need for clinical effect and the troublesomeness of the adverse effect, an adverse effect may temporarily halt the search for an effective regimen until it can be resolved or reduced to an acceptable level.

- **Treat a “Lynchpin” Symptom.** At times, a symptom seems to be the basis for other symptoms, for example, an anxious and inattentive adolescent who goes into a rage

### TABLE 13 Adverse Effects and Possible Monitoring of Atypical Antipsychotics

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Time course</th>
<th>Suggested monitoring</th>
<th>Medications most likely to cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergic</td>
<td>Early</td>
<td>During titration, at 3 mo and annually</td>
<td>Clozapine, olanzapine</td>
</tr>
<tr>
<td>Acute parkinsonism</td>
<td>Early</td>
<td></td>
<td>Paliperidone, risperidone</td>
</tr>
<tr>
<td>Akathisia</td>
<td>Early/intermediate</td>
<td>During titration, at 3 mo and annually</td>
<td>Aripiprazole</td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>Not known</td>
<td>EKG at baseline if taking ziprasidone or clozapine and during titration if taking ziprasidone</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>Late</td>
<td>Fasting blood glucose at 3 mo and then every 6 mo</td>
<td>Clozapine, olanzapine (but problem for all)</td>
</tr>
<tr>
<td>Increased lipids</td>
<td>Early?</td>
<td>Lipids at 3 mo and then every 6 mo</td>
<td>Clozapine, olanzapine (but problem for all)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Most likely within first 6 mo</td>
<td>Clozapine registry recommended CBC monitoring</td>
<td></td>
</tr>
<tr>
<td>Orthostasis</td>
<td>Early</td>
<td>Orthostatic blood pressure and pulse if symptomatic, blood pressure and pulse at 3 mo and annually</td>
<td>Clozapine, olanzapine, quetiapine</td>
</tr>
<tr>
<td>Increased prolactin and sexual dysfunction</td>
<td>Early</td>
<td>Sexual history during titration and then every 3 mo, prolactin level only if symptomatic</td>
<td>Paliperidone, risperidone, olanzapine</td>
</tr>
<tr>
<td>Decreased prolactin</td>
<td>Early</td>
<td>Prolactin level only if symptomatic</td>
<td>Aripiprazole</td>
</tr>
<tr>
<td>Increased QTc interval</td>
<td>Not known</td>
<td>EKG at baseline if taking ziprasidone or clozapine and during titration if taking ziprasidone</td>
<td>Ziprasidone</td>
</tr>
<tr>
<td>Sedation</td>
<td>Early</td>
<td>Each visit</td>
<td>Clozapine, olanzapine, quetiapine (but problem for all)</td>
</tr>
<tr>
<td>Seizures</td>
<td>During titration</td>
<td>At 3 mo and annually (abnormal involuntary movement scale)</td>
<td>Clozapine</td>
</tr>
<tr>
<td>Tardive dyskinesia</td>
<td>Late</td>
<td></td>
<td>Lower risk compared with first generation antipsychotics</td>
</tr>
<tr>
<td>Withdrawal dyskinesia</td>
<td>Early during fast switch</td>
<td>During titration</td>
<td>Aripiprazole, paliperidone</td>
</tr>
<tr>
<td>Wt gain</td>
<td>First 3–6 mo</td>
<td>Height, wt, BMI percentile, BMI z score each visit</td>
<td>All, but clozapine and olanzapine highest and aripiprazole and ziprasidone least</td>
</tr>
<tr>
<td>Other laboratories</td>
<td></td>
<td>Electrolytes, CBC, renal function test annually, and liver function tests at 3 mo and annually</td>
<td></td>
</tr>
</tbody>
</table>

### TABLE 14 Medications That May Increase Mood Cycling in Children and Adolescents

**Antidepressants**
- Tricyclic antidepressants
- Selective serotonin reuptake inhibitors
- Serotonin-norepinephrine reuptake inhibitors

**Aminophylline**
- Oral or intravenous corticosteroids
- Sympathomimetic amines (eg, pseudoephedrine)
- Antibiotics (eg, clarithromycin, erythromycin, and amoxicillin)

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or its treatment, (2) conditions that mimic mania, (3) conditions that occur more commonly in patients with bipolar disorder that appear unrelated to its treatment, and (4) conditions related to risk behaviors associated with bipolar disorder. The authors noted that little has been published specifically with regard to pediatric bipolar disorder and concurrent medical conditions, but a number of reports that focused on adults included pediatric subjects.

