

Bipolar Disorder in a Preschooler: Long-Term Ramifications of an Early Diagnosis and Treatment

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CASE HISTORY

Joe is a 12-year-old boy living in a Boston suburb with his mother, the younger of his two brothers (the older being a half-brother), his mother's boyfriend, and the boyfriend's son. He has been in treatment at a Boston hospital since the age of 6 years, receiving both medications and therapy for bipolar disorder and separation anxiety disorder. He has been tried on different medications and has experienced significant side effects (namely, weight gain and other metabolic problems). In July 2005, between fifth and six grades, he was transferred to his current psychiatrist, FTM (a PGY-4 resident), for psychotherapy and medication management.

At the time of this report (spring 2006), Joe is a sixth-grade student who has been in some form of psychiatric treatment since the age of 3 years. His mother reports that he was doing well until that time, when his younger brother was born. Joe was first referred for psychiatric treatment when his mother found him "jumping on the head of his younger newborn brother." The patient was referred for play therapy at a community mental health center, where he received therapy for a couple of years. After starting in kindergarten, he began to have outbursts at school and was re-

portedly disruptive and moody. His mother said that when things "wouldn't go his way," he either "shut down" and refused to do schoolwork, or became disruptive and aggressive. He frequently needed to be restrained at home and at school. Mother also reported that Joe was then a very "irritable child." She said that he was bossy and demanding, and that when he did not get what he wanted, he became threatening and aggressive. He was physically aggressive toward the teacher and also his younger brother. Both at home and at school, he had many "explosive outbursts" in which he threw things and broke furniture. Joe's mother needed to be trained in restraining him at home in order to control him and protect the safety of other family members. In addition to having racing thoughts, Joe had difficulty with falling, and staying, asleep at night. His appetite and level of energy were within normal range.

Joe's mother reported that he did not have any difficulty paying attention or concentrating at school when he "wanted" to do the school work and "decided" to participate. In addition, she reported that he was impulsive and that he had threatened on several occasions to leave home. This behavior and attitude have markedly improved since Joe has been in treatment. He has continued to show some impulsive behavior, however, and at one point last year, after an argument with his mother, he rode his bike to his father's house (five miles away) without getting his mother's permission.

In 2000, as a first grader, Joe was diagnosed with bipolar disorder and separation anxiety disorder, and was started on medications. He was initially started on risperidone, which he continued to take for three years. His mother reports that his behavior and mood markedly improved during this period, but the risperidone had to be discontinued because of the patient's weight gain (10–15 pounds). Joe's mother reported that his weight gain affected his self-esteem and put limitations on his daily activities (e.g., he had to stop playing

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Harv Rev Psychiatry 2006;14:319–329.

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DOI: 10.1080/10673220601082851

on the town baseball team because he could not run fast enough). In the fourth and fifth grades, Joe started showing signs and symptoms of a clinical depression. He talked about “hating himself” and “hating his life,” especially when other kids “made fun” of him at school. He felt that he was an easy target to bully at school because of his weight and his having to give up sports.

In addition to the bipolar disorder, Joe was diagnosed with separation anxiety disorder while in first grade. Mainly because of excessive worries that something “bad” was going to happen to his mother, he was having difficulty separating from her in order to go to school. For the same reason, he would also be reluctant to leave anyone behind at home when he had to leave the house. Joe was soon started on sertraline, which eased the anxiety symptoms.

After being first referred to our clinic at the age of six (when he was in first grade), Joe was seen on a regular basis for three years, when he was lost to follow-up. Around that time Joe’s mother was very busy taking care of her father, who was very sick, and then died, with lung cancer. A few months after dropping out of treatment—and, as a result, stopping his medications—there was an incident at school necessitating Joe’s transfer to the emergency room for an evaluation. He reportedly became “out of control” and started breaking furniture in the classroom; his teacher had refused to let Joe leave the classroom when Joe said he was “getting bored” and wanted to go home.

It was around that time that the school found out that Joe had not been following up with his psychiatrist. The school contacted the Department of Social Services; shortly thereafter, Joe’s care was reestablished in our clinic. Since November 2003, when he was in fourth grade, he has been followed on a regular basis for psychotherapy and medication.

Present Treatment

As noted earlier, Joe was transferred to FTM for therapy and medication treatment in July 2005, prior to which he had been seeing two different clinicians (a male child psychiatry fellow for medications, and a female psychology intern for therapy). Joe had had an intermittent relationship with his therapist; he missed many appointments, and during the few appointments that he came to, he was difficult to engage. It was hoped that having one male clinician for both medications and therapy would constitute a better match and improve treatment.

During the first session with FTM, Joe generally refused to talk, and said that he did not like to come for treatment. The therapist did most of the talking and told Joe that they could use the sessions in a way that they would both find helpful and interesting. When Joe then mentioned that he did not like to come in for morning appointments because “he is not a morning person,” the therapist accommodated his request and gave him the option to come for an afternoon

appointment the following week. Joe shrugged and said that he did not know whether he would come back. When his mother joined the session at the very end, she told FTM that she was surprised that Joe did not “flip out” around attending a whole session (as he had that day).

