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Practice Parameters for the Assessment and Treatment of Children and Adolescents with Depressive Disorders

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ABSTRACT

Child and adolescent major depressive disorder (MDD) and dysthymic disorder (DD) are common, chronic, familial, and recurrent conditions that usually persist into adulthood. These disorders appear to be manifesting at an earlier age in successive cohorts and are usually accompanied by comorbid psychiatric disorders, increased risk for suicide, substance abuse, and behavior problems. In addition, depressed youth frequently have poor psychosocial, academic, and family functioning, which highlights the importance of early identification and prompt treatment. Both psychotherapy and pharmacotherapy have been found to be beneficial for the acute treatment of youth with depressive disorders. Opinions vary as to which of these treatments should be offered first and whether they should be offered in combination. In general, the choice of initial therapy depends on clinical and psychosocial factors and therapist's expertise. Based on the current literature and clinical experience, psychotherapy may be the first treatment for most depressed youth. However, antidepressants must be considered for those patients with psychosis, bipolar depression, severe depressions, and those who do not respond to an adequate trial of psychotherapy. All patients need continuation therapy and some patients may require maintenance treatment. Further research is needed on the etiology of depression; the efficacy of different types of psychotherapy; the differential effects of psychotherapy, pharmacotherapy, and integrated therapies; the continuation and maintenance treatment phases; treatment for dysthymia, treatment-resistant depression, and other subtypes of MDD; and preventive strategies for high-risk children and adolescents. **Key words**: children, adolescents, depression, dysthymia, antidepressants, psychotherapy, practice parameters, guidelines.

Major depressive disorder (MDD) and dysthymic disorder (DD) are common and recurrent disorders in children and adolescents. These disorders are frequently accompanied by poor psychosocial outcome, comorbid conditions, and high risk of suicide and substance abuse, indicating the need for acute treatment and prevention. The objective of these parameters is to provide a guideline on the assessment and treatment of youth with depressive disorders.

Throughout this manuscript, the terms child, children, and youth, unless otherwise specified, refer to both children and adolescents.

LITERATURE REVIEW

The National Library of Medicine and psycINFO databases were searched covering a 15-year period through January 1998. In addition, relevant articles and descriptions of adult practice parameters were reviewed (American Psychiatric Association, 1993; Depression Guideline Panel, 1993; Persons et al., 1996; Prien and Kocsis, 1995; Thase and Rush 1995; Thase and Kupfer 1996). Due to space constraints, only the most relevant references have been cited in these parameters and pertinent reviews that contain most of the references of the literature on childhood depressive disorders have been included.

MAJOR DEPRESSIVE DISORDER

Epidemiology

The prevalence of MDD is estimated to be approximately 2% in children and 4% to 8% in adolescents with a male/female ratio of 1:1 during childhood and 1:2 during adolescence (Fleming and Offord, 1990; Kashani et al., 1987a,b; Lewinsohn et al., 1994a). The cumulative incidence by age 18 years is approximately 20% in community samples (Lewinsohn et al., 1993a).

It is not yet clear why the prevalence of depression increases during adolescence, particularly in girls, but it is possibly due to biological, psychosocial, and cognitive factors (Bemporad, 1994; Nolen-Noekesema and Girgus, 1994; Orvaschel et al., 1997; Rutter, 1991). In fact, it has been hypothesized that girls carry more risk factors for depression than boys. For example, even before adolescence, it appears that girls are more likely to deal with problems with a ruminative and self-focused style than boys. In addition, girls enter puberty earlier than boys, with the psychosocial and biological consequences that accompany it. During adolescence, girls tend to worry more about their body image, are more likely to be exposed to sexual abuse, and may experience more pressure to conform to restrictive social roles than boys (Nolen-Noeksema and Girgus, 1994).

Interestingly, studies in adults and one study in youth have suggested that each successive generation since 1940 is at greater risk for developing depressive disorders, and that these disorders are being recognized at a younger age (Kovacs and Gatsonis, 1994; Ryan et al., 1992).

Clinical Presentation

Every child can be sad occasionally and appropriately. However, to be given a *DSM-IV* (APA, 1994) diagnosis of MDD, a child must have at least 2 weeks of pervasive change in mood manifested by either depressed or irritable mood, and/or loss of interest and pleasure. In

addition, the child must have other clinical characteristics, including significant changes in patterns of appetite, weight, sleep, activity, concentration, energy level, self-esteem, and motivation (American Psychiatric Association, 1994). Symptoms must represent a change from previous functioning and produce impairment in relationships or in performance of activities. Furthermore, symptoms must not be attributable only to substance abuse, use of medications, other psychiatric illness, bereavement, or medical illness.

The clinical picture of childhood MDD is substantially different across different developmental stages and diverse ethnic groups, but parallels the symptoms of adult MDD (For a review, see Birmaher, et al., 1996a; Kovacs, 1996; Mitchell et al., 1988; Ryan et al., 1987). Children usually show more symptoms of anxiety (including phobias and separation anxiety), somatic complaints, and auditory hallucinations (Chambers et al., 1982; Mitchell et al., 1988; Ryan et al., 1987). Also, children may express irritability and frustration with temper tantrums and behavioral problems instead of verbalizing feelings. In contrast, perhaps due to their cognitive immaturity, they have fewer delusions and serious suicidal attempts. Adolescents tend to display more sleep and appetite disturbances, delusions, suicidal ideation and attempts, and impairment of functioning than younger children, but more behavioral problems and fewer neurovegetative symptoms than adults with MDD.

Clinical Variants

Very few studies have been done on the pediatric clinical variants of MDD. Research in this area is necessary because this work may provide guidelines for different intervention paths.

Psychotic Depression. Psychotic depression is defined as MDD associated with mood congruent or incongruent hallucinations and/or delusions. In prepubertal children, perhaps due to their cognitive development, psychotic depression appears to be manifested mostly by auditory hallucinations. In contrast, psychotically depressed adolescents may present with auditory hallucinations and delusions (Mitchell et al., 1988; Ryan et al., 1987). Psychotic depression has been associated with more severe depression, greater long-term morbidity, resistance to antidepressant monotherapy, low-placebo response, increased risk of bipolar disorder, and family history of bipolar and psychotic depression (Haley et al., 1988; Strober et al., 1993).

For appropriate treatment, it is important to differentiate psychotic depression from bipolar disorder, substance abuse, schizophrenia, dissociative states, and trauma-related "hallucinations" (Altman et al., 1997; Chambers et al., 1982; Haley et al., 1988; Livingston, 1987; Lohr and Birmaher, 1995).

