CHAPTER 1

An Integrated Approach to Bipolar Disorder

When Drew consulted our mood disorders clinic, he complained of depression, anxiety and suicidal thinking. Only 35 years old, he was on his third marriage and it had followed a pattern like all the others: Relationships were exciting and lively at the beginning, full of "great sex, all night conversations, and the feeling we could be anything we wanted to be." Within 6 months after each wedding, however, Drew would grow increasingly depressed and anxious. Many explanations were offered by the various therapists Drew consulted, including seasonal depression (even though his depression had not followed the seasons), "anniversary reactions" to his father's death, and, in one case, "buyer's remorse."

Drew, who was trying to get work as an actor in the highly competitive Los Angeles entertainment industry, felt that his depressive episodes coincided with losing out on a movie role or finding out that a friend had done better than he had. He felt they had little to do with his marriages. His most recent breakup illustrated a pattern that occurred in several of his prior marriages. After losing out in a string of auditions, he grew despondent and withdrawn. His wife attempted to cheer him up by reassuring him that she loved him and that he would get back on his feet. But after enduring a year of his sullenness, irritability, disinterest in sex, and suicidal threats, she said she would leave him unless he sought help. As he described it, the pressure from his wife made things much worse because "having my arm twisted into therapy is never a good beginning." He felt that most of the individual and couple therapists he (and his spouses) had consulted over the years were "charlatans" who gave "cookie cutter advice."

Despite having had multiple evaluations with various general practitioners and psychiatrists, Drew never believed that he had received a proper diagnosis. He had seen a counselor in high school because of "the usual adolescent mood swing stuff" and a psychologist for a few sessions in college because of anxiety. In fact, he felt it was his anxiety that had led him to drop out of

school. Most of these clinicians had told him he had depression, and some also suggested an anxiety disorder. Attention-deficit/hyperactivity disorder (ADHD) had been put forth by others. One had suggested that he had a narcissistic personality disorder, adding that "it may work well for you in the acting business." One called him "depressed with bipolar tendencies" but did not elaborate on what that meant.

Following the advice of his third wife, a nurse, Drew met with an outpatient psychiatrist who recommended trials of various medications, including lithium (Eskalith), valproate (Depakote), quetiapine (Seroquel), and a "cocktail that mixed them all together." He did not respond well to any of these agents, and typically tried them for only a week or two, after which his depression usually worsened. Then, a new psychiatrist, convinced that his problems were all due to a "biogenic depression," had recommended magnetic resonance imaging (MRI). Although the imaging results were inconclusive, the doctor had suggested that Drew discontinue all the other agents and try escitalopram (Lexapro) and methylphenidate (Ritalin) together. She also suggested he participate in Saturday morning group support sessions, which he attended only once, describing his fellow patients as "the clown brigade." Escitalopram and methylphenidate made him feel better at first and gave him more energy, but then "I couldn't sleep, I was nervous, angry as hell . . . it made me worse." He continued to feel anxious, fearful, irritable, and fatigued, and his thoughts began to speed up. He eventually stopped escitalopram and never went back to this psychiatrist, although he continued to take methylphenidate and began "doctor shopping" to renew his prescriptions. When he consulted our clinic, he was in a depressive episode that required hospitalization and a full reevaluation of his treatment.

OBJECTIVES OF THIS BOOK

Certainly, not all people with bipolar disorder receive the chaotic care that Drew received, but in our experience, his story is not unusual. On average, patients have 8–10 years of illness before they get the correct diagnosis, and many go even longer before finding an effective medication regimen.[1] Many report that they have never had any targeted or individualized psychotherapy related to their disorder, even if they have found therapists they liked. Some report little or no integration among the various treatments they have received; their medications have been dispensed by a general practitioner (GP) or a psychiatrist with minimal expertise in bipolar disorder, with follow-up appointments every 3 months. Their therapist, usually a practitioner in a different clinic, may have never spoken with their psychiatrist or GP, and rarely have any of the practitioners ever spoken to family members (often on purpose

because they view the confidentiality of psychiatric treatment to be unassailable).

