THE MANY FACES OF DEPRESSION in Children and Adolescents

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The Many Faces of Depression in Children and Adolescents

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There is a growing literature describing the stress–vulnerability model of illness, a model applicable to many, if not most, psychiatric disorders and to physical illness as well. Vulnerability comes in a number of forms. Genetic predisposition to specific conditions may arise as a result of spontaneous mutations, or it may be transmitted intergenerationally in family pedigrees. Secondary types of vulnerability may involve susceptibility to disease caused by the weakened resistance that accompanies malnutrition, immunocompromised states, and other conditions. In most of these models of illness, vulnerability consists of a necessary but not sufficient precondition; if specific stresses are avoided, or if they are encountered but offset by adequate protective factors, the disease does not manifest itself and the vulnerability may never be recognized. Conversely, there is increasing recognition of the role of stress as a precipitant of frank illness in
vulnerable individuals and of the complex and subtle interactions among the environment, emotions, and neurodevelopmental, metabolic, and physiological processes.

In this country, the years 2001 and 2002 contained stress of unprecedented proportions, with the terrorist attacks on September 11 and the events that followed that terrible day. Although the contents of Volume 21 of the Review of Psychiatry were well established by that date and much of the text had already been written, we could not introduce this volume without thinking about the relevance of this unanticipated, widespread stress to the topics already planned.

Certainly, major depression is one of the prime candidates among the disorders in vulnerable populations that can be precipitated by stress. The information presented in *The Many Faces of Depression in Children and Adolescents*, edited by David Shaffer and Bruce D. Waslick, is, then, timely indeed. Already identified as a growing problem in youth—all too often accompanied by suicidal behavior—depression in children and adolescents is especially important to identify as early as possible. School-based screening services need to be widespread in order to facilitate both prevention of the disorder in those at risk and referral for effective treatment for those already experiencing symptomatic depression. Both psychotherapy and pharmacotherapy are well established as effective treatments for this condition, making recognition of its presence even more important. In New York alone, thousands of children lost at least one parent in the World Trade Center disaster, a catastrophic event precipitating not just grief but also major depression in the children and adolescents at risk.

We now know that stress, and depression itself, affect not just the brain but the body as well. New information about this brain–body axis is provided in *Cutting-Edge Medicine: What Psychiatrists Need to Know*, edited by Nada L. Stotland. Depression as an independent risk factor for cardiac death is one of the new findings reviewed in the chapter on the mind and the heart, as we understand more about the interactions among emotions, behavior, and cardiovascular functioning. Similarly, stress and mood are primary players in the homeostasis, or lack of it, of other body systems, such as the menstrual cycle and gastrointestinal functioning, also re-
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<th>Degree of structure to instrument</th>
<th>Minimal qualifications to administer</th>
<th>Test-retest reliability for MDD</th>
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<th>Application to research on MDD</th>
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<td>Lay interviewers with some training (2–3 days)</td>
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<td>High</td>
<td>Epidemiological work mostly</td>
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<tr>
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<td>Lay interviewers with more training (2–4 weeks)</td>
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Table 1—Diagnostic instruments commonly used in pediatric depression research (continued)

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<th>Diagnostic instrument</th>
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<td>Interview Schedule for Children and Adolescents (ISCA; Sherrill and Kovacs 2000)</td>
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<tr>
<td>Children’s Interview for Psychiatric Syndromes (ChIPS; Weller et al. 2000)</td>
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<td>Trained lay interviewers</td>
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<td>Good</td>
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Note. MDD = major depressive disorder.
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<th>Instrument</th>
<th>Format</th>
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<td>Center for Epidemiologic Studies Depression Scale (CES-D; Garrison et al. 1991)</td>
<td>Self-administered</td>
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<tr>
<td>Reynolds Adolescent Depression Scale (RADS; Reynolds 1998)</td>
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<td>Self-rated symptom scale, treatment research as a measure of change</td>
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<tr>
<td>Beck Depression Inventory (BDI; Beck et al. 1961)</td>
<td>Self-administered</td>
<td>12–17</td>
<td>Self-rated symptom scale, treatment research as a measure of change</td>
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<tr>
<td>Children’s Depression Rating Scale (CDRS; Poznanski et al. 1979)</td>
<td>Semistructured interview</td>
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<td>Schedule for Affective Disorders and Schizophrenia for School-Aged Children (K-SADS) 17-item subscale (e.g., Ambrosini et al. 1991)</td>
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<td>Hamilton Rating Scale for Depression (Hamilton 1967)</td>
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the illness that warrant classifying it differently from other types of illness (e.g., because the diagnosis differentially predicts clinical course or response to certain interventions compared with other syndromes or illnesses). Beyond clinical description, validity of a disorder can be further demonstrated if specific etiological factors can be identified; quantified by physical, chemical, or other types of laboratory instrumentation; and controlled to alter the onset or clinical course of the illness and if the longitudinally determined natural history of the illness confirms future morbidity or mortality.