Bipolar Depression. Bipolar depression presents similarly to unipolar depression, however, symptoms such as psychosis, psychomotor retardation, pharmacologically induced hypomania, and family history of bipolar disorder may indicate that the depressed patient is at risk to develop bipolar disorder (Geller et al., 1994; Strober and Carlson, 1982; Strober et al., 1993). Youth may be more likely to present with rapid cycling or mixed episodes, which are difficult to treat and increase the risk for suicide (Brent et al., 1988, 1993a; Geller and Luby, 1997). It also is important to rule out the presence of bipolar II disorder, which appears to be more prevalent than bipolar I disorder in adolescents (Lewinsohn et al., 1995) and is often overlooked or misdiagnosed (Geller and Luby, 1997). For further information, see the Practice Parameters for the Assessment and Treatment of Children and Adolescents with Bipolar Disorder (AACAP, 1997).

Atypical Depression. Although no studies have been published in youth, atypical depression usually begins during adolescence. In adults, atypical depression appears to be a genetically distinct form of MDD (Kendler et al., 1996) and is manifested by increased reactivity to rejection, lethargy (leaden paralysis), appetite, and weight; hypersomnia; craving for carbohydrates (for a review see Stewart et al., 1993).

Seasonal Affective Disorder. Retrospective studies in adults, as well as a recent epidemiological study, support the presence of seasonal affective disorder (SAD) in youth (Swedo et al., 1995). SAD usually appears after puberty in adolescents who live in regions with distinct seasons, but also has been documented in prepubertal children. SAD manifests with symptoms similar to those described under atypical depression, except that SAD does not include increased reactivity to rejection and is episodic. SAD should be differentiated from depression triggered by school stress, because it usually overlaps with the school calendar.

Subclinical or Subsyndromal Depression. It is important to assess for subsyndromal symptoms of depression that may occur before or after an episode of MDD. These symptoms have been associated with psychosocial impairment and may increase the risk of subsequent MDD episodes (Lewinsohn et al., 1994a).

Treatment-resistant Depression. In contrast with depressed adults (Thase and Rush, 1995), there is no clear definition of treatment-resistant depression in youth with MDD (Geller et al., 1996). It has been reported that 6% to 10% of depressed youth may suffer from chronic depression (Kovacs, 1996; Sanford et al., 1995; Strober et al., 1993). In adult patients, in order to be classified as treatment-resistant, patients must have had at least two trials with two different classes of antidepressants administered at similar doses for at least 6 weeks each.

Comorbidity

Forty to 90% of youth with MDD have other psychiatric disorders, with at least 20% to 50% having two or more comorbid diagnoses (For a review, see Birmaher et al., 1996a; Goodyer et al., 1997a; Kovacs, 1996; Rohde et al., 1991).

The most frequent comorbid diagnoses are dysthymia (the so-called “double depression”) and anxiety disorders (both at 30% to 80%), disruptive disorders (10% to 80%), and substance use disorders (20% to 30%). MDD usually manifests after the onset of other psychiatric disorders, except for substance abuse (Biederman et al., 1995; Kovacs, 1996; Goodyer et al., 1997a; Lewinsohn et al., 1997a,b; Weissman et al., 1997). However, conduct problems may develop as a complication of the depression and persist after the depression remits (Kovacs, 1996). Comorbid substance abuse, conduct disorder, social phobia, and general anxiety disorder are more common in adolescents, while separation anxiety disorder is more common in children.

Differential Diagnosis

Several psychiatric disorders may co-occur with or mimic MDD. The diagnosis of MDD is made if the patient fulfills the appropriate criteria and the symptoms of depression cannot only be attributable to other conditions.

Non-affective Psychiatric Disorders. Patients with non-affective disorders (e.g., anxiety disorders, learning disabilities, or disruptive disorders) may have poor self-esteem and feel demoralized, but should not be diagnosed as having MDD unless they meet criteria for this disorder. Caution should be used in considering lack of concentration and irritability, because these may be part of both MDD and disruptive disorders. Also, patients may be suffering from attentional problems without overt ADHD symptoms and have symptoms of demoralization

secondary to academic and social difficulties. Children with separation anxiety often are quite dysphoric when separated from their parents, but in the absence of comorbid depression, the dysphoria is relieved by reunion with the parents. Patients with other anxiety disorders also may feel depressed, overwhelmed, irritable, and have symptoms similar to MDD including insomnia, changes in appetite, diminished concentration, and sometimes suicidal thoughts. Patients with anorexia nervosa may show depressive affect, but usually a diagnosis of depression is not made until nutritional status has been normalized. Patients with substance use disorders often show disturbances of mood. At times, the mood disorder may antedate and even predispose to substance abuse, but the mood disorder may be secondary to substance use and then will subside after detoxification. Premenstrual dysphoric disorder is marked by symptoms similar to MDD, however, no studies have been published regarding depressed youth. Finally, the differentiation between personality disorder and MDD is important, because some of the symptoms of personality disorder may be secondary to the mood disorder (Lewinsohn et al., 1997c; Marton et al., 1989).

Adjustment Disorder with Depressed Mood. Children with this disorder experience an excessive change in mood and impairment of functioning within 3 months of an identifiable stressor, but do not meet criteria for MDD. Overall, this disorder is self-limited and is associated with less severe mood disturbance, fewer symptoms, and no relapse (Kovacs et al., 1994a). If the patient begins to fulfill criteria for MDD, or if the symptoms of adjustment disorder last longer than 6 months, other diagnoses, such as dysthymia, should be considered. It is important to emphasize that MDD also often is precipitated by stressful events (Garber and Hilsman, 1992), so if a child has the appropriate symptoms, even if there is a stressful precipitant, he or she should receive a diagnosis of MDD.

General Medical Conditions. Depressed youth are more likely to have concomitant medical illnesses (Lewinsohn et al., 1996). In the same way, medical and neurological conditions, such as cancer, hypothyroidism, lupus erythematosus, acquired immune deficiency syndrome, anemia, diabetes, and epilepsy may be accompanied by symptoms of depression (Burke et al., 1989; Kovacs et al., 1996). These and other medical conditions usually impact the course of the depressive disorder, particularly when they disrupt patient's functioning (Lewinsohn et al., 1996).

The diagnosis of MDD can be made if depressive symptoms preceded or are not due solely to the illness or medications used to treat it. The differential diagnosis between depression and chronic medical illness can be difficult given that the incidence of depression may be higher with certain illnesses and that chronic illness may affect sleep, appetite, and energy. Feelings of guilt, worthlessness, and hopelessness, and thoughts of suicide, are unlikely to be attributable to the illness itself and if present, strongly suggest the presence of MDD.