Personalized and Integrated Treatment

A key theme of this book is that the treatment of bipolar disorder must be individualized in an ongoing collaboration with each patient. Our combined experience of over 60 years of working with people with bipolar disorder has convinced us that each treatment regimen, whether pharmacological or psychosocial, must involve careful planning to fit the needs of the individual. Moreover, it is critical to have a dialogue with the patient about the factors in the immediate milieu that play a role in the mood swings.

For most patients, a healthy balance of pharmacotherapy and psychotherapy are developed as an integrated and individualized plan. As shown repeatedly in the research literature, the integration of targeted forms of psychotherapy with pharmacotherapy enhances outcomes in functional as well as symptomatic domains.[2] To implement personalized treatment, there must be a number of factors in place: (1) an ongoing dialogue about treatment goals between the clinician and the patient; (2) ongoing communication between the physician and therapist (assuming that the patient is receiving both medication and psychotherapy and that the two clinicians are separate individuals), with each provider facilitating the goals of the other's treatment; and (3) flexibility over time, with the acknowledgment that the patient's needs will change over the course of treatment.

In individualizing pharmacological interventions, many factors need to be considered. A patient's history with certain medications (positive or negative), plus his lifestyle, economic resources, and support network, almost always influence what treatments are prescribed and when. Thus, a patient involved in a stressful relationship will often need a different medication regimen (or different dosages) than a patient who has a supportive partner. A cognitively disabled patient with a complex medication regimen will surely need support from family members to comply with the prescribed treatment. Ideally, Drew's psychiatrist would have designed an approach not only to treat his bipolar disorder, which was clearly the appropriate diagnosis, but one that also considered his dislike of medications and general mistrust of psychiatry, and the relationship problems and other situational factors contributing to his course of illness. Given his interest in an acting career, it might have meant avoiding medications that cause weight gain, even though some of them (e.g., quetiapine) would probably

stabilize his mood. And it certainly would have included establishing a strong therapeutic alliance to encourage his collaboration in his own treatment.

In terms of the type of psychotherapy to offer, this, too, will vary depending on the patient's circumstances—his age, the degree to which current family or spousal relationships are problematic, recent events (e.g., loss experiences or work problems), and the patient's working knowledge of how to cope with bipolar disorder. The type and intensity of therapy may also change over time as a function of changing illness states or emergent life events, during periods in which medications are changing, or when the patient has discontinued all medications.

Why place so much emphasis on psychotherapy? As Drew's story illustrates, the functional consequences of bipolar illness are as important as the frequency or severity of symptoms. Bipolar disorder has wide-ranging effects on a patient's school, work, social, or family life, even when the patient is on an optimal medication regimen. Many patients remain functionally impaired even when only minimally symptomatic.[3] Despite the difficulties inherent in measurement of functioning, clinicians must be attuned to the specific effects of the illness on the patient's quality of life and, furthermore, to the factors that may contribute to poor functioning, including unremitting depressive symptoms, cognitive impairment, loss of social supports, or adverse reactions to medications.

Treatment as a Moving Target

The treatment of bipolar disorder is a moving target and needs to be continually reassessed and revised as the patient's symptoms and life circumstances change. Yet many patients with bipolar disorder say that they have been repeatedly given the same treatments in the ill-conceived hope that eventually they will respond. If their practitioner has changed any aspect of treatment, it has generally been to increase the dosage of a given medication or substitute another in the same class. Likewise, psychotherapists have been known to stick to the same treatment well after it is clear that the patient is stalled. ***A second major theme in this book is the need to continually reevaluate a patient's situation—his symptoms, level of improvement, and functional capacity—such that treatment plans can be adjusted accordingly.*** Sometimes the best course of action is to stop a treatment rather than introduce a new one; in other cases, it may involve using novel pharmacological agents or introducing behavioral plans such as sleep–wake cycle regulation.