Tables 12 and 13 summarize medical adverse effects from medications commonly used to treat bipolar disorder: Pediatricians should familiarize themselves with these and monitor for them. Lithium treatment can result in hypothyroidism and, regardless of the cause, hypothyroidism can make bipolar disorder more difficult to treat. Elevated prolactin levels, typically from certain atypical antipsychotics, are associated with low bone mass for chronologic age, sexual dysfunction, menstrual irregularities, gynecomastia, galactorrhea, and retrograde ejaculation. Cardiovascular disease and type 2 diabetes mellitus may be associated with the illness itself. Conditions that may mimic mania are listed in Table 15. Elevated prolactin levels, typically from certain atypical antipsychotics, are associated with low bone mass for chronologic age, sexual dysfunction, menstrual irregularities, gynecomastia, galactorrhea, and retrograde ejaculation. Cardiovascular disease and type 2 diabetes mellitus may be associated with the illness itself. Conditions that may mimic mania are listed in Table 15. Elevated prolactin levels, typically from certain atypical antipsychotics, are associated with low bone mass for chronologic age, sexual dysfunction, menstrual irregularities, gynecomastia, galactorrhea, and retrograde ejaculation. Cardiovascular disease and type 2 diabetes mellitus may be associated with the illness itself. Conditions that may mimic mania are listed in Table 15.

Unrelated conditions more common in patients with bipolar disorder include migraine headaches, epilepsy, and at least in 1 large family, autosomal dominant medullary cystic kidney disease. Conditions associated with bipolar risk behaviors include complications of substance use and abuse, sexually transmitted diseases, and traumatic brain injury.

**CASE VIGNETTES**

The following fictitious cases are conglomerates based on the authors’ clinical experience and are designed to illustrate common diagnostic and treatment issues.

**Case 1**

Mary is a 16-year-old girl who presents for admission to psychiatry inpatient after sudden onset 1 week previously of euphoric and giddy mood, talking rapidly and jumping from topic to topic, and little sleep with almost none over the past 3 days. She has spent most of her time since then at her health club trying to “pick up” male patrons, a behavior very out of character for her. Before age 14, she was high achieving and well adjusted, earning mostly As in school, socially active, and described by her parents as a “model daughter.” At age 14, she broke up with a boyfriend and became severely depressed, responding after 2 months to a combination of sertraline and psychotherapy. She discontinued both treatments 4 months later because she had been doing well. She continued to do well until 1 year ago, when she developed an episode similar to the current one, but her behavior was controlled, and she was managed outside the hospital, responding after 2 weeks to a combination of lithium and psychotherapy. She had difficulty with moodiness and functioning in school for the next 6 months and again stopped the treatments. She then continued about the same until this current episode.

Mary is diagnosed with bipolar I disorder; current episode manic, severe, and without psychotic features. She has the narrow phenotype. She is restarted on lithium and also is started on quetiapine for sleeping, calming, and additional mood stabilization. Lithium is chosen because of her past response to this medication. Her psychiatrist decides to combine this with quetiapine immediately, despite treatment algorithms suggesting starting with monotherapy, for 2 reasons: (1) previous treatment with lithium yielded a good acute response but only a partial response long-term, even before she stopped the medication and (2)
Charles is a 15-year-old boy who presents to the psychiatrist’s office for his first mental health visit with the complaint of increasing, severe depression over the past month. He feels that the depression started 3 years ago when his parents divorced and he moved with his mother and siblings to a new city and new school. Additional questions reveal that depression probably existed on and off for quite some time before the divorce. Furthermore, the depression is not continuous. Even over the past week, he reports having 1 or 2 days at a time of feeling great and “energized,” spending most of the night playing an online game with little fatigue the next day, talking more, having racing thoughts, and having a more difficult time focusing on school work. He has other times, up to 2 days at a time, of being easily angered, punching a wall at times, ruminating about slights from peers and parents, and generally feeling “edgy.”