When Joe and his mother showed up for the second session, Joe was more forthcoming. He told the therapist that he had three dogs and that he liked the middle one best. The therapist commented that Joe was the middle child in his family. Joe agreed that that was something he had in common with his middle dog and that he had also many other things in common with him; they both have “bad knees” and both like the summer season. He then remarked that his grandfather who passed away the previous year had gotten him the dog as a present.

Joe has been showing up regularly, accompanied by his mother, for his every-other-week appointments with FTM. Most of the therapy work is done using the computer. Joe and the therapist play hockey games online at times. Joe’s favorite thing to do during the sessions is designing brochures for his ice hockey team using Microsoft PowerPoint.

With time, Joe was more able to talk in therapy about some of his feelings. During one session he drew the Irish flag and wrote his Irish last name on the flag. He also expressed his wish to visit Ireland, noting that his father had told him about the country. Later in the session he talked about his father’s sickness (referring to the alcoholism) and mentioned that it upsets him when he goes to see him and finds out from his stepmother that his father is “sick” and not available.

Other issues discussed in therapy include Joe’s body image. He talked about his frustration when his friends—and especially more recently, also the girls—tease him about his weight. He was able to say, though, that he likes it when his friends joke around with him and make puns based on his name.

During one of the sessions scheduled around Joe’s birthday, he and the therapist designed a birthday card for Joe on the computer. Joe proudly asked for more copies of the card to show to friends and family members.

Medication Management

When Joe was first transferred to FTM for treatment, he was taking sertraline and aripiprazole. He continued to gain weight on the latter, though at a much slower rate than he had while previously taking risperidone. Oxcarbazepine was added to address Joe’s mood lability, but it did not help and was therefore discontinued. Topiramate was added and slowly titrated to a dose of 150 mg twice daily. Sertraline was discontinued because of Joe’s ongoing mood irritability. With the current combination of topiramate and aripiprazole, Joe’s mood has remained more stable, as has his weight, and there have been no breakthrough anxiety symptoms.

He currently receives aripiprazole 15 mg per day and topiramate 150 mg twice daily.

Social and Developmental History

Joe was born to a single mother who already had a 7-year-old son from a previous relationship when Joe was born. Joe was the product of a normal vaginal delivery after a smooth, noncomplicated, term pregnancy. He was reportedly an easy-to-soothe infant and acquired his developmental milestones at the expected ages.

Joe's mother has a sister 12 years older than she. Their mother died when Joe's mother was 7 years old. Her father struggled with alcohol problems. After her mother's death, Joe's mother went to live with relatives. The living arrangements were not stable, however, and she would move in with different relatives three or four times a year. When she graduated from high school, she was pregnant with her first son (who is 19 years old now) and moved out to live with her sister. She never married. She was in a relationship with Joe's father for a few years and had two sons with him (Joe, now 12, and his younger brother, 7). She reports that Joe's father has been inconsistently involved in his sons' lives.

The father has been struggling with alcoholism. She reports that he would sometimes make plans to take his two sons to a ball game—and then not show up. There have also been times when she dropped off the children at his house (he is married and has started his own family), only to be told by his wife that he was sick and that the children must leave. On a few occasions, he allowed Joe's younger brother to visit for the weekend, but Joe was not allowed to go; according to Joe's mother, the father is unable to deal with Joe's "bipolar condition."

As noted earlier, Joe currently lives with his mother, his younger brother, his mother's boyfriend, and his 13-year-old son. His older half-brother recently moved out but continues to visit regularly. The mother has been with her current boyfriend for four years. She describes his relationship with Joe as being "close; they go to sport events together." The mother works as a longshorewoman. Her boyfriend is a carpenter. Joe likes ice hockey and is an active player on the town team; he has also been very active in baseball. Family history is significant for alcoholism on both sides (Joe's father and his maternal grandfather). Joe's mother reports that she was diagnosed with bipolar disorder and an anxiety disorder. She was treated with sertraline but stopped after a few months. Though not currently in psychiatric treatment, she is functioning well.

Medical History and Other Pertinent Data

Joe is 4'10" tall and weighs 146 pounds. His medical history is significant for hypercholesterolemia, a benign heart

murmur, and allergic rhinitis. Blood work done on a regular basis reveals normal CBC, BUN, Cr, and electrolytes, with elevated levels of total cholesterol (242 mg/dl) and LDL.

Cognitive testing done through the school system showed full-scale IQ of 92 (within the average range). Three out of the four composite IQ scales were also within the average range: 96, 94, and 102 for verbal comprehension, perceptual reasoning, and working memory, respectively. Processing speed was in the low-average range, with a score of 85.

QUESTIONS TO THE CONSULTANTS

1. What are the pros and cons of diagnosing and medicating a child with a possible bipolar disorder at the age of 6 years?
2. What are the clinical criteria for bipolar disorder at that age?
3. How would you determine whether to start experimenting with the possible discontinuation of medications as the patient grows older?
4. How would puberty affect his treatment course?
5. What are the pros and cons of including a psychodynamic play/talking therapy throughout this child's course of treatment?