The Role of the Family

When we asked Drew to tell us more about his experiences with psychotherapy, he grimaced. He had found insight-oriented individual therapy to be somewhat helpful, but he stopped after 6 weeks, saying "I got what I could out of the lady." He explained that his marital treatments were focused only on "things we could do to be nicer to each other." He felt particularly humiliated by an in-session exercise in which he was asked to rub his wife's back for 3 minutes whenever she said something that made him feel more confident about his acting career.

Drew's third wife, a nurse, had significant medical knowledge and was the first to suggest that he might respond to mood stabilizers. She encouraged him to put his work away and be in bed by midnight. Yet when Drew worsened (writing lengthy letters of introduction to movie directors, then trying to reach them well into the night) and she tried to contact his psychiatrist, the doctor never returned her calls. When Drew asked the psychiatrist about this, she explained that Drew had never given her permission to talk with his wife. Eventually, the psychiatrist invited Drew's wife in for a consult, but insisted that Drew not be present, to allow his wife to talk freely. Drew felt alienated by this encounter, which contributed to his decision to quit taking his medications.

In addition to the "one-size-fits-all" quality of his prior treatment experiences, none of Drew's treatment had involved *psychoeducation*. None of his clinicians had discussed the possibility that he had bipolar disorder, or explored the genesis of his depression or its effects on his relationships. Of course, milder cases of bipolar disorder can be easily missed by even the most experienced clinicians. Often, depression dominates the clinical picture to the extent that periods of hypomania or subthreshold mixed symptom states are missed.

In our view, the clinician should view the bipolar patient's interpersonal problems within the context of the symptoms of the disorder. For example, knowing that a patient tends to behave aggressively and be self-absorbed when hypomanic may help us to understand why he has recently lost his job, even though he might see and explain things quite differently. Marital or relational conflicts may have different implications if they only emerge during depressive episodes and resolve during periods of remission.

This brings us to the third theme of this book: ***Family members are integral members of the treatment team***. They provide information critical to making the initial diagnosis. Moreover, they are often the first to notice changes in the patient's mood or behavior, and can therefore help prevent worsening of manic or depressive symptoms. They

can offer immeasurable help in maintaining the patient's consistency with the treatment regimen. For example, they can help to ensure the bipolar person maintains regular daily routines and sleep–wake cycles. They may describe instances of medication nonadherence that the patient has either forgotten or thinks are insignificant.

Family members are often quite willing to give input into their relative's treatment, and are often bewildered by mental health professionals' seeming lack of interest. Throughout this book, we provide examples of how best to engage family members, so that they become allies in the treatment; how and when to set limits with them; and ways to make their involvement both palatable and helpful to patients.

HOW IS THIS BOOK DIFFERENT FROM ANY OTHER BIPOLAR BOOK?

Books on bipolar disorder have proliferated. Amazon.com lists over 100 books on the disorder, including first-person accounts; self-care books for patients, parents, or spouses; books about bipolar children or teens; managing bipolar disorder during pregnancy; and a host of "how-to" books for clinicians. Some of these books are clearly designed for psychopharmacologists, and others equally clearly are for psychotherapists. What has been missing is a clinically useful integration of pharmacology and psychotherapy as the foundation for treatment, including a realistic appraisal of the complexities of these interventions and what to do in specific situations.

What you do find in these books, for example, are discussions of medications, set out one by one. There is a chapter on lithium, one on valproate or carbamazepine, another on lamotrigine, one on antipsychotics, and one on "novel agents." These books usually survey the clinical trial literature on acute efficacy (e.g., how many studies have shown that the drug, when used as a monotherapy, does better than placebo in stabilizing a manic or depressive episode). We realize the importance of such reviews to an academic audience, but practicing clinicians may not find them useful. Although at times psychiatrists may have to decide among medications to treat patients' acute episodes, more often they seek information on what to do in very specific clinical situations. For example, they want to know how to consider the treatment options for bipolar I depression versus bipolar II depression—when to introduce changes, and how to make adjustments correctly. What these books miss, then, is helping clinicians resolve critically important treatment questions:

What combination of medications should a clinician choose for a particular patient in an acute episode?

In what order should they be given and at what starting dosage?