There is little doubt that children and adolescents meeting criteria for major depression, whether ascertained from clinical or community samples, experience significant concurrent functional impairment in several domains (i.e., academic, health, social). High levels of comorbidity, however, can call into question the specificity of the diagnosis because dysphoric reactions, even when prolonged, sometimes can be attributable to a variety of negative events and stresses. In addition, groups of individuals with subsyndromal depressive symptoms that do not meet criteria for the diagnosis of major depression have shown in some studies similar levels of impairment and similar longitudinal course of illness as those meeting full criteria (Lewinsohn et al. 2000). No specific laboratory tests are available to diagnose depressive illness at any developmental stage. In addition, as described later in this chapter (see “Natural History and Clinical Course”), there is a fair amount of discontinuity between depressive disorders arising in childhood and mood disorders in adults, especially in cases of prepubertal-onset depression. Outcomes for individuals with childhood-onset depressive illness vary, with a percentage of subjects in any given study having very good outcomes, others having prolonged problems with affective illness, and still others developing other types of nonaffective psychiatric illness. Therefore, ongoing research is needed to further refine diagnostic criteria to improve construct and predictive validity of depressive illness in youths, and to develop laboratory tests that can be used as independent validators of mood disorder in afflicted patients.
increased sleep latency, shortened rapid eye movement (REM) sleep latency, increased duration of REM sleep overall, and lower percentages of stage 2 and 3 non-REM sleep—that are similar to the findings of studies with depressed adults. Additionally, one study found that dysregulated sleep physiology may be a marker for an increased likelihood of depression recurrence after recovery (Emslie et al. 2001).

**Psychological Correlates**

**Cognitive Factors**

Cognitive theories of depression postulate that the presence in an individual of *dysfunctional attitudes*, including a pessimistic view of one’s self, world, or future, or *negative attribution style*, in which negative events in one’s life are conceptualized as the result of internal (self-related), stable (vs. transient), and global (vs. specific) causes, precede the development of depressive disorders. These cognitive factors are thought to create a diathesis for depression in youths and adults. Research supporting the presence of these “depressogenic” cognitive abnormalities in patients with depression forms the theoretical basis for the use of cognitive therapies in youths and adults (see Gotlib and Abramson 1999).

Animal models suggest that the behavioral manifestations that have certain features in common with depressive illness in humans can develop in animals that are subjected to negative events from which there is no opportunity to escape. A “learned helplessness” paradigm typically entails the organism being subjected to unwanted events over which it can exert only minimal regulatory control (Seligman 1984). Animals, and potentially humans, placed in circumstances from which no escape is possible can develop passivity to negative life events, which on superficial examination can resemble neurovegetative symptoms of depression, such as psychomotor retardation, listlessness, and loss of goal-directed behavior. It is tempting to correlate this type of animal model to depressive illness, in which an individual can become demoralized when confronted with unescapable negative life events, such as family discord, poverty, learning prob-


tion effect on depressive symptoms increased over time. Although the study had design limitations (lack of randomization, no attention control group, self-reported information), results suggested that cognitive interventions begun in late childhood might be effective in preventing future depression. The investigators are currently attempting to replicate this work with a randomized design.

Adolescents

Clarke et al. (1993) conducted two studies investigating school-based primary prevention of depressive symptoms in ninth- and tenth-grade adolescents. These first attempts at prevention showed little to no benefits. In 1995, Clarke and colleagues conducted another targeted prevention study of depression in an at-risk sample of high school adolescents. The adolescents were selected with a two-stage case-finding procedure. Those with an elevated Center for Epidemiologic Studies Depression Scale (CES-D) score (≥24) on initial screening were interviewed with the K-SADS. Those subjects with current affective diagnoses were referred for other treatment. The remaining 150 consenting adolescents were considered at risk for future depression and randomized to receive either “usual care” or the Coping With Stress Course (a modification of the longer Coping With Depression Course) consisting of three 45-minute sessions per week for 5 weeks. The treatment goal was to teach new coping strategies that would provide the adolescent with some measure of protection or resistance against later development of depression (Clarke et al. 1995).