RESPONSES OF THE CONSULTANTS

Robert G. Ziegler, MD

Many child psychiatrists see patients such as Joe—that is, if their families can get themselves and the child to the therapist—who have multiple issues, including parenting problems, insecure attachments, or psychosocial adversity. These children often have multiple symptoms that surround their reactive, impulsive aggression; these symptoms lead to the child's being presented for treatment, even though the diagnosis remains uncertain. The first question, about the pros and cons of "diagnosing and medicating" a child of six, is not one that we wonder about within the routine practice for children with attention-deficit/hyperactivity disorder (ADHD), who are often reactive and aggressive. While a bipolar diagnosis opens the path for the use of mood stabilizers or antipsychotics in younger children, there are unanswered questions about the use of such drugs in children so young. Whatever our working diagnosis is—ADHD, disruptive behavior disorder NOS, or bipolar—our interventions still need to be driven by our formulations, not diagnosis alone. Formulation guides treatment planning to respond to problems, or to move toward solutions, or may simply try to enhance strengths and minimize risks; in itself, a diagnosis in the case of a child (or their parents, for that matter) often does not determine exactly what we do. The same is true of other diagnoses until we have the

results of complex, longer-term studies (like the Multimodal Treatment Study of Children with ADHD¹ [MTA]) that will clarify outcomes from medications, behavioral treatments, or combined treatments.

Joe did not have core symptoms of ADHD, but as in the more complicated ADHD cases in the MTA study, he did have a large set of problems. The absence of ADHD symptoms is surprising in view of the level of comorbidity with ADHD that Wozniak² has documented in the early pediatric bipolar group. Joe meets some of the clinical criteria described in the American Academy of Child and Adolescent Psychiatry work group's article on bipolar disorder³—including irritable mood, decreased need for sleep, and racing thoughts—but no grandiosity, euphoric or expansive mood, pressured speech, distractibility, excessive involvement in pleasurable or risky activities, or psychosis is described. Many of his symptoms could make us entertain oppositional defiant disorder; this diagnosis would highlight the nature of Joe's attachment, a very important issue for a child's self-regulation in the preschool era, when the use of aggression can be the way that some children manage an insecure attachment.⁴

Although Joe's mother learned how to do safety holds when Joe was 3 and 4 years old, there is little suggestion of any other ways in which this child and parent had learned to manage conflict or emotion, or of how the mother set limits in those years. We know she brought Joe to "be fixed" when his sibling arrived and disrupted their world. Joe had trouble, and mother found his aggressive responses difficult to soothe or limit. A diagnosis of bipolar disorder—which implies to many people a "chemical imbalance"—might empower this mother by relieving her of feelings of guilt and responsibility for Joe's behavior, but there is the risk of minimizing the contribution of, and need to address, psychosocial and relational aspects of his difficulties. We would not be stretching a point to say that this mother's own sense of "love" had been affected by her own life history (early loss of a maternal figure, an alcoholic father, and then serial caretakers, with none of them able to make a commitment to her). Knowing mother's prior exposure to violence or trauma may be important, since she was clearly overwhelmed by Joe's aggressive behavior toward the new sibling. In those early years, it might have been helpful to do some relational work and directive-parenting education—which could have strengthened her capacity to love and to limit.

Regarding the future and Joe's use of medications, it is good to know that Joe's bipolar, anxious mother thinks that she is functioning well without medication herself (so might he be able to do so, now or later on). However, a medication reevaluation would mean reevaluating the ecology of Joe's relationships, level of function in different settings, and current resilience. We could begin a reconsideration of the third question (concerning the possible discontinuation of medications) by scheduling two or three mother-son meetings,

which would clarify mother's current parenting style and the nature of Joe and mother's relationship. Various studies show that parents with anxiety disorders or mood disorders can exacerbate children's symptoms. What is the parenting style of Joe's mother? How does she offer her parental love? What is the current quality of the attachment between Joe and his mother? How emotionally attuned is she to him, and what is her level of commitment to the activities that will keep him strong and growing?⁵ How does she support his current sense of competence and self-esteem? Even if Joe has bipolar disorder, the diagnostic assessment does not include observed relational data (which we could obtain from a reevaluation) beyond the perimeter of the child's play and the parent's report.

Other data about Joe come from the empathic alliance that begins in the first session with FTM, who offers words that are tolerated by Joe, and who responds to Joe's minimal cues. By the second session, Joe shares his place in the family as a middle child. We know, however, that it is no easy task to be the middle child of same-sex siblings (Toman's keenly observed work on sibling positions⁶ is of some relevance here, though some see it as akin to astrological forecasting); we would like to know if the "middle dog" is favored by anyone else in the family. FTM has offered Joe a chance to be himself, given him a new identification figure, and offered Joe opportunities for negotiation so important to a child who has lacked a comfortable ability to negotiate difficulties with others. Together they find joint activities that offer pride and a sense of self and accomplishment. The case history suggests Joe was "irritably" catapulted from the role of an "easy to soothe" baby to one whose behavioral response to challenges was a meltdown. FTM helps him to tolerate disclosure of his dilemmas of disappointment and aggravation. While the evidence base of outcome data for controlled, long-term psychodynamic intervention is limited, psychodynamic thinking does focus clinicians on explanatory narratives that can help patients integrate their experience with their emotions and help them endure the unpredictability of life. The therapeutic relationships we cultivate with patients in the hothouse of our consulting rooms, in which emotion, experience, and exchange can be carefully tended, are especially important; but these roots must bear transplanting into the relationships that exist in the child's world.