Charles is diagnosed with bipolar disorder not otherwise specified and the intermediate phenotype. He does not meet duration criteria for mania (7 days) or hypomania (4 days). Key features are the spontaneous and frequent changes of mood symptoms, unrelated or only very loosely related to environmental circumstances, and the lack of distinct, continuous manic or hypomanic states for even 4 days.

Medication management for Charles is similar to that for Mary in case 1; the primary initial objective is mood stabilization with ≥1 mood stabilizers and/or atypical antipsychotics. A difference is that Charles’s mood symptoms are not stable. He only has to wait a few days or less to switch to a different group of symptoms. Despite depression being the primary concern, antidepressants may make his condition worse by increasing the frequency or intensity of mood changes or undermining the effects of the mood-stabilizing medication. Even for treating the depression symptoms, the preference is typically to find more effective mood stabilizing medication rather than add an antidepressant. Exceptions are common, however, with the treatment of bipolar illness.

Cases 1 and 2 illustrate the findings of a recent study showing that in 90% of cases the first mood episode in pediatric bipolar disorder is depression.\(^{40}\)

**Case 3**

Dan is a 17-year-old boy who presents for psychiatric inpatient admission after damaging his father’s car with a crow bar and threatening to kill his parents and then himself after parents took away his cell phone. The patient reports having had difficulty with temper outbursts for years. This is the worst such episode, but the patient commonly yells or leaves the house when upset and tends to overreact to his parents’ attempts to set limits. Both patient and parents report that he does “fine” most of the time and just overreacts to frustration. He was diagnosed with ADHD in the third grade and has been on and off treatment for that (currently off). He has had mild to moderate depression at times but not recently. On interview, the patient reports that the incident with the car was “not a big deal” and says that he currently feels “fine,” although he appears quite edgy and becomes frustrated with the interviewer for “asking too many questions.”

The patient is diagnosed with mood disorder not otherwise specified and meets criteria for bipolar spectrum broad phenotype or severe mood dysregulation. He shows no evidence for mood cycling, except for the history of depression, but his mood changes quickly with minor provocation, and he is highly sensitive to frustrating circumstances.

Common practice is to treat the rage symptoms and edginess with mood stabilizers and/or atypical antipsychotics. Treatment of rage and edginess in this population has been poorly studied, but risperidone and aripiprazole are approved by the FDA for the treatment of irritability associated with autism (Table 8). With some patients, these symptoms may respond to ≥1

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**TABLE 15 Medical Conditions That May Mimic Mania**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Other Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroidism</td>
<td></td>
</tr>
<tr>
<td>Closed or open head injury</td>
<td></td>
</tr>
<tr>
<td>Temporal lobe epilepsy</td>
<td></td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td></td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td></td>
</tr>
<tr>
<td>Fetal alcohol spectrum disorder/alcohol-related neurodevelopmental disorder</td>
<td></td>
</tr>
<tr>
<td>Wilson disease</td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td></td>
</tr>
<tr>
<td>Lyme disease</td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td></td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td></td>
</tr>
<tr>
<td>Niemann-Pick disease</td>
<td></td>
</tr>
<tr>
<td>Familial leukoencephalopathy</td>
<td></td>
</tr>
</tbody>
</table>

Lithium can easily take 1 week or more to be effective, and Mary needs something with more immediate effect for calming and sleeping.

Mary is in a relatively consistent (abnormal) mood state. The primary treatment goals are, therefore, to help her out of this state, return her to a euthymic mood, and prevent the next mood episode. If her current mood state were depression instead of mania, mood-stabilizing medication would still be the first choice, but often, antidepressant medication is cautiously added should the depression prove resistant to the mood stabilizing medication alone. The caution is related to the possibility that the antidepressant could make it easier for her to go into a manic episode, even when combined with the mood-stabilizing medication. In addition, during the time she is in a manic state, an antidepressant is generally not recommended.

**Case 2**

Charles is a 15-year-old boy who presents to the psychiatrist’s office for his first mental health visit with the complaint of increasing, severe depression over the past month. He feels that the depression started 3 years ago when his parents divorced and he moved with his mother and siblings to a new city and new school.
medications for depression, anxiety, or ADHD.