Over the 12-month follow-up period, adolescents in the Coping With Stress condition had a total incidence of unipolar depressive disorder that was approximately half that of the control group: 15% of the students who received the Coping With Stress Course reported a new episode of depression compared with 26% of the students in the control group. The onset of new episodes tended to occur within the first 2–3 months of the project, suggesting that some of the adolescents may have been identified in the prodromal period of a full depressive episode. This is the conundrum of prevention research. Is there a meaningful differ-
population in clinics and private offices. Once efficacy is suggested for a treatment, future studies should have less stringent exclusion criteria to more closely approximate those patients seen in real-world clinical settings.

Additional efforts are needed to further broaden the study of psychosocial treatments for depressed children and adolescents. Relatively few studies have compared two or more empirically supported active treatments for depressed youth. No published studies have compared psychotherapy with medication, although the National Institute of Mental Health (NIMH)–sponsored Treatment for Adolescents With Depression Study is under way. In addition, there are no large studies of empirically based treatments for the prevention of relapse in adolescents successfully treated for depression. Amid criticism of the restrictiveness of efficacy studies and concerns about the generalizability of the findings, alternative treatment models have been proposed that may incorporate more flexibility for therapists. These include designs for studying the sequencing of treatments (both psychosocial and pharmacological) to better address comorbid disorders that accompany depression. Also proposed are modular psychotherapy manuals that provide treatment algorithms that correspond to particular comorbidity profiles. For example, an adolescent with depression and posttraumatic stress disorder (PTSD) might receive IPT-A to treat the depression followed by another module providing more CBT-like treatment for the PTSD. As of yet, no studies have examined the efficacy of sequencing or modular treatments and the potential for greater generalizability of findings.

Several studies have begun to explore the notion of continuation treatment to increase the likelihood of achieving remission and to accelerate the recovery of adolescents who still report symptoms after the acute phase of treatment as well as maintenance treatment. The notion of preventing depression given its significant social morbidity is an exciting one but also one that is complicated by the need to identify for whom these programs would be most beneficial and to decide what is an acceptable follow-up period. Ideally, one would need to follow up children through adolescence into young adulthood to monitor them
vention, and, in some cases, inpatient or partial hospitalization. Thus, outpatient care is intended to supervene when the patient’s condition has been stabilized and a reasonable degree of safety is assured (American Academy of Child and Adolescent Psychiatry 2001). Of course, this treatment “cycle” may be disrupted in instances when suicide risk cannot be managed effectively on an outpatient basis and acute care is again indicated. Although each of these stages is integral to a “wraparound” system of service delivery (Rotheram-Borus et al. 1996b), discussion of acute patient care in the context of suicidality is beyond the scope of this chapter.

**Background**

Whereas suicide among school-aged children (5- to 14-year-olds) is a relatively infrequent occurrence, adolescent suicide is now recognized as a major public health problem, accounting for nearly 2,000 deaths nationally each year among 15- to 19-year-olds. Suicide is the third leading cause of death for this age group. Moreover, recent studies indicate that approximately 20% of the adolescents in community samples report serious suicidal ideation and between 3% and 8% report having made at least one suicide attempt (Centers for Disease Control and Prevention 2000). A range of risk factors has been identified for completed suicide (e.g., Brent et al. 1993; Gould et al. 1996; Shaffer et al. 1996) and nonlethal suicidal behavior in adolescents (e.g., Andrews and Lewinsohn 1992; Gould et al. 1998), but efficacious treatments for suicidal youth are not currently available. This highlights the need for the development and empirical validation of innovative psychotherapy interventions that specifically target risk factors such as depression, hopelessness, suicidal thoughts, and self-harm behaviors in clinically referred adolescents.

Drug therapy with selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine has been suggested as a potentially effective treatment for suicidal adolescents with major depressive disorder (Greenhill and Waslick 1997), but at present, limited data are available. Because of concerns of safety and the lack of efficacy data, psychosocial treatment interventions provide a safe and effective alternative.
and comorbid disorders that may have higher response to placebo (Birmaher et al. 1996b). However, a recent study comparing imipramine, paroxetine, and placebo (Keller et al. 2001) in a sample of adolescents with MDD sufficiently large to accept the null hypothesis reported no significant differences between imipramine and placebo, indicating that the TCAs are not the first-line medication for the treatment of MDD in youths. However, it is important to emphasize that some individual patients may selectively respond to TCAs and not the newer antidepressants. Specifically, the TCAs may be indicated for the augmentation of the SSRIs (American Psychiatric Association 2000) and for the treatment of comorbid MDD and ADHD (Hughes et al. 1999). A recent report suggested that imipramine may be helpful, in combination with cognitive-behavioral therapy, for treatment of school-refusing adolescents with a combination of MDD and anxiety disorders (Bernstein et al. 2000).