Chronic fatigue syndrome has symptoms similar to those manifested in depressive disorders, but with more somatic complaints and less severe mood, cognitive, and social symptoms. It is not clear at present whether symptoms are part of a depressive disorder, a prodrome of depression, or due to an infectious or immunological disorder that mimics depression (Carter et al., 1996).

Medications, including stimulants, neuroleptics, corticosteroids, and contraceptives, among others, may induce changes in mood, cognition, and psychomotor activity.

Bereavement. The symptoms of bereavement and depression may be indistinguishable (Weller et al., 1991). The acute phase of uncomplicated bereavement usually remits spontaneously within 6 months to 1 year. However, the diagnosis of MDD in a bereaved youth

should be considered if bereavement is associated with moderate to severe functional impairment, psychosis, suicidality, and/or prolonged course. Previous episodes and family history of mood disorder may predispose to depression following bereavement (Brent et al., 1993b).

Clinical Course

Table 1 lists terms that have been used to describe the clinical course of MDD (Emslie, et al., 1997a; Frank et al., 1991; Kovacs et al., 1997a).

TABLE 1
Terms Commonly Used to Describe
the Clinical Course of Major Depressive Disorder

Response	Significant improvement of depressive symptoms during the initial or acute treatment phase. In general, response coincides with the onset of remission.
Remission	A period of at least 2 weeks and less than 2 months with no more than 1 clinically significant symptom.
Partial remission	A period of at least 2 weeks and less than 2 months with more than 1 clinically significant symptom but fewer symptoms than the full syndrome.
Recovery	An asymptomatic period of more than 2 months.
Relapse	An episode of depression during the period of remission
Recurrence	The emergence of symptoms of MDD during the period of recovery (a new episode).

Episode Duration. The median duration of a major depressive episode for clinically referred youth is 7 to 9 months, and for community samples, about 1 to 2 months. Approximately 90% of major depressive episodes remit 1 to 2 years after onset, with 6% to 10% becoming protracted (Emslie et al., 1997a; Harrington et al., 1991; Kovacs, 1996; Lewinsohn et al., 1994a; McCauley et al., 1993; Rohde et al., 1994; Strober et al., 1993).

Although controversial, predictors of longer duration of episode include greater severity of the depression, comorbid psychiatric disorders, presence of personality disorder, exposure to negative life events (e.g., family conflict, neglect, or abuse), presence of psychiatric disorders in parents, and poor psychosocial functioning (Clarke et al., 1992; Goodyer et al., 1997a,b; Kovacs, 1996; Kovacs et al., 1997a; Lewinsohn et al., 1997a,b; Reinecke et al, 1998; Sanford et al., 1995; Warner et al., 1992).

Relapse. After successful acute therapy, approximately 40% to 60% of youth with depression experience a relapse. This fact underscores the need for continuous treatment (Emslie et al., 1997a; Kovacs, 1996; Lewinsohn et al., 1994a; Vostanis et al., 1996; Wood et al., 1996). The high rate of relapse may be due to the natural course of MDD, lack of compliance, presence of negative life events, or rapid decrease or discontinuation of pharmacological and psychotherapeutic treatment.

Recurrence. Longitudinal studies of both clinical and community samples of depressed youth have shown that the probability of recurrence reaches 20% to 60% by 1 to 2 years after remission and climbs to 70% after 5 years, depending on the severity of the depression and time interval that is examined (Emslie et al., 1997a; Fleming et al., 1993; Kovacs, 1996; Lewinsohn et al., 1994a; Rao, et al., 1995).

Youth with recurrent episodes of depression appear to have different predictors of recurrence than youth with only one episode because of the negative psychological, social, academic, and perhaps biological changes that have been initiated (Emslie et al., 1997a; Kovacs et al., 1997a; Lewinsohn et al., 1994a,b). Predictors of recurrence include earlier age of onset; increased number of previous episodes; severity of index episode; psychosis; psychosocial stressors; dysthymic disorder or other comorbid disorder; and lack of compliance with treatment (Emslie et al., 1997a; Kovacs, 1996).

Risk of Bipolar Disorder. Follow-up studies of depressed children and adolescents have found that 20% to 40% develop bipolar disorder within 5 years after the onset of MDD (Geller and Luby, 1997; Kovacs, 1996; Strober and Carlson, 1982). Characteristics of MDD associated with a switch to bipolar I disorder include early onset, psychomotor retardation, psychotic features, family history of bipolar disorder, family history of psychotic depression, heavy familial loading for mood disorders, and pharmacologically-induced hypomania.

Factors Associated with Clinical Course

Demographics. The risk for depression increases by a factor of 2 to 4 after puberty, particularly in girls (Weissman et al., 1997).

Genetic and Familial Factors. Family, twin, and adoption studies have provided evidence that both genetic and environmental factors play a role in the pathogenesis of MDD (Kendler, 1995; Plomin, 1994). Among the environmental factors, non-shared (unique) intra- and extra-familial environmental experiences, including differences in how individual parents treat each of their children, are particularly associated with MDD (Kendler, 1995; Pike and Plomin, 1996; Thapar and McGuffin, 1997). Furthermore, individuals at high genetic risk appear to be more sensitive to the effects of adverse environment than individuals at low genetic risk (Kendler, 1995; Plomin, 1994).

Children with at least one depressed parent are approximately three times more likely to have a lifetime episode of MDD than children of non-depressed parents. The lifetime risk for MDD in children of depressed parents has been estimated to range from 15% to 60% (Hammen et al., 1990; Orvaschel et al., 1988; Weissman et al., 1997). Furthermore, among adult depressed patients, more than 50% report having their first depressive episode by age 20 years (Weissman et al., 1992). Factors in a depressed parent, including early-onset mood disorder, recurrent MDD, and other non-affective psychiatric disorders, as well as mood and/or anxiety disorders in both parents, confer the highest risk for MDD in children (see review by Birmaher et al., 1996a; Beardslee et al., 1996a; Weissman et al., 1997). Importantly, offspring of depressed parents are not only at risk for affective disorders, but they also are at increased risk for general psychopathology, including anxiety and disruptive disorders (see review by Birmaher et al., 1996a; Kovacs, 1996).

The prevalence rates of depression in first-degree relatives of depressed children range between 30% and 50%. In particular, mothers have high rates of depression (56% to 73%) (Harrington et al., 1997; Kovacs et al., 1997b; Kutcher and Marton, 1991; Neuman et al., 1997; Puig-Antich et al., 1989; Todd et al., 1993; Williamson et al., 1995), indicating the need for

assessment and treatment. Parents of depressed children also have high rates of other psychiatric disorders, including anxiety, substance use, and personality disorders (e.g., antisocial), increasing the risk of affective and non-affective psychopathology in their children (Beardslee et al., 1996a; Geller et al., 1996; Kovacs et al., 1997b; Puig-Antich et al., 1989; Rende et al., 1997; Weller et al., 1994).

