Managing Bipolar Disorder From Urgent Situations to Maintenance Therapy, Part 1: Urgent Situations

This ACADEMIC HIGHLIGHTS section of The Journal of Clinical Psychiatry *presents the highlights of the planning teleconference series "Managing Bipolar Disorder From Urgent Situations to Maintenance Therapy, Part 1: Urgent Situations," which was held in March and April 2007. This report was prepared by the CME Institute of Physicians Postgraduate Press, Inc., and was supported by an educational grant from Eli Lilly and Company.*

The planning teleconference series was chaired by ***Rakesh Jain****, M.D., M.P.H., from R/D Clinical Research, Inc., Lake Jackson, Tex. The faculty were* ***J. Sloan Manning****, M.D., from the Mood Disorders Clinic, Moses Cone Family Practice Residency, and private practice, Greensboro, N.C.;* ***Steven Garlow****, M.D., Ph.D., from the Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Ga.; and* ***Tracey G. Skale****, M.D., from the Greater Cincinnati Behavioral Health Services, Cincinnati, Ohio.*

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Introduction: Taking Control of Urgent Situations in Bipolar Disorder

Urgent is defined as "calling for immediate attention."[1] Rakesh Jain, M.D., M.P.H., emphasized that patients with bipolar disorder often demand immediate attention from clinicians because these patients are at a high risk for situations that are urgent or that may trigger urgency, such as suicidality, aggression, legal difficulties, functional disability, occupational disruption, and marital disharmony.

Patients with bipolar disorder have a significant risk for suicide. A longitudinal study[2] of patients with bipolar disorder reported a standardized mortality ratio of 9.77 (95% CI = 4.22 to 19.24) when compared with the general population. Further, clinicians have long been aware of the common occurrence of aggression or agitation in uncontrolled bipolar disorder.[3] The National Comorbidity Survey (NCS)[4] and the Epidemiologic Catchment Area Survey[5] found high rates of violence among patients with bipolar disorder (16% and 11%, respectively). Uncontrolled bipolar disorder also increases individuals' risk for criminal arrest, sending many patients with this condition on a collision course with the judicial system and creating clinical urgency for rapid intervention to avoid incarceration.[6]

Bipolar disorder is also associated with severe impairment of functioning in social, vocational, and cognitive domains.[7] Thus, Dr. Jain noted that functional disability appears to be the rule and not the exception. Relationships and marriages are adversely affected when a partner suffers from bipolar disorder. For example, evidence[8] has shown higher rates of sexual dissatisfaction and lower rates of affection, support, and consideration for spouses of patients with bipolar disorder, resulting in high rates of marital discord in this population. In terms of vocation, according to the NCS Replication,[9] patients with bipolar disorder lost 65.5 workdays per year. When compared with patients with major depressive disorder who lost 27.2 workdays per year, bipolar disorder emerges as one of the most disabling psychiatric conditions.

Clinicians have an important role in the quick and efficient identification and resolution of urgent situations for patients with bipolar disorder. Dr. Jain stated that although clinicians are moved by the plight of urgently ill patients afflicted by bipolar disorder, many do not feel confident on how to best diffuse urgent situations and move patients to stability. This Academic Highlights, featuring 3 experienced experts from multiple settings, provides evidence-based recommendations and clinical advice on helping urgently ill patients with bipolar disorder.

First, J. Sloan Manning, M.D., emphasizes that patients who present in an urgent situation may be in a mixed phase of bipolar disorder, and correct diagnosis is critical for stabilization.[10,11] Then, Steven J. Garlow, M.D., Ph.D., summarizes the pharmacologic management of urgently ill patients, whether in new-onset or breakthrough episodes. Oral, orally disintegrating, and intramuscular medication formulations are all effective treatment options available to clinicians. Additionally, the American Psychiatric Association

(APA) guidelines support the use of rational polypharmacy in treating severely ill patients who need urgent and rapid control of symptoms. Finally, Tracey G. Skale, M.D., recommends the practical application of the biopsychosocial approach in treating urgently ill patients with bipolar disorder, which can help clinicians comprehensively employ all treatment modalities. All the experts advocate implementing psychoeducation and psychotherapy, which have demonstrated effectiveness in helping optimize outcomes for patients with bipolar disorder.[12]

Bipolar Mixed States: The Importance of a Correct Initial Diagnosis

Bipolar illness is pleomorphic, according to Dr. Manning. Because manic and depressive symptoms often appear concurrently and are often comorbid with other features of psychopathology, these symptoms can be easily confused with those of other psychiatric illnesses or missed altogether in the clinical process. An assessment for mixed episodes and/or mixed states is an important part of the clinical evaluation of any depressed and anxious patient, because morbidity and comorbidity among bipolar mixed presentations are greater than among pure manic or pure depressive states, particularly in the realm of suicidality. Without an early and correct diagnosis, the patient may receive medications that could exacerbate the mixed state.