How does the clinician adjust this regimen if symptoms worsen, or if the patient switches into the opposite polarity?

What is the protocol when weaning patients off certain agents as they recover?

Clinicians often need to weigh cost–benefit ratios between side effects and efficacy at different points in the illness. They may want to know more about ways to prevent recurrence in a patient with subsyndromal symptoms than about how to stabilize an acute manic episode. In this book, our goal is to provide much-needed advice on how to make treatment decisions at different change points in the illness, based as much as possible on the available literature—what the science tells us and what it does not—and on our own experiences from treating numerous patients.

Most existing books on bipolar disorder address psychotherapy in a single chapter in which different treatment models (interpersonal therapy, family therapy, cognitive-behavioral therapy, or group psychoeducation) and their supporting evidence are reviewed. Although it can be useful to compare and contrast the models now in use, there are few studies that directly test these methods against each other or try to match patients to treatments. Other books focus on only one psychotherapy method and take the reader, chapter by chapter, through that type of therapy.

Most clinicians do not have the time or the resources to obtain extensive training in manual-based psychotherapies. Moreover, in our experience, clinicians want training in *strategies* as opposed to lockstep manualized treatments. These strategies cut across psychotherapeutic (i.e., psychodynamic, cognitive-behavioral, or interpersonal) models. For example, they seek ways to educate patients and family members about bipolar disorder; to help patients identify the early warning signs of recurrence and coach them on what to do when these appear; to assist them in coping with stressors that elicit symptoms; to clarify or challenge the patient's thinking about medications; or to counsel the patient about substance abuse. Indeed, adapting these principles of evidence-based psychotherapy and putting them into treatment individualized to the patient is both feasible for the clinician and beneficial to patients. Learning about these strategies involves borrowing from

the literature on specific psychotherapies and focusing on common elements. In this book, we emphasize common and effective psychotherapy strategies and how to time them to address the challenges of different stages of illness.

Finally, most of the existing books do not consider the heterogeneity of illness presentations with which clinicians in community mental health settings deal daily. Many clinicians do not see patients in an acute manic state. Most patients seek treatment because of subthreshold depressive or mixed states, or because they are functioning at a low level even though their symptoms do not appear to be severe. Some patients are chronically hypomanic, with occasional periods of depression, or they straddle the line between bipolar disorder and borderline personality disorder. Others may follow a bipolar illness course, but their real problems have more to do with anxiety.

In this book, we provide numerous cases of patients with a wide variety of clinical presentations. These examples illustrate the complexity of the illness, as well as the principles to follow when deciding what to do and when to do it. We offer ways to think about complex or highly comorbid patients from a longitudinal perspective, with changing treatment targets. There are suggestions on how to prioritize pressing concerns (e.g., suicidality) that may take precedence over other mood symptoms, and how to revise these priorities as the patient improves. It is our hope in presenting these examples that clinicians will be able to generalize the recommended approaches to the majority of patients in their practices.

We base our recommendations for clinical diagnosis and treatment on research evidence whenever possible. However, we have opted to use representative references on a given topic rather than an exhaustive list of references, or extensive comparisons of studies that went about addressing the same question differently. The reader who is well acquainted with the bipolar literature may at times wonder why we cite one study instead of another. Although we acknowledge the limitations inherent in noncomprehensive reviews, we believe that our approach improves accessibility and readability while maintaining our dedication to evidence-based practice. When appropriate, we refer the reader to comprehensive reviews of the literature on specific topics.

Given that we are writing this book for practicing psychotherapists *and* psychopharmacologists, we realize that readers will differ in the level of detail and amount of information they want or need. Psychopharmacologists may focus more on the details of constructing a pharmacological treatment plan for acute mania or hypomania, while psychotherapists may want more detail about the psychotherapeutic

strategies during maintenance treatment. Yet given our belief that treatment needs to be well integrated, we believe it would be helpful to peruse the entire volume.