Broadening the relational context, what is it like to sit with this mother and all three of her sons? How does this change in the presence of the stepfather? If one adds the new, older stepbrother? When I see that other relationships are working well, I feel myself more confidently able to withdraw some pharmacologic neurochemical modulators since the modulating capacities of good human relationships can support neural regulation and connectivity. If we examine another important relationship, is the biological father amenable to receiving help that might strengthen his

connection with his son? Can he step up to the plate by naming his disease (alcoholism) and admit its impact on Joe in a meeting with FTM? Even children of intact parents like to be able to turn to the alternate parent in the face of conflict with the other; and children of divorce, like Joe, show some stamina when they bike to the separated parent's home for help and comfort (even when it is unlikely to be forthcoming). Thinking about the father's struggle with alcoholism introduces the fourth question (concerning the impact of puberty on his treatment course). The onset of adolescence, coupled with Joe's actual and genetic relationship to an alcoholic, demands that we consider Joe's risk of substance abuse.

That risk might be minimized by an intervention about alcohol and substance abuse framed around his father's "sickness," as well as by continuing his medication (if we draw a lesson from the ADHD book). Psychoeducation about the parental disease of alcoholism can be integrated into a family treatment since his younger brother also needs to address the issue. This process might even create a new joining point between this mother's history (i.e., having an alcoholic parent) and that of her sons. The problem of turning to drugs and alcohol is one that could also be addressed ("People often use alcohol or substances to help them with feelings or moods that they feel they can't control. What helps you—in this family—stay in control and manage some very sad feelings?"). Therapeutic action that heightens awareness of risks, that highlights the role of choice in a preteen who has a sense of growing autonomy, and that stresses the importance of honesty (i.e., confronting denial as part of a disease) can help this family grieve and can strengthen the reality of their acceptance of one another. In addition, this contextual examination of Joe's current sense of competence and self-esteem can help address the third question (about the possible discontinuation of medications). If his therapist can engage Joe in thinking about issues of alcohol use and abuse in the family (past and ongoing) and about his own medication (which Joe sees as improving his level of function but at the cost of extra weight and a loss of self esteem), he will experience another level of both participation in risk/benefit discussions and ownership of his difficulties and choices.

The CATIE (Clinical Antipsychotic Trials of Intervention Effectiveness) study suggests that whether we use old medicines or new, we still need to stay connected to the other components of our care and treatment of these serious illnesses.⁷ This cautionary note applies—and may even apply with special force—to interventions on behalf of "early bipolar children." With this population, there are few "crisp" responses to medication intervention alone, and it remains an open question whether this diagnosis represents a bipolar disorder that would continue to be identified as such into adulthood.⁸ There is some evidence that children with early-onset anxiety disorders may be more at risk for adult depressive disorders and also that established cases of child or

adolescent depression may turn into adult bipolar, but we still cannot readily separate which will become what until we can mount larger, long-term, population-based studies using the most reliable diagnostic tools we have—and even then, if 50% with early-onset adolescent depression become bipolar, which 50%? We may continue to revise our terminology, just as the terminology for adult bipolar disorder is being deconstructed,⁹ but whatever name we use, we need to remember that these children are bearing the weight of considerable symptoms that need to be addressed. And if using the term *bipolar* causes us to move from diagnosis to medicine with less evaluation and less consideration of interventions, we may not have accomplished much or, indeed, anything.

Thankfully, our field continues to clarify the issues that surround a child's diagnosis and further impair his or her functioning. Even in the case of ADHD, an area of intense research, there are many unresolved questions concerning the impact of parenting and, more generally, of family. Research is ongoing; for example, a recent issue (March 2006) of the *Journal of the American Academy of Child and Adolescent Psychiatry* includes two articles on these very questions: "Relationship of Family Environment and Parental Psychiatric Diagnosis to Impairment in ADHD,"¹⁰ and "Family and Cognitive factors: Modeling Risk for Aggression with ADHD."¹¹ These articles remind us of the importance of the family environment and cognitive status in the presentation of any diagnostic entity in child psychiatry. Mentioning these articles here is a way of flagging that despite our having a decent amount of information on Joe's symptomatology and on the history of his family and treatment, we are still far short of understanding exactly his psychiatric situation or what needs to be done to improve it.

We do not know to what degree Joe witnessed or experienced violence in his home or community. Children who have been exposed to violence often have difficulties with how they manage their fears and anger. Because the exposure to violence frequently occurs in the intimate setting of the home, a natural distrust affects the way that children may communicate (or try not to) about their exposure, even to attuned clinicians like FTM. But it is not just the family setting that is at issue here. Among the teens who have been psychiatrically hospitalized on our adolescent unit, we found that although their past exposure to violence at home was a factor, their recent (past year), community-based exposure to violence was highly associated (by self-report) with their own violent acts.¹² In addition, in a school-based survey of sixth-, seventh-, and eighth-grade children, self-reported concerns about depression were associated not only with school difficulties and getting into fights, but also with high levels of social and personal adversity.¹³ These questions are ones that we need to consider in Joe's case, though it may take the current therapy in a somewhat different direction. Cues

about trauma will often emerge in play, whereas Joe's recent focus in therapy appears to be in accepting the pleasures of consolidating a sense of competence with FTM.