Concepts of Mixed States

The key concept in understanding the bipolar mixed state, according to Dr. Manning, is that mood, cognition, and psychomotor energy can move independently of each other in bipolar disorder. This independence gives rise to superimpositions of the extremes of a pure mood state with cognitive or psychomotor features of the opposite mood. Thus, bipolar disorder can present in these mixed states with a perplexity of symptomatology that can be clinically confusing.[13]

DSM-IV-TR concept of mixed states. Dr. Manning stated that the concept of mixed episodes from the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (DSM-IV-TR)[14] is categorical and limited. The DSM-IV-TR concept requires at least 1 week when the criteria for both a manic episode and a major depressive episode are met nearly every day. The characteristics discussed in the DSM-IV-TR include rapidly fluctuating mood, agitated states, severe insomnia, psychotic features, and an increase in suicidal thinking. The DSM-IV-TR excludes mixed features that would be direct physiologic effects of general medical conditions. For example, the omission of neurologic disorders, such as multiple sclerosis or stroke, and hypermetabolic states, such as adrenal dysfunctions or thyrotoxicosis, may complicate the recognition and diagnosis of mixed states. The DSM-IV-TR also excludes the effects of substances and treatments such as amphetamines, neurotoxins, antidepressants, and electroconvulsive therapy. The issue of whether antidepressant-induced manic switches or mixed states are specific to bipolar I disorder remains a matter of controversy.

Other concepts of mixed states. Non–DSM-IV-TR concepts for mixed mood states include dimensional mixing and trait mixing. Dimensional mixing includes dysphoric mania[15] and depressive mixed states.[16] Dysphoric mania is a manic state combined with either 2 or 3 depressive symptoms, depending on which definition of dimensional mixing is observed.[15] Depressive mixed states are defined as major depression with 3 or more hypomanic symptoms.[16] An even newer concept, trait mixing,[17] was described in which patients with predominantly depressive temperaments (early-onset habitual personality traits) carried those depressive temperaments into a manic episode. Conversely, people who had early-onset habitual manic temperaments carried that mania into a major depressive episode, thus producing a mixing of symptoms that was clinically evident.

Akiskal and Mallya[18] created a clinically useful list (Table 1) of features of mixed states. One feature is the presence of unrelenting dysphoria. These bipolar patients get very little rest from their psychic pain. They are generally severely agitated, have refractory anxiety, often present with unendurable sexual excitement, and have difficult-to-treat insomnias. These patients also suffer from suicidal obsessions and impulses. Patients can present with histrionic demeanors, appearing to seek attention for attention's sake, and yet it is obvious during examination that their suffering is genuine and intense.

Epidemiology of Bipolar Mixed States

Dr. Manning reported that epidemiology studies of mixed states suggest a lifetime prevalence of approximately 40% in hospitalized patients with bipolar I disorder.[19,20] Mixed states seem to be more common in women than in men. This point was illustrated by Suppes et al.,[21] from the Stanley Foundation Bipolar Treatment Outcome Studies, in which depression was found in those who met the criteria for hypomania significantly more often in women than in men (72% vs. 42%, respectively; $p < .001$). High levels of anxious symptomatology are also present in mixed states and seem to correlate with the presence and severity of depressive symptomatology.[22,23] Anger, irritability, and impulsive irritability are also increased during mixed states,[20] perhaps leading to the observed elevated suicide risk in mixed states.[13,23–27]

Table 1. Features of Mixed States[a]

Unrelenting dysphoria
Severe agitation
Refractory anxiety
Unendurable sexual excitement
Intractable insomnia
Suicidal obsession and impulses
Histrionic demeanor
Genuine, intense suffering

[a]Data from Akiskal and Mallya.[18]

Mortality Associated With Bipolar Mixed States

Suicidal behavior, both nonfatal and fatal, is increased during mixed episodes.[23] Risk factors for suicide include a family history of suicide, a history of physical or sexual abuse, an early age at onset of bipolar disorder, severe depressive symptoms (especially when presenting with hopelessness), and any comorbid Axis I disorder, particularly anxiety disorders or substance use disorders.[24] The presence of a mixed state or extreme rapid cycling also increases patients' suicide risk.[23]