Additionally, we assume that readers will differ in their familiarity with some of the technical language used, especially with regard to medication names and side effects. In general, whenever we introduce a medication in a chapter, we use its generic name, with its more commonly known trade name in parentheses, as in "fluoxetine (Prozac)." Thereafter, the medication is referred to by its generic name only. If that same medication is referred to in another chapter, both names are again provided. Appendix B is a table that provides both generic and trade/proprietary names for easy reference. It is a comprehensive list of all medications relevant to the treatment of bipolar disorder.

Similarly, some side-effect names—such as dry mouth—are self-explanatory. Others, such as agranulocytosis—when the bone marrow stops making white blood cells—require explanation and are provided for those readers unfamiliar with these terms.

A word about gender terminology: We refer to the patient as "he" in some places and as "she" in others. We realize this can be confusing, but we find referring to each patient as "he or she" is awkward. We at times refer to the treating clinician as "the psychiatrist" and at other times as "the therapist" or "the clinician," recognizing that patients with bipolar disorder are treated by health care professionals of all trades and degree status. All of the case studies have been disguised so that individuals cannot be identified, but the reader can be assured that the cases are all based on real-life situations we have faced in our practices.

STRUCTURE OF THE BOOK

This book is organized by the illness phases in which clinicians typically encounter patients with bipolar disorder, with both pharmacological and psychosocial advice to consider at every phase. Chapter 2 describes the basics of bipolar disorder: how manic and hypomanic episodes differ and the significance for treatment of diagnosing bipolar I disorder, bipolar II disorder, or subthreshold bipolar disorder; how bipolar disorder is distinguished in DSM-5 from "near-neighbor" disorders; and the significance of the duration of episodes. We explore the controversies currently being debated among clinicians and researchers, including issues such as whether a major depression with only one or two manic symptoms should be considered a part of the bipolar spectrum and the distinctions between bipolar disorder and borderline

personality disorder. Chapter 2 covers the most recent research on the phenomenology of bipolar disorder, and new ideas on how to approach the more diagnostically ambiguous cases in practice.

Chapter 3 offers recommendations for conducting intake evaluations. The psychiatrist, psychologist, or social worker undertaking the evaluation—whether this occurs on an inpatient or outpatient basis—should be aware of biological, genetic, and environmental factors that may be relevant to the patient's diagnostic presentation. We are trying to help clinicians avoid the situation Drew faced in never receiving a full diagnostic evaluation, or if he did, never getting the results.

In discussing the initial encounter and history taking, suggestions are offered on how to ask certain questions and probe further when a clinician is not getting her questions answered. We emphasize obtaining information from key relatives or other "collaterals" whenever possible, and offer strategies as to how to address the patient's concerns about the involvement of parents or spouses.

Chapters 4 and 5 describe modern pharmacological approaches to treating acute mania and acute depression, respectively. Acute episodes present challenges for planning both pharmacological and psychosocial interventions, although most of the research literature deals only with pharmacotherapy. The careful balancing act of finding the most effective but tolerable dosage requires some trial and error, yet following a basic algorithm—with opt-in and opt-out decisions along the way—can stabilize the episode and set the stage for maintenance treatment. The strategies will be different when the patient is acutely manic, mixed or depressed, psychotic, cognitively impaired, or younger versus older, but there are common themes as well.

Chapter 6 discusses pharmacological treatment during the maintenance phase, during which medication regimens may be simplified. Here, the challenge becomes one of controlling subsyndromal symptoms to reduce the likelihood of relapse, and trying to enhance the patient's return to functioning in the community. One of us (M. J. G.) has shown that even minor subsyndromal depressive symptoms (scores as low as 6 on the Beck Depression Inventory) can be associated with functional impairment in the maintenance phases after a bipolar depressive episode.[3]

Psychotherapy can be effectively introduced during acute episodes. The strategies may be very simple, such as offering emotional support to the patient and family, encouraging practical strategies such as the monitoring of mood states, or explaining the importance of consistency with medications. In fact, the strong therapeutic alliance that is often built during the most extreme phases of illness sets the stage for

more intensive treatment during the maintenance phases. Chapter 7 addresses the challenges of maintenance treatment from the psychosocial viewpoint. We emphasize psychosocial *strategies* rather than particular manualized treatments. The approaches include educating the patient (and family, if available) about bipolar disorder, social and circadian rhythm tracking, behavioral activation, and relapse prevention planning. Family caregivers play a key role during maintenance treatment in helping to track residual symptoms and identifying prodromal periods (i.e., the beginning of new episodes) or other change points. During Drew's maintenance treatment, he and his wife agreed to collaborate in identifying daily changes in his irritability and activity levels (his position: "I'll do it if you'll also do it on yourself").