How will modulation of behavior, good functioning in school, and healthy relationships be supported for Joe—whether with or without medication—as treatment continues? Good prognosis is suggested by Joe's school function; his intellectual capacity appears “good enough,” even with some slow processing speed. Mother's relationship to her boyfriend seems not to have exaggerated, or added to, past tensions. Joe's connection to treatment may help him begin to add some dietary practices that would, in conjunction with his sports activities and training, help him to manage the adverse metabolic consequences of his medication treatment—which would further increase his self-esteem and sense of control. Although the last of the questions posed to us presents a mutually exclusive choice between medication follow-up or talking therapy, Joe's problems and progress might be best addressed through a flexible, multimodal therapy¹⁴ that could provide different treatment types, with the possibility of moving flexibly among them (at least until we find out that it's “all about the medicine,” as the MTA study suggested for the majority of the ADHD subjects).¹ But until we know that, it would be best if a single provider could maintain a connection to Joe and his family over the course of his development, adjusting the schedule of visits to meet the needs of the patient (at times using referrals to support different aspects of Joe's development), and working, as necessary, with Joe and other family members as new risk factors emerge.

Steven Schlozman, MD

The treatment of juvenile bipolar disorder remains a highly charged and often controversial issue. Although the reasons for these controversies are multifaceted, it is likely that the overall stigma associated with adult bipolar disorder, the multiplicity of often unchecked information about all childhood psychiatric challenges, and the incomplete knowledge of juvenile bipolar illness itself all play a role in the strong public and professional response to discussions of this complex issue. Suffice it to say that the treatment of children, especially preadolescents, for suspected bipolar illness often generates strong, and not always positive, feelings among clinicians and the public. Any clinician reckoning with these issues must take these reactions into consideration when generating a treatment plan.

That said, there is growing, very solid evidence that some behavioral disturbances in younger children do not easily meet criteria for disorders other than bipolar disease. These behaviors are increasingly well documented and include sudden and very intense bouts of rage over relatively minor insults, rapid mood cycling throughout the day, frequent

nightmares, and extreme difficulty with self-soothing once the intense tantrums have begun. Although these symptoms are somewhat nonspecific, the apparent grandiosity inherent in a massive tantrum has frequently been conceptualized as the developmental equivalent of adult grandiose notions of entitlement and rage that characterize more traditional descriptions of mania.¹⁵ Additionally, epidemiological data suggest that children with these behavioral patterns have a higher percentage of first-degree relatives with bipolar illness, and that a percentage of these children will go on to manifest more traditional symptomatology of bipolar disease as they enter adolescence and adulthood.¹⁵ Finally, treatment data show that these children do not respond to interventions that target other symptoms. These behaviors do not seem to stem from severe ADHD alone; in fact, stimulants have been found in some circumstances to make this behavior worse. Similarly, the use of antidepressants to treat suspected unipolar depression has been successful in some cases but has had the opposite effect in others, leading to severe agitation and controversy about whether this response suggests a bipolar diathesis. Given these data, it seems clear that children with intense rage and tantrums, very much like Joe's in the case detailed above, suffer from a syndrome that is best described as pediatric bipolar illness.^{16,17}

For the clinician, these controversies pose a special set of problems. We do not have complete data on the side effects of mood-stabilizing agents on the rapidly developing brain. We do not possess a good understanding of why some children with behavior like Joe's present with unipolar depression and perhaps comorbid ADHD, and why others have something more consistent with recent conceptualizations of pediatric bipolar illness. Finally, we are not very good at predicting which of these children will go on to develop more classic bipolar presentations. As with much in child psychiatry, we are left with incomplete data with which to make potentially far-reaching decisions that will affect the child's sense of self and the parent's sense of their child's capacities, and that will have potentially unknown effects on the developing brain.

What, then, do we know—with more certainty—that can guide us in our treatment approach? First, we have good longitudinal documentation of children and adolescents with poor frustration tolerance and untreated psychiatric syndromes. Poor school performance, struggling peer relations, substance abuse, early pregnancy and promiscuity, accidents, conduct disturbances, and suicidality are all higher in untreated or poorly responding populations of psychiatrically ill youth.¹⁷ We also know that bipolar illness is extremely heritable; research first done by Strober and colleagues¹⁸ suggests that up to 30% of preadolescents with bipolar illness have a first-degree relative with bipolar disease. Finally, although there remain regional differences about whether traditional mood stabilizers or atypical

antipsychotics should be the first-line treatment for preadolescent bipolar illness, both pharmacological approaches have been found effective in the preadolescent and adolescent populations.¹⁷

Put more succinctly, the positive aspects of early recognition and treatment include primary and secondary prevention of more severe problems later in life, as well as the potential to vastly improve the child's current quality of life. The negative aspects involve reckoning with the inevitable uncertainty that a newly defined syndrome brings to the clinical table. Given these issues, one should realize that *all of medicine* is characterized by a level of uncertainty. The worst mistake in the face of these ambiguities is to do nothing. Parents and the treating clinician are best served by a careful discussion of the risks and benefits of all approaches, and by frequently updated, forthright appraisals of the current standard of care.