Other Antidepressants

Other antidepressants, including bupropion, venlafaxine, nefazodone, and mirtazapine, have been found efficacious for the treatment of depression in adults, but only a few open studies of treatment in children and adolescents have been published (e.g., Daviss et al. 2001). Randomized controlled trials with some of these compounds are under way.

Bupropion may be useful in treating youths with MDD and ADHD (Daviss et al. 2001). Because of the sedative effects of mirtazapine and trazodone, these medications have been used as adjunctive treatment for patients with severe insomnia.

Treatment of Subtypes of Major Depressive Disorder

Psychotic Depression

Overall, only 20%–40% of the adults with psychotic MDD respond to antidepressant monotherapy, and the range of placebo response is from very low to null (American Psychiatric Association 2000). Although monotherapy with antidepressants may be
effective, recovery appears to be both more robust and more rapid when antidepressants are combined with an antipsychotic. However, the long-term use of the typical neuroleptics has not been evaluated and carries the risk for tardive dyskinesia. Therefore, the antipsychotic should be tapered after remission of the depression. The newer antipsychotic medications (e.g., risperidone, olanzapine) may prove to be useful alternatives to the typical neuroleptics and deserve further investigation, especially because they have a secondary effect as a serotonin type 2 receptor agonist. Electroconvulsive therapy (ECT) is particularly effective for this subtype of depression in adults, but it has not been well studied in depressed youths (American Psychiatric Association 2000; Rey and Walter 1997).

Atypical Depression

Adult patients with atypical depression respond significantly better to the MAOIs and SSRIIs than to the TCAs (American Psychiatric Association 2000). However, this has not been studied in younger patients.

Seasonal Affective Disorder

Studies in adults and a few studies in children and adolescents have suggested that bright-light therapy is efficacious for the treatment of seasonal affective disorder (see review by Swedo et al. 1997). The most widely used protocol consists of using the light box with 10,000 lux at 1-foot distance from the face of the patient for 30–45 minutes. Treatment can be extended to 1 hour in cases of partial response. Studies of light visors and other head-mounted devices have been controversial. Also, it is unclear at which time of the day light exposure is more efficacious, but some patients may respond better during the morning hours. However, morning treatment sessions may be difficult during the school calendar and for adolescents who refuse to wake up early. Bright-light therapy has been associated with some side effects such as headaches and “eye strain.” Some authors have recommended an ophthalmological evaluation before initiating light therapy, but this practice has been frequently questioned unless patients have previous eye illnesses. Treatment with light
cious and safe for the treatment of MDD in children and adolescents, but further research on the other available antidepressants (e.g., bupropion, venlafaxine, nefazodone, mirtazapine) is needed. At standard doses (e.g., citalopram 20 mg/day; sertraline 50 mg/day; paroxetine 20 mg/day), child and adolescent patients should receive twice-a-day doses for at least 4–6 weeks before declaring lack of response to treatment (see “Treatment-Resistant Major Depressive Disorder” later in this chapter).

To plan an adequate treatment, the clinician should take into account factors such as the severity of the depression, subtype of depression (e.g., presence of psychosis, seasonal depression, bipolar depression), presence of comorbid disorders (e.g., ADHD, anxiety disorders, substance abuse, eating disorders, learning disabilities), treatment history, parental psychopathology, child’s and parents’ motivation toward treatment, clinician’s motivation and expertise to perform the treatment, and presence of ongoing stressors (e.g., conflicts, abuse, academic difficulties).

The optimal pharmacological management of child and adolescent MDD involves some educative and supportive psychosocial interventions and management of daily problems. Education of the patient and family about the disease, nature of treatment, and prognosis is critical to engagement in treatment and enhancement of compliance (Brent et al. 1993).

The high degree of comorbidity, as well as the psychosocial and academic consequences of depression, emphasizes the importance of the use of adequate and carefully monitored polypharmacy treatments (e.g., SSRIs and stimulants for depressed patients with ADHD). Moreover, multimodal pharmacological and specific psychosocial (e.g., cognitive-behavioral therapy and interpersonal therapy) treatment approaches may be necessary (Birmaher et al. 1996a, 1996b; Hughes et al. 1999), especially in the face of family discord, a history of trauma, or “double depression.”

Problems at school, academic issues, school refusal, abuse of drugs, exposure to negative events (e.g., abuse, conflict with parents), and peer issues must be addressed. For example, family discord is associated with slower recovery and greater chance of recurrence (Birmaher et al. 2000a; Emslie et al. 1998), and ongoing
(e.g., suicidality, psychosis, functional impairment), number and severity of prior depressive episodes, chronicity, comorbid disorders, family psychopathology, presence of support, patient and family willingness to adhere to the treatment program, and contraindications to treatment.