Psychopathological Factors. A history of a previous depressive episode, subsyndromal symptoms of depression, dysthymia, and anxiety disorders increase the risk for future depression (Kovacs et al., 1994b; Kovacs, 1996; Lewinsohn et al., 1994a,b; Reinherz et al., 1993).

Educational Functioning. It is difficult for a child to feel adequate if he or she is not succeeding in school, since a child's educational success measures his or her ability to succeed outside of the family. Parental satisfaction with a child also can vary with the child's grades in a direct fashion. Language and learning disabilities, ADHD, school phobia, and any other condition that interferes with a child's learning, therefore, easily can increase the risk for depression (American Academy of Child and Adolescent Psychiatry, 1998a). Likewise, a depressed child's response to treatment may be measured in part by increased academic success.

Depressed patients with comorbid disruptive disorders tend to have worse psychosocial outcome but apparently fewer recurrences of MDD (Asarnow et al., 1994; Goodyer et al., 1997a; Harrington et al., 1991; Hughes et al., 1990; Kutcher et al., 1989; Puig-Antich et al., 1989).

Psychodynamic Factors. Personality dynamics, such as unrealistic, often overly harsh, internal judgment of the child's own impulses, thoughts, and affects, particularly those that are aggressive or angry in content, may contribute to the development of depression. These dynamics contribute to low self-esteem and shame, which are prominent in MDD. A child faced with environmental frustrations, disappointments, or abuse beyond his or her power to change may adapt by developing a conscious attitude of self-blame, or more subtle mechanisms, that turn the anger and frustration toward the self. Exaggerated dependency needs or other internal conflicts over autonomy are additional psychodynamic factors that may influence the course of depression in children and adolescents (see reviews by McCracken and Cantwell, 1992; McCracken and James, 1992).

Cognitive Style and Temperament. Youth who have negative attributional styles for interpreting and coping with stress and negative life events tend to become hopeless and dysphoric and appear to be at higher risk to develop MDD (Garber and Hilsman, 1992; Joiner and Wagner, 1996; Marton and Kutcher, 1995). It is unclear, however, whether a depressogenic cognitive style is a trait or a state characteristic and if it is specific for depression. It appears that a negative cognitive style becomes more fixed during adolescence (Nolen-Hoeksema et al., 1992), emphasizing the need for early intervention.

Early Adverse Experiences. There is evidence that adverse experiences (e.g., parental death or separation) during childhood and adolescence raise the risk for depression or anxiety in adulthood (For a review, see Birmaher et al., 1996a; Garber and Hillsman, 1992). It appears, however, that the effect of exposure to parental loss through separation or death may be mediated by psychosocial factors before or after the event.

Exposure to Negative Life Events. Several cross-sectional studies using both clinical and community samples of depressed youth and adults have reported significantly more negative life events, especially in the domains of school, relationships with friends or parents, health, work, and romantic relationships, in depressed patients 12 months prior to the onset of depression when compared with normal controls (Birmaher et al., 1996a). The negative events may be either independent of the person's behavior (e.g., death of a parent) or generated by the person's

maladaptive behaviors. It seems that in order to have an effect, the negative life events must interact with other risk factors.

Family Relationships. Studies of depressed adults recalling their early family relationships, children of depressed parents, and depressed youth have shown that their family interactions are characterized by more conflict, child maltreatment, rejection, and problems with communication, and less expression of affect and support, compared with families of normal controls (Beardslee et al., 1996a; Harrington et al., 1997; McCauley and Myers, 1992). Depressed parents often experience difficulties in the parenting that may reflect the symptoms of their own disorders. On the other hand, parenting role problems may be secondary to interaction with a depressed, irritable, or oppositional child. Furthermore, parenting difficulties may be due to comorbid psychopathology (e.g., alcoholism, personality disorders). The stress caused by these factors may have more impact on parenting than parental depression (Downey and Coyne, 1990; Goodman and Brumley, 1990; Stubbe et al., 1993)

Several studies suggest that parenting difficulties may not be specific to depressed parents but common to parents who are distressed because of family, marital, economic, medical, and psychological problems. There is an increased risk of any psychiatric disorder in children when parents have poor baseline functioning or conflicted relationships with their children. This risk has been reported to be independent of the parents' psychiatric status (Downey and Coyne, 1990; Fendrich et al., 1990; Lee and Gotlib, 1991; Mufson et al., 1994; Schwartz et al., 1990; Weissman et al., 1992).

Biological Factors. It is unclear whether the dysregulation found in some biological systems in youth with depression is specific for depression or is associated with psychopathology in general and the clinical relevance of these findings is not yet known (for a review, see Birmaher et al., 1996a). An area of current interest is dysfunction in the ability to regulate emotions or distress, which may predispose youth to develop depression (Gross and Munoz, 1995). This is a promising area of study because affect regulation integrates innate biological processes, temperament, and emotional, cognitive, and psychosocial factors.

Sequelae

If untreated, MDD may affect a child's development of social, emotional, cognitive, and interpersonal skills, and the attachment bond between parent and child (Kovacs, 1996; Puig-Antich, et al. 1985, 1993; Rohde et al., 1994). Children and adolescents with MDD are at high risk for suicidal behavior; substance abuse, including nicotine dependence; physical illness; early pregnancy; exposure to negative life events; and poor work, academic, and psychosocial functioning (Birmaher et al., 1996a; Kovacs, 1996). After an acute episode of depression, a slow and gradual improvement in psychosocial functioning may occur unless there are relapses or recurrences (Kandel and Davies, 1986; Nolen-Hoeksema et al., 1992; Rao et al., 1995; Rohde et al., 1994). On the other hand, psychosocial difficulties frequently persist after the remission of the MDD episode, underscoring the need of continuing treatment.

It is important to emphasize that not only the MDD, but other factors, such as comorbid psychopathology, poor family functioning, parental psychiatric disorder, physical illness, low socioeconomic status, and exposure to negative life events may affect the psychosocial functioning of depressed youth (Asarnow et al., 1993, 1994; Lewinsohn et al., 1994b, 1997a,b; McCauley and Myers, 1992; Warner et al., 1995).