Pediatric bipolar illness is far too complex to be treated through a single modality such as pharmacologic intervention alone. While all children meeting the criteria for pediatric bipolar disease will likely require some medication, the treatment plan should never stop with the administration of medications alone. School discussions, family work, individual psychosocial interventions, and careful attention to the meaning of both the diagnosis and the medications to patient and family are extremely important.¹⁷

Responsive treatment requires careful consideration of the rapidly changing developmental trajectory that characterizes normal growth. The patient's capacity to understand his or her challenges will grow in concert with cognitive and emotional development, and the clinician can help the patient to better cope with these issues by keeping careful track of where a child is expected to be developmentally throughout the course of treatment. The onset of puberty is therefore especially relevant from multiple vantage points.

One central consideration is that the child's capacity to metabolize medications may change with maturation of liver and kidney function. If medications are continued throughout puberty, adjustments may be necessary to maintain response. Also, the child's capacity to think recursively and abstractly will increase rapidly throughout adolescence. Frustration that was poorly understood before adolescence may now make more sense to the patient. Children like Joe might very well become more adept at predicting what situations are especially difficult; praise for, and attention to, these changes in the child's sense of self are fundamental to both the therapeutic alliance and the response to treatment.

Although estimates vary, the prevalence of bipolar illness in children and adults is something close to 1% for each population.¹⁷ Since some percentage of these children will *not* subsequently develop significant psychiatric illness, the clinician needs to consider when it would be appropriate, if ever, to taper medications. Taking into consideration factors

such as family/biological history, the family's and patient's desires regarding ongoing treatment, the reliability of the patient and family in reporting difficulties such as those that might occur in the absence of medications, and the patient's course over time all play vital roles in this decision. As suggested above, the patient-doctor alliance is absolutely essential. Any decision to change treatments needs to be a team decision, and to the extent that the team feels connected, these decisions can be made safely and effectively.

The treatment of pediatric bipolar illness can be immensely harrowing but also immensely rewarding. The severity of the illness demands a close working relationship among patient, family, and clinician. The psyche of children, regardless of psychiatric burden, is always changing. To this end, paying attention to dynamic changes within this psyche—the crux of psychodynamic therapy itself—is an ideal venue through which issues of self-esteem, fantasy, and identity can be worked through and understood. In some ways, the close relationship between clinician and patient that bipolar disorder necessitates makes psychodynamic work more feasible. Since psychosocial interventions with children are typically multifaceted, it is inevitable that this work would involve, at the very least, supportive therapy, behavioral approaches, and psychodynamic attention to the meaning of the administration of medications. Lack of attention to any of these issues runs the risk of missing vital opportunities to improve the patient's course.

The psychiatrist's exact approach to treating Joe remains to be seen. While the clinician needs to consider all of the nuances involved in treating any patient as complex as Joe, the overall theme of the treatment is clear: the psychiatrist must be empathically connected to his patient, well-informed regarding the particulars of a rapidly developing field, and heterogeneous in his approach to easing the patient's suffering. Perhaps most importantly, Joe likes and trusts his psychiatrist, who balances an understanding of the illness with an appreciation of all that makes Joe special. In the end, these qualities are the best possible indicators that things will go well for Joe and his family.

Jefferson B. Prince, MD

Joe's case history provides an excellent opportunity to discuss pediatric bipolar disorder (BPD). Although controversy persists about the nosology, phenomenology, assessment, diagnosis, and treatment of pediatric BPD,^{3,17,19,20} clinicians in mental health and pediatric settings regularly evaluate children for BPD.^{21–23} Moreover, bipolar children suffer impaired relationships, experience academic difficulties, and are at high risk of self-injurious behaviors and psychiatric hospitalization. Helping clinicians to identify and properly assess pediatric BPD is critical; early identification, assessment, and diagnosis may lead to appropriate treatments

that could alleviate suffering, improve outcome, and provide hope to children with BPD and their families.

In recent years our understanding of the clinical characteristics, correlates, and course of pediatric BPD has grown. For example, mania has been recognized in an unexpectedly large number of pediatric patients referred to an outpatient psychopharmacology clinic in an academic medical center.^{24,25} These children suffered marked psychosocial impairment and had high rates of comorbidity with ADHD, oppositional defiant disorder (ODD), depression, multiple anxiety disorders, and psychosis. Mixed mood states with a pattern of chronic ultradian cycling (i.e., daily cycling during the episode) appears to predominate in bipolar youth.^{26–28} Symptoms of increased energy, irritable moods, accelerated speech, distractibility, elation, poor judgment (e.g., hypersexuality, daredevil acts, silliness, uninhibited people seeking), grandiosity, flight of ideas/racing thoughts, psychosis, suicidal thoughts/self-injurious behaviors, and decreased need for sleep are frequently seen in bipolar children.^{26,28} In one study, presence of psychosis appeared to increase the likelihood of mania/hypomania persisting in two-year follow-up.²⁸