Factors associated with increased risk for recurrence in naturalistic studies of depressed children and adolescents may serve as guidance to the clinician to decide who needs maintenance treatment. These factors include history of depressive episodes, female sex, late onset, suicidality, double depression, subsyndromal symptoms, poor functioning, personality disorders, exposure to negative events (e.g., abuse, conflicts), and family history of recurrent depressive episodes (≥2 major depressive episodes) (Birmaher et al. 1996a, 1996b; Goodyer et al. 1998; Jinks et al. 2001; Lewinsohn et al. 1999; Rao et al. 1999; Weissman et al. 1999).

Depressed adults (American Psychiatric Association 2000) who have only a single uncomplicated episode of depression, mild episodes, or lengthy intervals between episodes (e.g., 5 years) probably should not start maintenance treatment. Also, the consensus in adults is that patients with three or more episodes (especially if they occur in a short time and have deleterious consequences) and chronic depression should have maintenance treatment.

More controversy exists about whether to provide maintenance treatment to patients with two previous episodes. Overall, maintenance treatment has been recommended for adult depressed patients with two episodes who have one or more of the following criteria (Depression Guideline Panel 1993): 1) there is a family history of bipolar disorder or recurrent depression, 2) the first depressive episode was of early onset (before age 20), and 3) both episodes were severe or life threatening and occurred during the past 3 years. Given that depression in youths has a clinical presentation, sequelae, and a natural course similar to that in adults, the above-noted guidelines probably should be applied for youths with two previous major depressive episodes.

Which Therapy Should Be Used?

Practically, unless any contraindication (e.g., medication side effects) is present, the treatment that was efficacious in the induction of the
chosis, severe impairment, or severe suicidality or that proved very difficult to treat should be considered for longer periods of or lifelong treatment (American Academy of Child and Adolescent Psychiatry 1998).

In summary, during the maintenance treatment phase (prevention of recurrences), pharmacological treatment has been found beneficial to prevent recurrences. Psychosocial (in particular, interpersonal therapy and cognitive-behavioral therapy) treatments also are efficacious, but in adults the current evidence is stronger for pharmacotherapy (American Psychiatric Association 2000). Also, it is not clear whether psychosocial treatments are efficacious to prevent recurrences for severe depressions. Psychosocial treatments may have promise in improving outcome in bipolar depression as well (Miklowitz et al. 1996). Also, in chronic, bipolar, and chronic depressions require use of medications.

TCAs, SSRIs, and lithium have been found efficacious for the prevention of depressive recurrences in adults (American Psychiatric Association 2000). However, given the above-noted advantages of the SSRIs and their efficacy in the acute treatment of MDD and dysthymia, this group is considered the first-choice medication. The antidepressant medication, unless it is not tolerated, should be continued at the full dose used to exert the initial therapeutic effect.

For children and adolescents with severe, chronic, or comorbid depression, history of trauma, or family discord, multimodal therapies are recommended. However, if antidepressant medications are used initially as monotherapy, psychosocial maintenance strategies should be implemented if residual social skills deficits or interpersonal conflicts are evident. The reduction of family stress, promotion of a supportive environment, and effective treatment of psychiatric disorders in parents and siblings also may help diminish the risk for recurrence.

**Treatment-Resistant Major Depressive Disorder**

Similar to the adult literature (American Psychiatric Association 2000), approximately 20%–30% of the youths with MDD have a
Psychoeducation with the patient and family is required to avoid the development of hopelessness both in the patient or family and in the clinician. Comparing these strategies with other treatments of medical disorders can be useful to help patients and their families understand the medication plan and to improve compliance and tolerance with treatment. The example of hypertension is appropriate: diuretics may be used alone or combined with other antihypertensives in different trials, according to response.

**Optimizing Initial Treatments**

Although few studies have evaluated the efficacy of optimizing the initial treatments, the initial treatment can be maximized by increasing the length of the trial or increasing the dose.

**Extending the Initial Medication Trial**

For patients with at least *partial response* after receiving a therapeutic dose of antidepressant for 6 weeks, the first and simplest strategy would be, if the patient’s clinical and functional status allows, to extend the treatment for another 2–4 weeks (American Psychiatric Association 2000). This makes the most sense in the face of gradual and steady improvement.

**Increasing the Dose**

With partial or nonresponders, the dose can be increased and the patient observed for another 2–4 weeks (American Psychiatric Association 2000).