Suicide and Suicide Attempts. Suicide attempts and completion are among the most significant and devastating sequelae of MDD. Paralleling the increase in MDD, the adolescent

suicide rate has quadrupled since 1950 (2.5 to 11.2 per 100,000), and currently represents 12% of the total mortality in this age group (Lewinsohn et al., 1993b). In addition to mood disorders, other predisposing factors for suicidality include past suicide attempts, family history of mood disorders, family history of suicidal behavior, exposure to family violence, exposure to abuse, impulsivity, availability of lethal agents (e.g., firearms), and comorbid psychiatric disorders (substance use, anxiety, disruptive, and personality disorders) (Brent et al., 1987; 1993a,b,c; Brent, 1995; Fergusson et al., 1996; Lewinsohn et al., 1993b; Pfeffer et al., 1993). Even controlling for psychiatric factors, specific socio-environmental circumstances, including family history of suicidal behavior, poor parent-child communication, school problems, and negative life events, are associated with increased risk of suicide (Gould et al., 1996).

DYSTHYMIC DISORDER

Epidemiology

The few epidemiological studies on DD have reported a prevalence of 0.6% to 1.7% in children and 1.6% to 8.0% in adolescents (Garrison et al., 1992; Kashani et al., 1987a,b; Lewinsohn, et al., 1993a, 1994a).

Clinical Presentation

DD consists of a persistent, long-term change in mood that generally is less intense but more chronic than in MDD. As a consequence, DD is often overlooked or misdiagnosed. Although the symptoms of dysthymia are not as severe as in MDD, they cause as much, or more, psychosocial impairment (Kovacs et al., 1994b). For a *DSM-IV* diagnosis of DD, a child must have depressed mood or irritability on most days for most of the day for a period of 1 year, as well as two other symptoms from a group including changes in appetite, sleep, self-esteem, concentration, decision-making, energy, and hope (American Psychiatric Association, 1994). Other symptoms associated with DD, but not included in the *DSM-IV* criteria, include feelings of being unloved, anger, self-deprecation, somatic complaints, anxiety, and disobedience (Kovacs et al., 1994b).

Comorbidity

Approximately 70% of youth with DD also have superimposed MDD. In addition, 50% have other pre-existing psychiatric disorders including anxiety disorders (40%), conduct disorder (30%), ADHD (24%), and enuresis or encopresis (15%). Approximately 15% have two or more comorbid disorders (Ferro et al., 1994; Kovacs et al., 1994b).

Clinical Course

Childhood DD has a protracted course with a mean episode length of approximately 3 to 4 years for clinical and community samples, and is associated with an increased risk for subsequent MDD, bipolar disorders, and substance use disorders (Keller et al., 1988; Klein et al., 1988; Kovacs et al., 1994b; 1997a; Lewinsohn et al., 1991). Comorbid disruptive disorder increases the duration of dysthymia (Kovacs et al., 1997a).

The first episode of MDD usually occurs 2 to 3 years after the onset of dysthymia, resulting in the so called “double depression” and suggesting that DD is one of the gateways to developing recurrent mood disorders. The need for preventive interventions targeted at this population is clear (Kovacs et al., 1994b). The high rate of comorbidity with MDD may explain

the poor outcome of dysthymia (Ferro et al., 1994; Keller and Shapiro, 1982; Kovacs et al., 1994b).

Factors Associated with Clinical Course

There are few studies of the correlates associated with onset, maintenance and recurrence of DD (Kovacs et al., 1997a). Factors associated with MDD, however, also may be related to DD (Klein et al., 1995, 1997). Risk factors associated with DD include exposure to chaotic family environment (Warner et al., 1995) and high family loading for mood disorders, in particular dysthymia (Klein et al., 1988; 1995, 1997).

Sequelae

Similar to MDD, dysthymia, in particular double depression, is usually accompanied by a high a degree of psychiatric and psychosocial morbidity (Klein et al., 1997; Kovacs et al., 1997a).

ASSESSMENT

The comprehensive psychiatric diagnostic evaluation is the single most useful tool currently available to diagnose depressive disorders. For a detailed description and recommendations on psychiatric evaluation of children and adolescents, see Practice Parameters for the Psychiatric Assessment of Children and Adolescents (American Academy of Child and Adolescent Psychiatry, 1997).

Evaluation frequently requires separate and/or conjoint initial interviews with the patient and his or her parents or caregivers. Multiple interviews are usually required, as are contacts with collateral informants, including teachers, primary care physicians, and social services professionals. Comorbid psychiatric diagnoses, psychosocial and academic problems, early and recent-onset negative life events, psychiatric family history, social support, medical and medications history, and substance use (including nicotine) are among the areas covered in assessment interviews. A developmentally appropriate mental status examination (MSE) is performed. For example, with younger children, MSE can be performed using play techniques. Physical examination, and as indicated, laboratory tests, also are included in the evaluation. An assessment of global functioning also should be performed.

A diagnosis of MDD or dysthymia is made when the required *DSM-IV* target symptoms are present, either currently or by history, and other disorders (e.g., schizophrenia) have been ruled out. It is important to assess symptom clusters, such as seasonality, atypical symptoms, psychosis, or hypomania, which characterize different subtypes of depression, because these subtypes require different treatment strategies. Importantly, manic and depressive symptoms may be mixed (mixed episode), a common presentation of bipolar disorder among youth (see review by Geller and Luby, 1997). Also, hypomanic symptoms may be quite brief at the onset of bipolar disorder and may be overlooked or misdiagnosed. Comorbid symptoms of ADHD, anxiety, posttraumatic stress disorder (in patients who had exposure to trauma), substance abuse, and sleep disorders (including usual changes in sleep patterns in adolescents) are often overlooked and require careful assessment and treatment (American Academy of Child and Adolescent Psychiatry, 1997a-f; AACAP, 1998c). The diagnosis and treatment of youth with subclinical depression should be considered because these children are at high risk to develop or

have recurrences of depression, and early intervention may be beneficial (Clarke et al., 1995; Lewinsohn et al., 1994a).

Assessment should be ongoing, and the interventions in the assessment phase have begun the treatment process creating hope, offering a new relationship with an adult, the clinician, and allowing for crisis management in the child's environment. The continuity or disruption of these therapeutic factors must be managed as treatment planning proceeds.

During assessment, it is imperative for the clinician to be alert to ethnic and cultural factors that may influence the presentation, description, or interpretation of symptoms and the approach to treatment. For example, children from many cultures are encouraged to be silent and to avoid direct eye contact when in the presence of authority figures. These behaviors easily could be misinterpreted as indicators of depression, anxiety, or another psychiatric disorder.

The psychiatric assessment of depressed children and adolescents can be difficult and must be performed by a clinician trained and knowledgeable about the patient's current developmental stage. Depressed children and adolescents frequently are irritable and uncooperative, and have difficulty identifying and expressing their feelings. For example, a child may deny feeling sad, and the only observable affect may be irritability, temper tantrums, boredom, or persistent behavior problems at home and/or school. Alternatively, parents and teachers may notice that a depressed child or adolescent has become withdrawn, anxious, or moody. Importantly, a child may act out serious suicidal intentions in a manner that is dismissed by parents and teachers as harmless or manipulative (e.g., holding his or her breath).