**Case 4**

Claire is a 13-year-old girl who presents to the psychiatrist's office because of daily episodes of rage, which have been present for years but increasing over the past year. She has the rage only at home and does well academically and socially. She denies any history of significant depression, although she does report a strong tendency to worry and has had this for most of her life. With further questioning, she reports multiple different ritualistic behaviors, such as needing to touch the doorframe in a certain way before going through it and needing to do household tasks in groups of 3. She becomes enraged when parents inadvertently interfere with her ability to complete a behavior.

Claire is diagnosed with OCD as well as generalized anxiety disorder. She does not have a mood disorder despite the rage outbursts. The rage would probably diminish with a mood stabilizer or atypical antipsychotic, but a better treatment is medication and psychotherapy for OCD and anxiety.

**Case 5**

George is a 14-year-old boy who presents to the pediatrician having recently moved from another state. According to his mother, he has been doing fairly well for the past 6 months and has been diagnosed with bipolar disorder and ADHD. He is currently taking lithium, methylphenidate, quetiapine, aripiprazole, sertraline, and clonazepam. He last saw his previous psychiatrist 2 months ago, and the mother requests a refill for his medications, because he does not have a psychiatrist currently. George's mother said that he has been in general good health but gained 40 pounds over the past year. George's mother attributes this to the medication. In addition to her routine for a new patient visit, the pediatrician does the following:

- Asks more questions to confirm clinical stability, such as potential adverse effects of the medications and clinical course, including depression, suicidality, and behavioral problems.
- Asks about medication dosing adherence.
- Contacts the previous psychiatrist to confirm medications and doses, obtain history, and obtain the psychiatrist's opinion on recent stability.
- Orders laboratory studies, including lithium concentration 12 hours after last dose, electrolytes, thyroid studies, calcium, lipids, and glucose (a fasting glucose may be ordered later if the random one is abnormal).
- Performs physical examination, including vital signs, height, and weight, and calculates BMI percentile.
- Refers George to a local child and adolescent psychiatrist for ongoing mental health care and arranges to partner with the out-of-state psychiatrist for care in the meantime.
- Renews the current medications unless there is a compelling reason otherwise. Given 6 months of stability, a slow medication taper may be safe, but this should be conducted under psychiatric supervision. Not renewing the medications is dangerous, because it may precipitate a major relapse as well as withdrawal symptoms.
- Refers George to a dietitian, recommends an exercise program, and plans to work with the psychiatrist on adjusting medications to reduce weight.

If it were determined that George may not be stable in some respect, resources include phone consultations with the out-of-state psychiatrist (and the out-of-state therapist, if there was one), urgent referral to a local child and adolescent psychiatrist, urgent referral to a local psychologist or other therapist for psychotherapy, and evaluation at a local hospital emergency department.

**SUMMARY**

Pediatricians have a collaborative role in diagnosis and management of adolescents with bipolar disorder, a common and often debilitating illness. Interviewing for current or past mania or hypomania, the defining feature of bipolar disorder, may be challenging but may be simplified by asking about red flag symptoms that, when present in the history, signal reasonable suspicion of bipolar disorder. In suspected or previously diagnosed cases of bipolar disorder, patients with current or recent symptoms or impairments should be referred for treatment. Pediatricians can actively monitor for and manage medication adverse effects, particularly weight gain, hyperlipidemia, and diabetes mellitus.

**ADVICE FOR PEDIATRICIANS**

1. Have some familiarity with diagnostic criteria and different types of bipolar disorder.
2. Maintain communication with child and adolescent psychiatrists and other mental health professionals.
3. Maintain familiarity with adverse effects and suggested monitoring protocols for mood-stabilizing and atypical antipsychotic medications.
4. Assist in monitoring for and managing medication adverse effects, particularly weight gain, hyperlipidemia, and diabetes mellitus.
5. Carefully and thoroughly document all recommendations, including referrals, medications prescribed, and instructions for observing and reporting adverse reactions.
REFERENCES


Collaborative Role of the Pediatrician in the Diagnosis and Management of Bipolar Disorder in Adolescents

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