**Switching Strategies**

For patients who do not respond to a specific antidepressant medication or who do not tolerate its side effects, other antidepressants of the *same class* or *different classes* (e.g., venlafaxine for a patient treated with an SSRI) can be tried. In adults, about half of the SSRI nonresponders will respond to a switch to a second


occurs frequently, and can be quite severe, confusion with other disorders has not been a problem (Carlson et al. 1994). Response to lithium is generally considered good (Abou-Saleh 1993). The type of mania is termed pure rather than mixed, and one might call the kind of bipolar disorder classical or uncomplicated (Black et al. 1988).

Adolescent and young adult onset of bipolar disorder also may be classical, although more frequently these patients appear to have complicated forms of bipolar disorder. Traditionally, the diagnosis of mania was missed much more frequently in young patients than in bipolar patients with onset after age 30 (Joyce 1984). Severe psychosis used to be misdiagnosed as schizophrenia, but the tightening of schizophrenia criteria has lessened this (Carlson et al. 1994). Substance abuse both precipitates mania and may produce an organic psychosis difficult to differentiate from mania (Carlson et al. 1999; Goldberg et al. 1999). Comorbid and less psychotic forms of mania are confused with borderline personality disorder and “adolescent turmoil” (Weller et al. 1986).

Younger children with manic symptoms have never functioned well, have psychopathology that cuts across all disorders (anxiety, disruptive behavior, neuropsychiatric, cognitive, and developmental), and have mood symptoms that merge with other disorders, making episodes difficult to define. Although this form of “mania” and bipolar disorder is very different clinically from adult-onset, classical manic depression, it may relate to chronic “mixed” mania complicated by substance abuse and antisocial behavior in adults (Biederman et al. 2000b).

What is so different about mania delineated in children is the almost complete absence of classical manic-depressive illness, the co-occurrence of multiple other symptoms, and the presence of developmental problems as well (Faraone et al. 1997). If one examines the criteria for what had been called “organic mood disorder” in DSM-III-R (American Psychiatric Association 1987) (affective instability, e.g., marked shifts from normal mood to depression, irritability, or anxiety; recurrent outbursts of aggression or rage that are grossly out of proportion to any precipitating psychosocial stressors; marked impairment of social judgment,
e.g., sexual indiscretions; marked apathy and indifference; and suspiciousness or paranoid ideation), one finds a perfect description of children who are receiving “bipolar” diagnoses. It is quite conceivable that the etiology of this condition will be different from the etiology of more classical, nonorganic manic-depressive illness.

Differential diagnosis of mania is also increasingly complicated by secondary agitation that occurs while taking multiple medications (Walkup and Labellarte 2001; Wilens et al. 1998). Activation and disinhibition may be difficult to distinguish from acute mania. Prospective study of children who become activated has not been done. Without such data, it is impossible to conclude whether the implications of this response are the same as they are with a switch into mania from a clinically depressed state. Practically speaking, it is sometimes necessary to hospitalize a child and discontinue all medications to really separate baseline disorder from secondary medication reaction.

Family Studies

Offspring of parents with bipolar disorder have 2.7 times greater risk for mental disorder and 4.0 times greater risk for developing a mood disorder than do offspring of parents with no mental disorder (LaPalme et al. 1997). This observation is so compelling that the trend in recent years has been to diagnose bipolar disorder in a child almost regardless of his or her symptoms if anyone in the family, no matter how distantly related, has a diagnosis of bipolar disorder. However, families of patients with early-onset bipolar disorder also have high rates of spectrum disorder (alcoholism, substance abuse, unipolar depression), antisocial personality, and comorbid bipolar disorder with ADHD, which are also heritable (Todd et al. 1996). Although there is a 9-fold increased risk for bipolar disorder in an offspring if he or she has one bipolar parent (1% unselected risk; 9% risk in offspring), the risk for Tourette’s disorder if a parent has it is 25-fold, the risk for panic disorder is 12-fold, and the risk for ADHD is 5-fold (Nurnberger and Berrettini 1998). Thus, the notion that any bipolar disorder anywhere in the family negates any other psychiatric disorder or
response is similar to that in adults (Geller et al. 1998; Kowatch et al. 2000; Wagner et al., submitted). These data appear to be consistent with those from studies of adults with mixed mania or, similarly, mania spectrum disorders. Case series for atypical antipsychotics are encouraging, but more systematic data are needed (Frazier et al. 1999, 2001; Soutullo et al. 1999).

There are two studies of long-term mood stabilizer use. In a sophisticated chart review, Biederman et al. (1998) found that over a 2-year period, children with a clinically significant manic syndrome appeared to be functioning significantly better when mood stabilizers were continued. Delong and Aldershof (1987) collected 196 patients over the course of 10 years who were treated with lithium. They divided their sample into subgroups with either clear mood disorder or other disorders with manic-like symptoms. They determined response and whether patients continued taking lithium over a 10-month period. They also commented on whether a relapse occurred on discontinuation. Not surprisingly, bipolar children of parents who had responded to lithium treatment had higher rates of response than did children with ADHD and affective symptoms or explosive behavior.