Several studies have documented higher levels of suicidality in patients with mixed states versus patients with pure mania: Dilsaver and colleagues[25] showed a 55% suicidality rate in mixed states versus 2% in pure mania, Strakowski et al.[26] found a 26% suicidality rate in mixed states versus 7% in pure mania, and Marneros et al.[27] found a 14% rate of suicidality in mixed states versus 0% in pure mania. Dr. Manning emphasized that patients' potential mortality should always be in the clinician's mind during evaluations for mixed states. This mindfulness will lead to both an accurate diagnosis of the bipolar diathesis and an accurate gauge of the extent of clinical severity of the disorder.

Opportunities for and Consequences of Misdiagnosis

Bipolar disorders are prevalent in primary care settings, yet misdiagnosis and diagnostic delays are common. In 2 studies, 27.9%[28] and 25.9%[29] of patients presenting with depression or anxiety in primary care settings had some form of bipolar disorder. Dr. Manning stated that, over the last decade, there has been a broad focus on unipolar depression and a variety of anxiety disorders, which may have distracted some clinicians from bipolar disorder as an important clinical entity. The manifestations of mania are much less familiar to clinicians in nonpsychiatric settings where the majority of mood disorder treatment is administered.[28,30]

Table 2. Social and Economic Consequences of Mixed States

Marital disruption(s)[31]
Work disruption(s)[32]
Job loss(es)[31]
Arrests[32]
High use of medical resources[31]

Because the concept of mixed states is unfamiliar to many clinicians, there is a tendency for physicians to focus on a comorbidity or state descriptors in these patients and miss the larger picture of the underlying bipolar diathesis. Physicians may also attribute social or economic consequences of mixed states to issues that are unrelated to the mood disorder (Table 2).[31,32] Misdiagnosis can cause patients to remain in mood states with high levels of suicidal thinking, impulsivity, anger, and/or aggressive tendencies, which may cause further difficulties at home, at work, in community activities, and other areas of life.

Anxiety disorders and suicidal-like behaviors—including self-mutilation—occur often in patients with bipolar disorder, with many patients experiencing panic attacks or prolonged panic states, symptoms of obsessive-compulsive disorder, generalized anxiety disorder or social phobia, and substance use disorders.[23,33,34] These symptoms can distract physicians from the presence of a bipolar mixed state. Additionally, clinicians may focus on agitation and make a diagnosis of agitated depression.[13] Not all agitated depressions are signs of bipolar disorder; however, agitation in a patient who presents with depression is an indication to look carefully for other elements of the bipolar diathesis. Dr. Manning noted that another potential misdiagnosis is borderline personality disorder.

Patients may receive inappropriate treatment if physicians fail to diagnose a bipolar diathesis.[29,30] For example, patients with refractory insomnia may get overmedicated with sedative-hypnotics.[18] Clinicians may also focus on depression or anxiety and treat patients with an antidepressant, as opposed to using treatments more specific for a bipolar mixed state. Treatment with antidepressant monotherapy tends to increase the potential for suicidality, impulsivity, and aggressive tendencies.[35,36] Dr. Manning stressed that it is possible to exacerbate the condition of already ill individuals if they are not accurately diagnosed and treated.

Conclusion

Symptoms of mania and major depression may be mixed in patients with bipolar disorder, and increased morbidity and mortality are associated with mixed states. Dr. Manning stated that early recognition of the bipolar diathesis and mixed states permits appropriate interventions that may reduce morbidity and mortality, and thus, improve patient outcome.

Interventions for Acute Mood Episodes in Patients With Bipolar Disorder

Types of Acute Mood Episodes

Dr. Garlow discussed pharmacotherapy for 3 types of acute, rapid-onset mood episodes in bipolar disorder—manic, depressive, and mixed. These mood episodes are defined by DSM-IV criteria[14]; however, Dr. Garlow added that, in manic episodes, patients can have severe behavioral disturbances, activation, psychosis, and severe agitation; in depressive episodes, patients can have significant neurovegetative symptoms and psychosis; and in mixed bipolar episodes, which are a mixture of manic and depressive symptoms, patients can have significant agitation and distress, as well as psychosis.

Treatment Goals

The first treatment goal for an acute mood episode is rapid and robust relief of symptoms. For manic episodes, initial interventions should calm patients to de-escalate their mania, relieve psychotic symptoms, and alleviate behavioral disturbances not only for patients' well-being, but for those around them as well. For depressive episodes, the goal is rapid relief from the negative symptoms, cognitive disturbances, and impairments resulting from depression. When treating an acute episode, Dr. Garlow recommended that clinicians select a treatment that facilitates the transition into maintenance therapy and prevents cycling and further decompensation.