Although irritable moods are reported in most patients with pediatric BPD,^{26–28} there is debate about the significance of this symptom. Some investigators find grandiose, euphoric, but not irritable moods to be most characteristic of bipolar youth.²⁹ These investigators argue that irritability is a nonspecific symptom that, while commonly observed in youth with BPD, lacks specificity, therefore limiting its value in diagnosing pediatric BPD or in differentiating BPD from disruptive behaviors disorders.^{30,31} However, other investigators have observed that usually severe irritability, not euphoria, is the principal mood disturbance in bipolar youth.³² Moreover, in this study the presence or absence of euphoria did not alter the pattern of manic symptoms, rate of grandiosity, or pattern of comorbid disorders. These data challenge the belief that euphoria represents a “cardinal symptom” of pediatric BPD. Building on this concept, Mick and colleagues³³ studied the quality of the irritability observed/reported in 274 children with ADHD and BPD ($n = 30$), unipolar depression ($n = 100$), or no mood disorder ($n = 174$). These authors found that “ODD-type” irritability usually occurred in subjects with ADHD and was mildly impairing. In contrast, the subjects with unipolar depression were likely to display a “mad/cranky” level of irritability, and those with BPD were most often “super-angry/grouchy/cranky.” These data suggest that early-onset mood disorders may manifest as “extreme, explosive irritability.” Taking such research findings into consideration will help us make sense of Joe. He was initially brought to a community mental health center because he had physically assaulted his helpless younger brother. Despite his level of severe aggression, Joe is treated in play therapy for

several years. It is not until kindergarten that he is diagnosed with a mood disorder. The course of Joe’s condition is reflective of two common phenomena: in preschoolers a diagnosis of BPD is not usually considered, and children are often symptomatic for several years prior to diagnosis and treatment.^{25,27} Only when Joe’s moodiness appears severe enough—as evidenced by his alternating moods between being “shut down” and so disruptive/aggressive/explosive that he requires restraint at home and in school—is the diagnosis of a mood disorder considered.

Assessment of BPD in a prepubertal child is challenging. Although the DSM-IV-TR criteria for BPD were not written specifically for children, these criteria are used to diagnose patient of all ages. Mood disturbances in children are likely to be expressed in a manner commensurate with their developmental age. If and when the DSM-IV-TR criteria are met, a manic episode can and should be diagnosed.³⁴ The diagnosis of BPD not otherwise specified (NOS) is often appropriately made in severely impaired children with a mood disturbance who are irritable, aggressive, and explosive.²⁰ Appropriate assessment requires gathering of information from available sources and clinical interviews of both the child and parent(s). These data should then be integrated with other information, such as likelihood of mania in this particular setting/community, family history of affective illness, and whatever other considerations might be relevant to particular patients.³⁵ In clinical practice, rating scales are a simple and useful way to gather information and to supplement, but certainly not substitute for, the clinical interview. The Child Behavior Checklist has been shown to be a helpful guide in screening for pediatric BPD.³⁶ The General Behavior Inventory, a nonproprietary scale available in self-report and parental-report forms, has demonstrated good ability to discriminate bipolar from nonbipolar youth in both academic and community mental health settings.³⁷ Clinicians and parents may use the Young Mania Rating Scale to track severity of mania and treatment response. An array of information about rating scales to evaluate pediatric BPD can be found at www.manicdepressive.org, www.bpkids.org, or www.schoolpsychiatry.org. Clinicians should assess the frequency, intensity, number, and duration of manic symptoms in children being evaluated for BPD. Prospective mood-charting may be a useful means to gather longitudinal data on the child.³⁸ Clinicians and families may either develop a mood chart together or, instead, access www.bpkids.org/learning/6-02.pdf for a sample chart. Mood charting engages the family in a structured observation of the child’s symptoms, helps to track non-somatic therapies, and may improve both compliance and the observation of medication side effects.

Not surprisingly, children with pediatric-onset BPD experience more trauma and psychosocial distress than either ADHD children or normal controls.³⁹ These adverse life

events may significantly delay diagnosis and contribute to poor outcome.⁴⁰ Joe suffered significant losses and stressors that appear to have adversely affected his development and also his initial engagement in treatment. Our understanding of the association between anxiety disorders and pediatric BPD is emerging. Recently, a broad range of anxiety disorders has been observed in youth with BPD.⁴¹ In Joe's case, he had many understandable reasons to be anxious. Once mood stabilization is achieved, management of Joe's anxiety may be addressed through therapy or medications. In this context, consideration of potential alternative causes of manic symptoms is essential. While BPD is the most common cause of mania, clinicians should recognize that there are additional causes, including psychological trauma, communication disorder, developmental disorders, seizure disorder, head injuries, neurodevelopmental disorders (e.g., fetal alcohol syndrome/effect), hyperthyroidism, and activation by medications (e.g., stimulants, antidepressants, steroids, antibiotics, pseudoephedrine).³