There are age-specific concerns about side effects of medications used to treat mania. For instance, the development of polycystic ovary disease (characterized by truncal obesity, hyperandrogenism, hyperinsulinemia, and lipid abnormalities) has been observed in only seizure patients taking divalproex as an anticonvulsant (Isojarvi et al. 1993, 1998). However, the fact that the subjects were young women who had taken the medication for several years has raised concern about the long-term implications of this drug for pubertal bipolar women. Certainly the prospects of chronic weight problems caused by any of the mood stabilizers or long-term renal effects of lithium might be expected to be more of an issue in people who have, by virtue of their young age at onset, been exposed to treatment longer.

**Follow-Up**

Considered a critical test of validity, follow-up as a way by which to clarify and differentiate outcomes has become complicated by...
different definitions of onset (episode onset or admission to study), recovery (how long without symptoms; symptomatic recovery or functional recovery), and sample characteristics (first vs. multiple episode, psychotic vs. nonpsychotic, comorbid/mixed/rapid cycling vs. “pure” manic). In studies of childhood mania, samples of youths with ADHD and comorbid mania have provided the major information.

A brief review of the data indicates that a tremendous difference exists between the outcomes of childhood or early adolescent mania and those of adolescent or adult onsets of more or less classical (even including comorbid) mania. Using an extremely liberal definition of recovery (2 weeks without manic symptoms in a highly comorbid sample of children with ADHD), Geller et al. (2000) found 6-month recoveries of less than 20%. This contrasts with a 90% recovery (2 months without symptoms) from pure mania and a 70% recovery from mixed mania in a hospitalized sample of adolescents with bipolar disorder (Strober et al. 1995). Keller et al. (1986) reported rates of recovery of about 80% in adults with pure mania and 55% in adults with mixed mania or rapid cycling from the National Collaborative Depression Study. However, some investigators have found a clear effect of age at onset on outcome (for review, see Suppes et al. 2000). Even adjusting for sex, education, and comorbidity, psychiatrically hospitalized psychotic bipolar patients with an age at onset before 19 years had an odds ratio of not remitting completely of 4.57 (1.57–13.20, \( P < 0.01 \)) (Carlson et al., in press). Reasons for these differences have yet to be clarified.

Summary

As the concept of bipolar disorder in adults has broadened and has come to include patients with chronic emotional dysregulation (Akiskal et al. 2000), it has been easier to find a diagnostic home for children with severe behavior problems that also include mood instability. Classic manic-depression is, in fact, rare before puberty. However, given the prognostic ramification of what Biederman et al. (2000b) called “a clinically significant manic syndrome,” research interest in these children is both timely and necessary.
Dasari M, Ferreira L, Essberger L, et al: A magnetic resonance imaging study of the thalamic area in adolescent patients with either schizophrenia or bipolar disorder as compared to healthy controls. Psychiatry Res 91:155–162, 1999


(Centers for Disease Control and Prevention 2000; National Center for Health Statistics 2001a). Many suicides occur under circumstances in which timely discovery was possible and death can reasonably be seen as an “attempt gone wrong.” Finally, after standardizing for gender, no clear differences between attempters and completers have ever been identified other than choice of method. There is, in other words, an almost inextricable net of similarity and difference. And for most clinical purposes, it is sensible, if frustrating, to assume that the most minor manifestations of suicidality could presage a tragic outcome, although it is highly unlikely that they will.

**Epidemiology**

**Suicidal Ideation**

The Youth Risk Behavior Survey (YRBS) conducted by the Centers for Disease Control and Prevention (CDC) obtains information about ideation from between 12,000 and 16,000 school attendees aged 14–17 years every 2 years. Since 1991, the survey has recorded endorsements of the question “Have you seriously considered suicide within the last year?” ranging between 25% and 37% among girls and 14% and 21% among boys (Centers for Disease Control and Prevention 2000). Of the ideators, 75% had also formulated a suicide plan.