Urgent treatment is critical for patients experiencing acute mood episodes for 3 reasons: (1) To prevent hospitalization or to shorten the hospital stay. Often, patients will feel demoralized and discouraged as a result of hospitalization.[37] Further, this treatment modality is costly, not only for the patient, but for society as a whole.[37] (2) To reduce the risk for suicide, which is high among patients with bipolar disorder.[38] Dr. Garlow commented that mixed episodes may combine the energy and activation of mania with the negative mood of depression, which has the potential to result in fatal outcomes for patients. (3) To reduce the psychosocial consequences that adversely affect patients' familial relationships, employment, and status with the law.[32]

According to Dr. Garlow, mental health practitioners typically encounter 2 treatment scenarios: new-onset mood episodes or breakthrough episodes. Patients with new-onset mood episodes are either at the beginning of the disease and not yet in treatment or were on maintenance therapy but have stopped taking medication for a variety of reasons. Patients with a breakthrough episode are on active maintenance therapy but nevertheless experience an acute mood episode. Dr. Garlow described each treatment scenario and discussed available treatment options, including those with U.S. Food and Drug Administration (FDA) indications, to promote optimal patient outcomes.

Table 3. FDA-Approved Agents for the Treatment of Various Bipolar Disorder States

Agent	Agitation	Type of Mood Episode: Manic	Mixed	Depressed	Maintenance Therapy
Aripiprazole[40]	✓[a]	✓	✓		✓
Carbamazepine[45]		✓[a]	✓[a]		
Chlorpromazine[47]		✓			
Divalproex[44]		✓[a]	✓[a]		
Lamotrigine[59]					✓
Lithium[43]		✓			✓
Olanzapine[39]	✓[a]	✓	✓		✓
Olanzapine-fluoxetine[50]				✓	
Quetiapine[49]		✓	✓	✓	
Risperidone[48]		✓	✓		
Ziprasidone[41]		✓	✓		

[a]Extended-release or intramuscular injectable formulations indicated.
Symbol: ✓ = approved by the U.S. Food and Drug Administration (FDA).

Acute Manic and Acute Mixed Episodes

Agitation. An emergent symptom of acute mania (either new-onset or breakthrough) is psychomotor agitation, which is generally defined as excessive motor activity associated with a feeling of inner tension and requires definitive and immediate intervention. Patients can manifest high levels of motor agitation, impulsivity, and lability, which may lead to exhaustion. The experience has a large component of fear and uncertainty and can be highly distressing and uncomfortable for patients, who can be threatening because they themselves feel threatened. Agitation can interfere with care via threatening and escalating behaviors that lead to high-risk situations with untoward consequences. When agitation is combined with psychosis, misperceptions of the world are added to patients' already negative and fearful experiences and may result in self-injury or dangerous situations for family members and staff.

Rapid physical intervention may be necessary, such as putting the patient into seclusion or restraints. However, Dr. Garlow strongly recommended using oral agents to treat acute agitation if possible, because convincing patients to take medication allows for the development of a therapeutic alliance with the treatment provider, whereas restraining patients and forcing medication through injection creates a conflictual relationship. Dr. Garlow acknowledged that, in extreme cases, an intramuscular medication may be necessary, with the treatment goal of helping patients remain calm, awake, and able to participate in their evaluation and treatment.

Although 2 second-generation antipsychotics, intramuscular olanzapine[39] and intramuscular aripiprazole,[40] have been approved by the FDA to treat psychomotor agitation in bipolar I mania, Dr. Garlow stated that intramuscular ziprasidone[41] (a second-generation antipsychotic) and lorazepam[42] (a benzodiazepine with anxiolytic properties that is often used alone or in combination with an antipsychotic medication) are other agents typically used in acute interventions for agitation (Table 3). At one time, haloperidol was the standard treatment for agitation and is still currently used; however, Dr. Garlow recommended using second-generation antipsychotics instead.

New-onset manic or mixed episodes. For patients without agitation, treatment options are greater for acute manic and acute mixed episodes. Dr. Garlow advised that, when making a pharmacotherapeutic decision, clinicians should consider patients' past experiences with particular agents, such as response, allergic reactions, contraindications, route of administration, and onset of action, including the introduction of an agent at a full therapeutic dose or an extended period of dose titration and the ease of transition of an agent into maintenance therapy.