Minor issues frequently make depressed children irritable or tearful, and they tend to experience relatively normative situations as negative or overwhelming. As a result, depressed youth frequently interact less with others, develop behavioral problems, have poor school performance, and withdraw from favorite activities such as sports, social events, or other extracurricular activities.

Persistent pessimistic evaluation of self and others is usually less prevalent in early childhood. In contrast, during middle and late childhood, the child may begin to report the cognitive components of their dysphoric mood and expressed low self-esteem, guilt, and hopelessness (Bemporad, 1994). Furthermore, they may make positive or negative attributions to the events that are causing their distress. With adolescent patients, whose sense of self and cognitive abilities are increasing, the evaluation of psychiatric symptoms is similar to that for adults. Developing rapport with and eliciting descriptions of symptoms from a depressed and irritable adolescent may present a challenge, however, because the patient is in a developmental period in which autonomy is favored over any form of dependence on adults.

Diagnostic classification systems, including the International Classification of Diseases (ICD) (World Health Organization, 1994), have been developed to diminish the variability in the interpretation of symptoms and to standardize diagnostic procedure. To this end, several standardized interviews are available (See reviews by Costello, 1995; Hodges, 1994; Kaufman et al., 1997). However, many of these interviews are too long to be carried out in clinical settings, require special training, and are not suitable for young children. Overall, for mood disorders in children at least 8 years of age, standardized interviews have demonstrated interrater reliability, and test-retest reliability, but low parent-child agreement. The parent-child finding is not surprising, since children usually give a better account of internalizing symptoms (including suicidal ideation), whereas parents are more aware of behavior difficulties (Cantwell et al., 1997). Parents' reports also may be influenced by their own psychopathology, highlighting the importance of obtaining information not only from parents, but also from the child and other sources, including teachers. Standardized interviews usually are best used for empirical studies or as teaching tools for ascertaining a comprehensive review of psychopathology and asking developmentally appropriate questions to children and adolescents in a reliable manner.

A mood lifetime chart, using school years as anchors, and a mood diary are very helpful in the assessment of mood disorders. Mood is rated from very happy to very sad, and/or very irritable to non-irritable, and normative and nonnormative stressors noted. The chart can help the child visualize the course of her or his illness and identify events that may have triggered the depression.

Psychiatric symptom checklists derived from standardized interviews and the *DSM-IV* symptom categories also have been developed (e.g., The Stony Brook [Carlson, unpublished manuscript] and Western Psychiatric Institute and Clinic's Psychiatric Checklists [Birmaher and Polling, unpublished manuscript]). These checklists may be useful in clinical settings, but require further validation.

Several self-administered and clinician-administered rating scales, such as the Beck Depression Inventory (BDI) (Marton et al., 1991), the Child Depression Inventory (CDI) (Kovacs, 1992), and The Center for Epidemiologic Studies Depression Scale (CES-D) (Roberts et al., 1991), among others, have been designed to ascertain depressive symptoms (for a review, see Costello and Angold, 1988). However, due to low specificity, these scales are not useful for diagnosing clinical depression. They can be used to screen for symptoms, assess the severity of depressive symptoms, and monitor clinical improvement.

While rating scales may show clinical improvement at the end of treatment, the patient's functioning may still be impaired. Therefore, functioning can be tracked using scales such as The Children's Global Assessment Scale (Shaffer et al., 1983) or The Global Assessment of Functioning (American Psychiatric Association, 1994).

TREATMENT

MAJOR DEPRESSIVE DISORDER

The evidence-based research on treatment of MDD in children is sparse, and most treatment, efficacy, and safety data are based on clinical experience or research on adults. Caution must be used in extrapolating adult research to children. Furthermore, treatment always should be adapted to the developmental stage (e.g., cognitive functioning, social maturity, capacity to sustain attention) of the child or adolescent.

The treatment of depressive youth should be provided in the least restrictive treatment setting that is safe and effective for a given patient. Selection of treatment setting in the continuum of care (e.g., outpatient, partial hospitalization or day treatment, inpatient, or residential) depends on the patient's clinical picture, as well as the parents' support, motivation for treatment, and ability to keep the patient safe. Movement among levels of care is based on ongoing assessment of the patient's ability to function in and benefit from less restrictive settings.

The treatment plan should indicate the frequency of sessions based on the severity of symptoms, the age and developmental status of the patient, the degree of current exposure to negative life events, and other clinical factors. Multiple sessions per week may be needed during the acute treatment phase. Additionally, the plan should recommend involvement of the parents in treatment, and other interventions directed at the child's care-taking environment. .

Treatment planning also requires determining the number and roles of the clinicians who will provide treatment. There is little research data to guide this decision. Treatment by one clinician simplifies coordination of care. However, there may be both clinical and practical reasons to divide the treatment. Clinical reasons encompass issues of maintaining continuity of care, transference, patient autonomy, and patient confidentiality. Practical reasons for splitting treatment may include the inability of one clinician to perform both psychotherapy and pharmacotherapy treatments, the need for specialized psychotherapy, or policy and procedure within the system providing the care. Although splitting care has been touted as less costly, a recent study with adults suggests that, in fact, care by a single clinician is less costly (Goldman et al., 1998). When the treatment is split, the role of each clinician should be defined and a mechanism for collaboration established. It often is helpful if one clinician is designated as primary.

Treatment Relationship and Education

An effective therapeutic alliance should be fostered very early in treatment, to maintain patient and family involvement over the course of treatment. Another critical component of early treatment for MDD is education of the patient and his or her family about the disorder and its treatment (Beardslee et al., 1997a,b; Brent et al., 1993d; Fristad et al., 1996) to help patients and their families become informed partners in the treatment team. There is evidence that depressed youth often do not seek treatment (Weissman et al., 1997) and clinical experience has shown that withdrawal from treatment greatly diminishes with the addition of an educational component. Education on the illness of depression allows discussion of treatment to proceed with less parental self-blame ("I'm a bad parent") and blame of the child ("She's just manipulative," or "He's just lazy"). Furthermore, it appears that educating parents about their child's depression helps them identify their own depressive symptoms and potential need for treatment.

Education should be offered to all family members because the symptoms of depression (e.g., lack of interest, fatigue, irritability, and isolation) usually affect each of them (Beardslee et al., 1997a,b). Family and friends may take the patient's behaviors personally or otherwise become emotionally overinvolved, causing more stress and guilty or angry feelings for the patient to cope with. Regardless of whether interpersonal circumstances precede or follow onset of the depressive episode, a reduction in these problems is important in the resolution and prevention of future episodes. Furthermore, supportive and understanding relationships improve the patient's and family's global functioning and treatment outcome (Asarnow et al, 1993, 1994).