The medically nonadherent patient presents special challenges (Chapter 8), but clinicians can enhance the outcome of pharmacological treatment by exploring the issues that get in the way of adherence. Often, nonadherence can simply be traced to the side effects of a particular medication. In other cases, nonadherence is associated with psychological conflicts of the individual (e.g., equating medications with a loss of independence), cognitive limitations (e.g., forgetting pills), or family factors (e.g., caregivers who constantly remind the patient that he is ill or insist on evidence of medication consistency). Drew was in constant conflict over his medications, which to some degree derived from their side effects (e.g., weight gain on quetiapine) or their meaning (i.e., feeling like a child) within his marital relationships. Chapter 8 includes many examples of how to talk to patients about nonadherence and to normalize it, and how to avoid setting oneself up as an authority figure who must be obeyed. Exploring the patient's long-term values or goals—and how medications do and do not fit with those goals—can be quite powerful, especially in the aftermath of an episode.

The unique issues faced by women during pregnancy and the postpartum period are covered in Chapter 9. Certain medications pose dangers to the developing fetus, but these dangers must be balanced against the risks of untreated bipolar disorder during pregnancy. Psychosocial interventions such as mindfulness-based cognitive therapy can enhance the patient's resilience during and following pregnancy. Current guidelines for the pharmacological treatment of postpartum bipolar depression, including the risks of breastfeeding when on lithium or other agents, are reviewed in this chapter.

In Chapter 10, on suicide prevention, we highlight the importance of an integrated, team approach to illness management. There are few data to guide the treatment of suicidality among bipolar patients, even regarding the oft-repeated recommendation to add lithium to

every regimen. Safety must be maximized during the postdepressive-illness phases, when many patients are still at risk despite their denial of suicidal intention. Including family members in suicide prevention planning is crucial because of the loss of insight among patients during acute episodes. Communicating closely with family members to enhance support can be protective during these high-risk intervals.

Finally, in Chapter 11—a "special topics" chapter—we discuss comorbid disorders such as ADHD, anxiety disorders, substance or alcohol abuse, personality disorders, or general medical illnesses, all of which frequently co-occur with bipolar disorder. Sometimes, the solutions to treating these complex combinations of disorders are straightforward (e.g., avoiding divalproex [Depakote] with patients who have hepatic problems). In other cases, they require weighing the benefits and costs of adjunctive treatments, such as when a patient has significant anxiety but has been destabilized by selective serotonin reuptake inhibitors (SSRIs) in the past. The dilemmas faced by clinicians when treating patients who have bipolar disorder and borderline personality disorder—such as when to rely on pharmacotherapy to stabilize mood and when to introduce dialectical behavior therapy or other psychosocial strategies—are discussed in this chapter.

In Chapter 11 we also discuss a related special topic: how to implement "split treatment" effectively when pharmacotherapy and psychotherapy are provided by different providers. There are ways to make shared treatment plans effective even when both practitioners are extraordinarily busy or do not fully comprehend each other's approach. Simple principles, such as optimal (rather than frequent) communication, mutual respect for another's area of expertise, and consistent messages to patients about the importance of both approaches, can make split treatment work quite effectively in practice.

In all, it is our hope that this book will help the clinician view the treatment of bipolar disorder in a fresh and new way: one that integrates individualized approaches to pharmacotherapy and psychotherapy, considers treatment as a moving target, offers flexibility when treating nonadherent patients or those with complex clinical presentations, and involves family members as important allies throughout treatment. But first, let us consider what we mean by bipolar disorder.

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