Lithium[43] is the standard treatment for acute manic episodes; however, extended-release divalproex sodium[44] and carbamazepine[45] also are indicated for treating acute manic episodes (see Table 3). Dr. Garlow described treatment strategies to gain rapid control for an acute manic episode: with divalproex, aim for a blood level above 100 μg/mL; with carbamazepine, aim for a blood level about 12 μg/mL; and with lithium, the blood level should be raised to between 1.0 and 1.2 mEq/L. Dr. Garlow advised that all 3 agents may present issues when titrating dosages.

Several antipsychotic agents are indicated for treating acute manic episodes,[46] including the oral and injectable formulations of chlorpromazine.[47] The second-generation oral antipsychotics risperidone,[48] olanzapine,[39] quetiapine,[49] ziprasidone,[41] and aripiprazole[40] are also approved for the treatment of acute mania as well as for the treatment of acute mixed episodes. Other agents approved for the treatment of mixed episodes are the extended-release formulations of carbamazepine[45] and divalproex[44] (see Table 3).

Breakthrough mania. Dr. Garlow stated that maximizing the dose of the current agent should be the first intervention for patients on maintenance therapy who have persistent symptoms or who have an emergent manic episode. Dr. Garlow suggested that, for patients treated with lithium, the blood level should be raised to between 1.0 and 1.2 mEq/L, and for patients treated with valproic acid, the blood level should be brought up above 100 μg/mL, in the 100 to 120 μg/mL range. If symptoms persist after optimizing the maintenance agent, Dr. Garlow recommended adding a second-generation antipsychotic, several of which have shown benefit in an adjunctive capacity.[46] For example, for patients taking lithium or valproic acid, risperidone[48] and olanzapine[39] are indicated for emergent mania or mixed episodes and quetiapine[49] is indicated for emergent mania. Consideration should be given to the agent's rapid onset of action and symptom relief, as well as the potential of the medication to transition into maintenance therapy.

Acute Depressive Episodes

New-onset bipolar depression. Treatment decisions for people who have been diagnosed with bipolar disorder but are not currently on maintenance therapy depend on individual patient's past experiences, the clinician's understanding of the patient's preferences, and the patient's course of illness. The olanzapine-fluoxetine combination[50] is indicated by the FDA for treatment of bipolar depression, as is quetiapine[49] (see Table 3). Other pharmacologic interventions supported by evidence[51] include lithium alone or in combination with an antidepressant, valproic acid alone or in combination with an antidepressant, and lamotrigine.

Treating bipolar disorder with antidepressants is a controversial issue because these agents may lead patients to switch rapidly from depression into mania and thus begin a rapid-cycling phase.[52,53] Dr. Garlow stressed that, if antidepressants are used in patients with bipolar disorder, a mood-stabilizing medication, such as lithium, valproic acid, or olanzapine, should be co-administered to prevent rapid-cycling. Meta-analyses[54,55] have shown that antidepressants relieve acute depressive symptoms in bipolar disorder; however, the long-term value is yet to be established. In terms of treatment for patients who switch into a manic episode, selective serotonin reuptake inhibitors (SSRIs) may be less problematic than tricyclic antidepressants (TCAs).[55]

Breakthrough depression. For a patient currently receiving maintenance therapy, the first intervention for breakthrough depression should be to check the patient's blood drug level and titrate the maintenance agent up to a full therapeutic dose. Dr. Garlow reminded clinicians that when a patient who has previously been stable on maintenance therapy begins to present with some mood symptoms, previous mood cycles predict the next one.[56] For example, someone who has had several depressive episodes is more likely to have another depressive episode rather than a manic episode. An antecedent of breakthrough mania is sleep disturbance, whereas the antecedents of a depressive episode are anxiety, poor concentration, and indecisiveness, as well as depressive symptoms.

If the patient is still depressed after optimizing the current mood stabilizer, the next step should be to consider additional medications, such as a second-generation antipsychotic, lamotrigine, or an antidepressant.[57,58] Scant definitive evidence is available to aid in decision-making, but clinicians should take into account previous beneficial treatments for the patient, contraindicated medications, and the patient's opinions, expectations, and concerns regarding particular treatments.