It also is critical that the clinician educate parents and teachers about how the patient's developmental level affects manifestation of and recovery from the disorder. Educational materials should be appropriate to the developmental level of the patient.

Within the context of the treatment relationship, patients and family members can develop a concept of depression as an illness, identify affect, address psychosocial deficits, learn the importance of compliance with treatment, and reduce feelings of stigmatization. Information should be presented at a developmentally appropriate level and review the developmental variation in clinical presentation of depression. Topics may include the signs and symptoms of depression, the role of psychiatric medication, common misconceptions about medications, relapse and recurrence, impact on school attendance and academic functioning, the role of the parents and teachers in recovery, and impact on peer and family relationships.

Acute Treatment Phase

Opinions vary about whether psychotherapy or pharmacotherapy, or a combination, should be offered as first line treatment for children and adolescents with MDD. Furthermore, there are differing opinions regarding which of the psychotherapies or which components of the psychotherapies are most efficacious (Jacobson et al., 1996). Overall, the choice of the initial acute therapy depends on several factors, including severity, number of prior episodes, chronicity, subtype, age of the patient, contextual issues (family conflict, academic problems, exposure to negative life events), compliance with treatment, previous response to treatment, and patient's and family's motivation for treatment. For example, an adolescent may refuse family therapy, a socially phobic patient may refuse group therapy, and an anxious parent or patient may refuse medications as the first line of treatment, so alternate treatments may be required. In addition, clinician availability, motivation, and expertise with a specific therapy may modify the choice and outcome of treatment (Jacobson et al., 1996; Spanier et al., 1996).

Based on the clinical experience and the few child and adolescent randomized treatment studies available, psychotherapy appears to be a useful initial acute treatment for mild to moderate depression (Geller, 1994). Cognitive-behavioral therapy (CBT) has been studied extensively, and other forms of psychotherapy, such as psychodynamic psychotherapy, interpersonal psychotherapy, and family therapy, have been found to be effective and are used clinically. Studies comparing the complementary and differential effects of these therapies are needed.

Antidepressant medications may be indicated for children and adolescents with non-rapid cycling bipolar depression, psychotic depression, depression with severe symptoms that prevent effective psychotherapy, and depression that fails to respond to an adequate trial of psychotherapy. For patients requiring pharmacotherapy, SSRIs are the antidepressants of choice given their safety, side effects profile, ease of use, and suitability for long-term maintenance.

Given the psychosocial context in which depression unfolds, pharmacotherapy is never sufficient as the sole treatment. There is evidence that the environmental and social problems associated with MDD remain when the patient's mood has been stabilized with medication-only treatment. Combined treatment increases the likelihood not only of mitigating depressive symptomalogy, but increasing self-esteem, coping skills, and adaptive strategies and improving family and peer relationships.

Specific interventions should be provided to parents and other caregivers during the acute treatment phase to help them effectively manage the child's irritability, defiance, isolation, or other behavioral problems. Parental mental health issues should be addressed, and, if indicated, parents should be offered treatment (Brent et al., 1997; Kovacs and Bastiaens, 1995; Lewinsohn et al., 1990).

Furthermore, education in the community, in particular teachers, is needed, because many children and adolescents with MDD are not identified and most of those who are depressed are under-treated (Brent et al., 1988; Keller, et al., 1991; Lewinsohn et al., 1991).

Psychotherapy. Psychotherapeutic techniques are used to teach patients and their families to cope with past and current stressors, improve social skills and self-esteem, understand themselves, and cope with interpersonal conflict and the social, familial, academic, and occupational problems that are associated with depression. Psychodynamic psychotherapy, IPT, CBT, behavior therapy, family therapy, supportive psychotherapy, and group psychotherapy each has been used for the treatment of youth with MDD (see reviews by Bemporad, 1994; Birmaher et al., 1996b). In-depth descriptions of these approaches are available (Bemporad, 1988; Moreau et al., 1991; Mufson et al., 1993; Wilkes et al., 1994).

Many clinicians have found psychodynamic psychotherapy useful for the treatment of depressed youth. Controlled studies using psychodynamic psychotherapy for the treatment of depression in children and adolescents are particularly difficult to design and expensive to conduct but are greatly needed. Psychodynamic psychotherapy can help youth understand themselves, identify feelings, improve self-esteem, change maladaptive patterns of behavior, interact more effectively with others, and cope with ongoing and past conflicts (Bemporad, 1988, 1994).

IPT focuses on problem areas of grief, interpersonal roles, disputes, role transitions, and interpersonal difficulties. A recent open study suggested that IPT may be useful for the acute treatment of adolescents with MDD (Mufson and Fairbanks, 1996). Furthermore, the rate of relapse may be relatively low after acute IPT treatment (Mufson and Fairbanks, 1996). Controlled studies are ongoing to evaluate this treatment.

CBT is one of the most frequently studied psychotherapy treatments. Its use for MDD is based on the premise that depressed patients have a distorted view of themselves, the world, and the future. These cognitive distortions contribute to their depression, and can be identified and counteracted with CBT. In non-clinical samples, four studies have shown group CBT to be better than no intervention for children and adolescents in the reduction of depressive symptomatology and improvement of self-esteem (Kahn et al., 1990; Lewinsohn et al., 1990; Reynold and Coates, 1986; Stark et al., 1987) (for a review see Reinecke et al., 1998).

In clinical samples, most, but not all, CBT has been found to be superior to other manualized treatments, including relaxation training, and family and supportive therapy (Brent et al., 1997; Kroll et al., 1996; Vostanis et al., 1996), but further research is necessary. All clinical studies of CBT have found a high rate of relapse on follow-up, suggesting the need for continuation treatment.

Supportive group treatment was found to be more helpful than a problem-solving group in the reduction of depression in one study of depressed adolescents (Fine et al., 1991). On the other hand, individual supportive treatment was found to be considerably less efficacious than CBT in another study of depressed adolescents (Brent et al., 1997).

Several factors appear to be related to the response to psychotherapy, including age at onset of depression, severity of depression, presence of comorbid psychiatric disorders (anxiety, dysthymia, substance abuse), lack of support, parental psychopathology, family conflict, exposure to stressful life events, socioeconomic status, quality of treatment, therapist's expertise, and motivation of both patient and therapist (Brent et al., 1997; Clarke et al., 1992; Jacobson et al., 1996; Jayson et al., 1998; Krupnick et al., 1996; Lewinsohn et al., 1990; Spanier et al., 1996).