In regular high-school students, both ideation and attempts were more common in Hispanics than in whites, although in a separate survey of alternative high schools (Centers for Disease Control and Prevention 1999), the highest rates were found in whites. Although these rates of ideation seem high, similar rates have been reported in samples of 15-year-olds (Garrison et al. 1991b; Reinherz et al. 1995), in 12- to 14-year-old urban high-school students (Kandel et al. 1991), and in Canadian teenagers (Dubow 1989). Community-based studies indicated that approximately half of all teenaged ideators had ideated only once, whereas 10% had ideated more than three times in the past 6 months (Choquet and Menke 1989; Reifman and Windle 1995). Ideation is nearly always episodic, and Garrison et al. (1991a), in a longitudinal study of 12- to 16-year-olds, found relatively weak
the large majority of suicides occur in teenagers with a psychiatric disturbance (Apter et al. 1993; Brent et al. 1999; Groholt et al. 1997; Ho et al. 1995; Marttunen et al. 1991, 1995; Shaffer et al. 1988, 1996). The most common forms of psychiatric disorder are

- **Some form of mood disorder**, which is found in about two-thirds of all suicides (Apter et al. 1993; Brent et al. 1999; Shaffer et al. 1988, 1996). In girls, this usually takes the form of an uncomplicated major depression, whereas in boys, it is often comorbid with conduct disorder and/or substance abuse (Shaffer et al. 1996).
- **Substance or alcohol abuse**, which is present in up to two-thirds of older boys (Brent et al. 1999; Shaffer et al. 1996) and usually is complicated by comorbid mood and/or conduct problems.
- **An anxiety disorder**, which is present in between a quarter and a third of all suicides (Brent et al. 1999; Shaffer et al. 1996), nearly always with an associated mood disorder. Performance and anticipatory anxiety are particularly prominent and are sometimes viewed by others as a sign of “perfectionism.”
- **Conduct or oppositional defiant disorder**, which is present in between a third and a half of all suicides (Brent et al. 1999; Shaffer et al. 1996), more often among males and older teenagers and, again, often comorbid with a mood or substance abuse disorder.
- **Schizophrenia**, which is present in fewer than 10% of suicides in the child and adolescent age group. Thus, even though the suicide rate is greatly increased in schizophrenia, because of its rarity, it accounts for very few suicides.

Similar diagnoses are found among both boys and girls (Brent et al. 1999; Shaffer et al. 1996), but they differ markedly in their relative importance (Shaffer et al. 1996). In girls, the most significant risk factor for suicide is major depression, which increases the risk of suicide 20-fold (Shaffer et al. 1996). In boys, the most significant risk factor is a previous suicide attempt, which increases the risk more than 30-fold (Brent et al. 1999; Shaffer et al. 1996). Although alcohol abuse and disruptive behavior disorders are among the most prevalent diagnoses in suicide victims, their
identified formerly or currently suicidal students (Shaffer et al. 1991). Most programs require a teenager to either persuade a friend who has shown depression or suicidality to obtain help themselves or, if that fails, disclose their observations to a responsible adult. These are daunting tasks for a teenager, and it should be no surprise that students who have received systematic training in counseling their friends to obtain help are no more likely to do so than are control subjects who received no training (Shaffer et al. 1990, 1991; Spirito et al. 1988; Vieland et al. 1991).

**Professional Education for Physicians**

Even though primary care physicians commonly prescribe antidepressants to adolescent patients (Goodwin et al. 2001; Rushton and Whitmire 2001), considerably fewer than half of physicians and pediatricians regularly ask their patients about suicide risk conditions (Frankenfield et al. 2000; Halpern-Felsher et al. 2000). Professional education to primary care physicians to teach them how to best identify and treat suicidality in teenaged patients can be helpful in this regard. This was shown on the Swedish island of Gotland (Rihmer et al. 1995; Rutz et al. 1992), where a 2-day training program for primary care physicians on how to assess mood disorders and suicidality was associated with a significant reduction in the female suicide rate (Rihmer et al. 1995; Rutz et al. 1995) and an increase in antidepressant prescriptions and hospitalizations for mood disorders.

**Stress Events**

Stresses commonly precede a suicide or attempted suicide (Brent et al. 1993; Gould et al. 1996). For the most part, these are common teenage stresses and could not be reasonably eliminated. However, treatments such as DBT (Linehan et al. 1993) emphasize stress avoidance and stress tolerance in suicidal individuals and may be one of the reasons that treatment is effective. Attempts have been made to teach these skills prophylactically to unselected teenagers (Friedberg et al. 2001), but the clinical use of these approaches has a highly personal orientation, and it is difficult to see how more generic “coping skills” classes could be of
Given the burden of suicidality, there is a great need for more information on optimal treatment. The quality of psychopharmacological research on suicidality is generally poor; most studies are small and unreplicated. This is especially unfortunate because of the efficacy of psychotropic medication in other conditions, its low cost, and its transportability. Well-designed studies on candidate medications must be conducted as a matter of urgency. DBT, the only form of psychotherapy that has been shown to be effective in adult attempters, needs to be studied in young people, along with ways to reduce its cost and complexity.

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