Two second-generation antipsychotics are approved for treating breakthrough bipolar depression—the olanzapine-fluoxetine combination[50] and quetiapine[49] (see Table 3). Olanzapine monotherapy is FDA-indicated for maintenance therapy in bipolar disorder,[39] which may facilitate patients' transition into maintenance therapy when treated with the olanzapine-fluoxetine combination for acute depression. Other agents with indications for maintenance treatment are lamotrigine[59] and lithium,[43] and the efficacy of aripiprazole has also been demonstrated for maintenance treatment in patients stabilized after recent manic or mixed episodes[40] (see Table 3).

Conclusion

Dr. Garlow emphasized that when making treatment decisions for patients with acute mood episodes, clinicians should consider patients' cycling history, course of illness, past and current treatment history, and the urgency of the clinical situation. If catastrophic events are likely, agents with rapid onset of action should be chosen to avoid adverse social consequences and hospitalization. Additionally, clinicians should opt for pharmacotherapeutic options that will ease patients' transition into maintenance therapy.

Practical Strategies for Assessing and Stabilizing Patients With Bipolar Disorder in Urgent Situations

Dr. Skale recommended that, when faced with a patient in an urgent bipolar situation, clinicians ask specific questions on a routine basis (Table 4). If clinicians do not inquire about important issues, patients could face negative consequences. In urgent situations, the clinician has a responsibility to act as quickly as possible to rapidly reduce acute symptoms and help the patient avoid hospitalization and the loss of relationships, independence, and employment, as well as the resulting demoralization from these events. Fortunately, multiple treatment modalities and management strategies are available for clinicians to stabilize the patient in acute distress.

Table 4. Questions to Ask About a Patient When Managing an Urgent Situation

Is there a risk for suicidality/homicidality/aggression?
Is there a comorbid alcohol or other substance use disorder?
Is the patient currently experiencing psychotic symptoms?
Is this an acute manic episode?
Is this an acute depressive episode?
Is this a mixed state?
Is the patient pregnant?
Are there any medical concerns?
What medications/supplements is the patient taking?
Are there adherence issues?
What are the familial/social/occupational issues?

Biopsychosocial Model

Effective management of bipolar disorder involves all aspects of patients' lives—biological, psychological, and social—that can trigger acute manic, depressive, or mixed episodes. Therefore, Dr. Skale described the biopsychosocial model of bipolar disorder and stated that this model helps physicians, patients, and patients' families to understand what may have caused the development of an urgent situation and how to best resolve it (Figure 1).

Biological Management of Urgent Situations

Biological factors may complicate the pharmacologic management of patients with bipolar disorder and may also induce urgent situations. These factors include nonadherence to treatment regimens, comorbid medical conditions, hormonal changes due to pregnancy or childbirth, substance use, sleep disturbance, and overall worsening of bipolar illness. For example, comorbid medical illnesses and hormonal changes may affect the successful management and stabilization of patients' moods. If comorbid medical conditions are present, the acute psychiatric condition should be controlled as soon as possible so that the nonpsychiatric condition may be addressed. For pregnant patients with bipolar disorder, clinicians' threshold for hospitalization in a high-risk situation may be lower than for patients who are not pregnant. However, when treating patients who are pregnant and in urgent situations, Dr. Skale recommended that lithium, valproate, and other anticonvulsants be avoided during the first trimester.[60–62] In addition, women with bipolar disorder are at a high risk for relapse (approximately 50%) into mania, depression, or psychosis immediately postpartum, which also increases their risk for developing an urgent situation.[63]

Patients with bipolar disorder have higher rates of substance use than the general population (41% vs. 6%, respectively),[64] and those with comorbid substance use disorders are more likely to harm themselves than those without substance use disorders.[65] Additionally, alcohol-related dehydration may increase blood lithium levels to toxic levels, and hepatic dysfunction from chronic alcohol use or hepatitis from intravenous substance use may adversely affect plasma levels of valproate and carbamazapine.[66] Dr. Skale noted that, ideally, clinicians would have access to patients' history, drug screening, and baseline laboratory results prior to prescribing medications.[67] However, many clinicians work in settings such as community mental health care facilities where severely ill patients are seen on a daily basis and the clinician is required to act quickly and effectively with limited information.

According to Dr. Skale, sleep disturbances can negatively impact patients' personal and workplace relationships, which can then trigger an urgent situation. To manage this biological factor, physicians should educate patients on the benefits of regulated sleep, which may reduce the occurrence of urgent situations and allow physicians to treat the primary psychiatric condition of bipolar disorder.