Treatment follows diagnosis. Given the severe morbidity of pediatric BPD, families and patients usually benefit from a coordinated treatment plan that integrates medications (often more than one is necessary), psychotherapies (individual, group, family), and educational interventions (accommodations or modifications in school, or therapeutic schools), as well as psychoeducation and parental support (available through national organizations such as the National Alliance for the Mentally Ill or the Child and Adolescent Bipolar Foundation).³

Although medications are usually a fundamental part of the treatment plan, our knowledge of their safety, tolerability, and efficacy is limited. Lithium remains the only treatment approved by the Food and Drug Administration for pediatric BPD (in children older than 12 years).⁴² Pharmacotherapy is directed at the presenting symptoms. It is recommended that in patients presenting with BPD type I without symptoms of psychosis, monotherapy with either a mood stabilizer (i.e., lithium, valproic acid, or carbamazepine) or atypical antipsychotic (AAP) (i.e., risperidone, olanzapine, or quetiapine) is indicated.³ In patients with only partial response, the initial medication should be augmented with either an additional mood stabilizer or an AAP. The combination of lithium and valproic acid has been shown to substantially reduce symptoms of mania and depression in children.⁴³ If the initial treatment is poorly tolerated or there is poor response, then switching to an alternative monotherapy is suggested. Clinicians are encouraged to continue this process, gradually moving up, if needed, to two mood stabilizers plus an AAP. Depending on response, treatment with oxcarbazepine, aripiprazole, or ziprasidone may be necessary. The final stage includes treatment with either clozapine or electroconvulsive therapy. In patients with BPD type I with psychosis, it is recommended that both a mood stabi-

lizer and an AAP be started concurrently, and that the same augmentation strategy be followed.

In Joe's case, the combination of aripiprazole and topiramate has been, it seems, both useful and well tolerated. Although topiramate does not appear efficacious in treating adults with BPD, retrospective, open, and pilot data in children and adolescents are promising.^{44–46} Topiramate has been reported to impair cognition; we may wonder whether topiramate contributes to Joe's slow processing speed (which may, however, also be a result of his condition). Although controlled data is lacking in youth with BPD, recent chart reviews found aripiprazole effective in reducing manic symptoms.^{47,48}

Treatment with AAP in pediatric patients warrants careful monitoring; various side effects may be anticipated. Sedation and extrapyramidal symptoms may occur during the early phases of treatment, while akathisia or dyskinesia/dystonias may develop after several months of therapy.⁴⁹ Clinicians are encouraged to monitor for these side effects and to document abnormal movements using the Abnormal Involuntary Movement Scale. Patients treated with AAP should also be monitored for weight gain and development of a metabolic syndrome. Although not specifically written for children, the American Diabetes Association guidelines recommend that clinicians inquire about family history of diabetes and that they regularly monitor patients' body mass index, waist circumference, blood pressure, fasting blood glucose and fasting lipid profile.⁵⁰

The decision about if and when to taper medication(s) requires clinical judgment, collaboration with the family, and wisdom. Clinicians and parents should balance the past level of impairment, the current level of functioning, and the tolerability of the treatment. The goal of treatment is to achieve remission and prevent relapse. Once the patient's BPD is in remission, it is suggested that at least an additional 18 months of pharmacotherapy is required.³

Although clinicians and parents may reasonably expect that pubertal maturation will influence affective illness, the impact of puberty on the symptoms, course, and treatment of prepubertal-onset BPD is understudied. Pubertal developments challenge clinicians and families to distinguish pathologic symptoms of mania, hypomania, or depression from appropriate adolescent behaviors. In a large group ($n = 100$) of youth with affective illness, children (Tanner stage 1) were most likely to display manic/hypomanic symptomatology, whereas adolescents (Tanner stages 3–5) most commonly displayed a depressive pattern.⁵¹ Although few data are reported on the impact of pubertal maturation on the efficacy of ongoing pharmacologic treatment for BPD, we can expect adolescent maturation to affect the pharmacokinetics of medications and perhaps their pharmacodynamic actions. Clinicians should also consider the possibility that, as in Joe's case, the long-term use of an antipsychotic may

potentially cause elevations of prolactin that might affect the onset of puberty.

Although pharmacotherapy provides a cornerstone to the treatment of pediatric BPD, nonpharmacologic treatments are an essential component of most treatment plans.³ Talking treatments help identify seasonal patterns, improve self-awareness, address parental concerns, acknowledge the stress generated by these children, and enhance the self-efficacy of the parent (and the child). In Joe's case it appears that his adherence to treatment occurred only after a connection with the therapist was established. Innovative treatments such as collaborative problem-solving may be of great benefit helping children regulate their emotions.⁵² In addition, child- and family-focused cognitive-behavioral therapy appears to be well received by families managing a child with BPD, reduces the severity of manic symptoms, and improves adherence to treatment.⁵³ Additional psychosocial interventions such as psychoeducation may provide additional support to families of children with BPD and also improve outcomes.⁵⁴ In summary, Joe's case history provides an excellent opportunity for clinicians to review the discussion of the presentation, assessment, diagnosis, and treatment of BPD in children.

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