The APA guidelines,[67] Texas Medication Algorithm Project (TMAP),[68,69] and Expert Consensus Guidelines[70] for the treatment of bipolar disorder offer rational, evidence-based intervention options for urgently ill patients. Dr. Skale stated that the recommended pharmacologic interventions should be tailored to individual patients and should also be effective, well-tolerated, and have a rapid onset of action. If the patient has had a known positive response to a medication in the past, that medication may be a good choice for the current episode. The patient may have confidence in this medication that has been effective and tolerated previously. For the treatment-naïve patient, the clinician should choose medication based on clinical presentation and other pertinent data such as comorbid medical issues, substance use disorders, and so on.

If the patient is in maintenance treatment, resolution of the acute situation may be achieved by the temporary increase of medication dose.[67,69] Once the crisis is resolved, the patient's symptoms can typically be managed at a lower dose. When raising the dose of atypical antipsychotics, it is helpful to remind acutely manic patients that they will likely sleep regularly while taking

Figure 1. Biopsychosocial Model for Urgent Situations in Patients With Bipolar Disorder

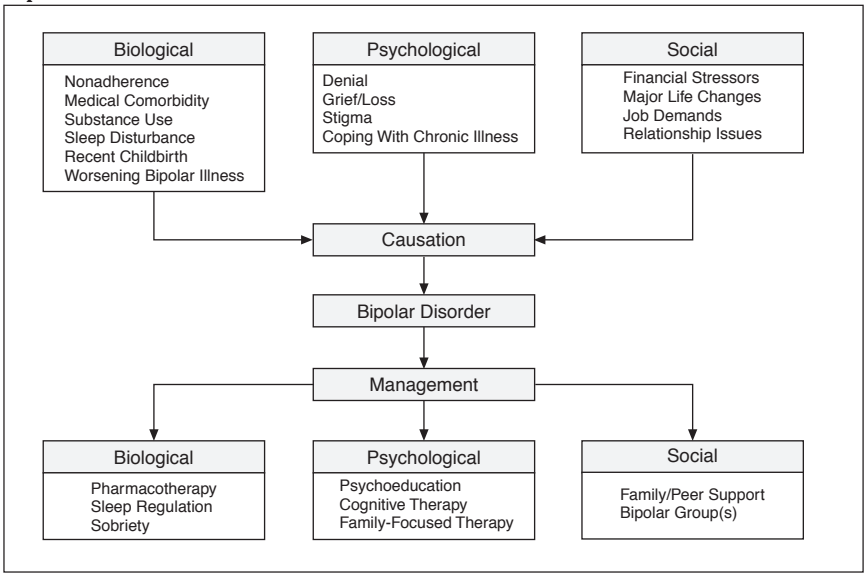

Table 5. Medications Available With Alternate Delivery Mechanisms

Medication	Potential Use
Intramuscular Formulations	In emergency department or inpatient setting where rapid control may be needed for safety reasons
Ziprasidone[41]	
Olanzapine[39]	
Aripiprazole[40]	
Orally Disintegrating Tablets	To help family/staff ensure adherence to oral dosing
Risperidone[48]	To help patients who do not like swallowing pills
Olanzapine[39]	
Aripiprazole[40]	

the higher dose and that they will feel more calm and focused within the next few days. Conventional antipsychotic medications should be used with caution because of the risk of acute dystonic reactions. Dr. Skale noted that conventional antipsychotics are not highly recommended by the APA or TMAP treatment guidelines.[67,69]

Dosages of mood stabilizers can also be raised during acute mania,[67,71] but in Dr. Skale's clinical experience, for an outpatient in an urgent situation, adding lithium may not be the most effective intervention because lithium has a relatively long onset of action and a narrow therapeutic window. Further, raising the lithium level quickly to a high but safe range is easier in an inpatient setting than in an outpatient setting. If needed, the clinician may augment the current treatment with another mood stabilizer or an atypical antipsychotic.

Short-term use of benzodiazepines may be considered if anxiety or insomnia is present.[67] Benzodiazepines can diminish manic symptoms quickly but are usually avoided with outpatients. If benzodiazepines are added in a hospital setting, they should be tapered and discontinued, if possible, prior to discharge.

Dr. Skale reiterated Dr. Garlow's recommendation that clinicians should minimize the use of antidepressants and, if antidepressants are used, clinicians must be cautious and watchful. Antidepressant treatment may need to be stopped if the patient is in a manic or mixed state.[67]

Dr. Skale suggested using alternate delivery mechanisms if urgency is particularly critical or if patients have trouble swallowing pills (Table 5). Finally, electroconvulsive therapy is an option in extremely urgent situations.[67]

Psychological Management of Urgent Situations

Psychological factors that can contribute to patients' development of urgent situations are denial of having bipolar disorder, grief over personal loss (e.g., of job, of independence, of a loved one), stigma associated with the illness, and inability to cope with this chronic illness.

Dr. Skale outlined psychological tools that may be helpful in treating a patient who is urgently ill. Simply providing medical expertise and adopting a calm approach to the patient and family in distress is a part of good clinical care. When the acute crisis has ended, psychoeducation about the recurrent nature of this neurobiological illness, the need for ongoing pharmacotherapy, the recognition of unique triggers or target symptoms, and healthy coping mechanisms to keep stress under control can reduce the number of future recurrences and hospitalizations.[72] Cognitive therapy specifically designed for relapse prevention in bipolar disorder is effective when used in conjunction with mood stabilizers.[73] Additionally, the combination of family and individual therapy, along with medication, can also offer protection from relapse.[74]

Social Management of Urgent Situations

In addition to pharmacologic and psychological treatment interventions, the management of social factors that trigger mood episodes, such as financial difficulties, major life changes, and work and relationship problems, may require referral to a crisis stabilization center or help from support groups within the community. The National Alliance on Mental Illness is one such group, as is the Depression and Bipolar Support Alliance. The patient may also need substance abuse treatment services if alcohol or other substance abuse has caused or exacer-

bated the current acute episode.[65,75] Dr. Skale stated that clinicians can also reassure the patient and family that there is hope that the patient will regain stability and act as a mediator to facilitate patient and family communication.

Addressing the Needs of the Suicidal Patient

Suicidality can be present in any phase of bipolar disorder.[76] APA guidelines[67] advocate that clinicians routinely assess for patients' suicidal or homicidal ideation, intent, and planning, as well as the availability of means to commit suicide and the lethality of those means.[67] Assessment for the presence of hallucinations and other psychiatric symptoms, including severe anxiety, and for the presence of alcohol or substance use is essential.[65] Clinicians should also assess patients' history of and seriousness of previous suicide attempts and self-harm and family history or recent exposure to suicide.[77] Dr. Skale stressed that using both pharmacologic and nonpharmacologic interventions is critical when suicidality is present.[76]

Conclusion

Urgent situations present frequently in clinical settings. Optimizing outcomes for patients in crisis situations requires clinicians to rapidly and accurately assess the biological, psychological, and social precipitants of urgent situations and offer appropriate interventions. Dr. Skale concluded that this biopsychosocial approach offers the most useful opportunity for positive patient outcomes.

Summary

Dr. Jain reiterated that bipolar disorder is a common problem, and psychiatrists and nonpsychiatrists alike face urgent situations in clinical practice. Many stakeholders have a vested interest in optimizing patients' outcomes, including the patients themselves,[78] their families and caregivers,[78,79] their workplaces,[80] and society at large[81]; each one can be dramatically and adversely affected by the devastating impact of this debilitating disorder. Bipolar disorder not only can cause loss of life through suicide or other mortality but also can lead to family dysfunction and occupational and educational disruption,[2] and therefore, society as a whole suffers from urgently ill bipolar disorder patients who are not quickly and efficiently stabilized. In summation, Dr. Jain offered the following take-home points:

- Urgent presentations of bipolar disorder are common in all physicians' offices
- Accurate diagnosis of the various phases of bipolar disorder (manic, depressive, or mixed) is critical to effectively manage patients
- Quick and accurate assessment for patient self-harm or harm to others is necessary to treat urgent situations appropriately
- Offering systematic interventions that are rapidly effective is mandated, and focusing on efficacy and tolerability will help guide clinicians
- Full patient and support system involvement in psychoeducation and psychotherapy will help reduce the burden of bipolar disorder

Drug names: aripiprazole (Abilify), carbamazepine (Carbatrol, Equetro, and others), chlorpromazine (Thorazine, Sonazine, and others), divalproex sodium (Depakote), haloperidol (Haldol and others), lamotrigine (Lamictal and others), lithium (Eskalith, Lithobid, and others), lorazepam (Ativan and others), olanzapine (Zyprexa and Zyprexa Zydis), olanzapine-fluoxetine (Symbyax), quetiapine (Seroquel), risperidone (Risperdal), valproic acid (Depakene and others), ziprasidone (Geodon).

Disclosure of off-label usage: The chair has determined that, to the best of his knowledge, lamotrigine is not approved by the U.S. Food and Drug Administration for the acute treatment of bipolar depression, and intramuscular lorazepam and intramuscular ziprasidone are not approved for agitation in bipolar disorder.

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