Pharmacological Interventions. There are very few studies on the use of medications for youth with MDD and these studies are open or have methodological problems (Mandoki et al., 1997; Ryan et al., 1988a; Wilens et al., 1997). Furthermore, very few pharmacokinetics and dose-range studies have been done in children (Findling et al., 1997; Geller et al., 1987). The few extant studies in children have focused solely on MDD, and most have evaluated the effects of the tricyclic antidepressant (TCAs), with few addressing the selective serotonin reuptake inhibitors (SSRIs). Other antidepressants, including the heterocyclics (e.g., amoxapine, maprotiline), the monoamine oxidase inhibitors, buproprion, venlafaxine, and nefazodone, have been found to be efficacious for the treatment of depressed adults (Thase and Kupfer, 1996).

Before using antidepressants, clinicians should inform parents and patients about side effects, dose, the timing of therapeutic effect, and the danger of overdose, particularly with the TCAs. In addition, the symbolic meaning of taking medication, which will be different for each child and family, should be addressed. For younger patients and those risk for suicide, it is recommended that parents assume responsibility for storing and administering medications, especially during the acute and during the first 2 to 4 months after complete remission. Due to the TCAs' potential to induce a fatal overdose, the amount of medication given at each appointment should be determined with care.

Currently, there is no indication for baseline laboratory tests before and during the administration of SSRIs. For the TCAs, baseline electrocardiogram (EKG), resting blood pressure and pulse (supine or sitting, standing), and weight should be obtained. No other tests are indicated in a healthy child before starting antidepressants.

The reports that SSRIs are efficacious for the treatment of adults (Thase and Kupfer, 1996) and youth (Emslie et al., 1997b) with MDD, together with the findings that SSRIs have a relatively safe side effect profile, very low lethality after overdose, and easy administration (once a day), favor the SSRIs as first line medications (DeVane and Salee, 1996; Kutcher, 1997; Leonard et al., 1997; Preskorn, 1994).

Open studies have reported 70% to 90% response to the SSRIs for the treatment of adolescents with MDD (DeVane and Salee, 1996; Leonard et al., 1997; Rey-Sanchez and Gutierrez-Casares, 1997). A double-blind, placebo-controlled study in a small sample of adolescents with MDD did not find significant differences between placebo and fluoxetine (Simeon et al., 1990). However, a recent 8-week, double-blind study of the treatment of a large sample of youth with MDD showed that both children and adolescents responded significantly better to fluoxetine than to placebo (58% vs. 32%) (Emslie et al., 1997b). Despite the significant response to fluoxetine, however, many patients had only partial improvement and only 31% achieved full remission. A possible explanation for the partial response is that the effective

treatment may involve variation in dose or length of treatment. Also, it is possible that the ideal treatment may involve a combination of pharmacological and psychosocial interventions.

Except for lower initial doses, the administration of SSRIs in children and adolescents is similar to those used for adult patients (DeVane and Salee, 1996; Kutcher, 1997; Leonard et al., 1997). Patients should be treated with adequate and tolerable doses for at least 4 weeks. At 4 weeks, if the patient has not shown even minimal improvement, the clinician should consider increasing the dose. If, at this time, the patient shows improvement, the dose should be continued for at least 6 weeks. On the contrary, if at 6 weeks no improvement has been observed, other treatment strategies should be considered (see section on treatment-resistant depression). This recommendation should be applied cautiously, however, because it is not clear if longer trials with SSRIs would increase the number of patients with late improvement. Overall, the SSRIs possess a relatively flat dose-response curve, suggesting that maximal clinical response may be achieved at minimum effective doses (DeVane, 1992; Preskorn, 1994). Therefore, adequate time should be allowed for clinical response, and frequent, early dose adjustment should be avoided. Blood levels are rarely indicated in clinical settings, but sometimes they may help clarify concerns about toxicity or medical compliance.

The side effects of all SSRIs are similar, dose-dependent, and may subside with time (Leonard et al., 1997; Preskorn, 1994). SSRIs may induce the mania, hypomania, and "behavioral activation," in which patients become impulsive, silly, agitated, and daring. Other side effects include gastrointestinal symptoms, restlessness, diaphoresis, headaches, akathisia, bruising, and changes in appetite, sleep, and sexual functioning (Leonard et al., 1997). The long term side effects of SSRIs are not yet known.

A small number of case reports have described a putative association between SSRI administration and increased suicidality (perhaps linked to behavioral activation or akathisia) (King et al., 1991; Teicher et al., 1990). However, while such phenomena may have occurred in a small number of cases, several studies suggest that SSRIs, like other antidepressants, generally reduce the risk of suicide in adult depressed patients.

Abrupt discontinuation of SSRIs with shorter half-lives, such as paroxetine, may induce withdrawal symptoms, some of which may mimic a relapse or recurrence of a depressive episode (e.g., tiredness, irritability, and severe somatic symptoms) (Zajecka, et al., 1997). The withdrawal symptoms can appear after as few as 6 to 8 weeks on the SSRI.

It is important to be attentive to possible interactions with other medications. The SSRIs inhibit, to varying degrees, the metabolism of several medications that are metabolized by the diverse clusters of hepatic cytocochrome P450 isoenzymes (e.g., TCAs, neuroleptics, antiarrhythmics, benzodiazepines, carbamazepine, theophylline, warfarin, and terfenadine) (Leonard et al., 1997; Preskorn, 1994). In addition, interactions of SSRIs with other serotonergic medications, in particular MAOIs, may induce the serotonergic syndrome, marked by agitation, confusion, and hyperthermia. The SSRIs also have a high rate of protein binding, which can lead to increased therapeutic or toxic effects of other protein-bound medications. It is important to emphasize that the MAOIs should not be given less than 5 weeks after discontinuation of fluoxetine, and less than 2 weeks for other SSRIs. Also, the SSRIs should not be administered within 2 weeks after stopping the MAOIs.

Although open studies using TCAs suggest their usefulness in treatment youth with MDD, several randomized controlled studies have shown 50% to 60% response to both TCAs (nortriptyline, desipramine, amitriptyline) and placebo (For a review, see Birmaher et al., 1996b). These results should be considered with caution because of methodological limitations,

including small sample sizes, short-duration trials, and inclusion of patients with mild depression and comorbid disorders that may have had good response to placebo.

Despite these methodological limitations, given the lack of efficacy and potential side effects, the TCAs are no longer considered the first line treatment for youth with depressive disorders. Nevertheless, individual cases may respond better to TCAs than other medications, and TCAs may be useful for youth with comorbid ADHD, enuresis, and narcolepsy, as well as for augmentation strategies. Further information and guidelines for the use of TCAs in children and adolescents is available (Clein and Riddle, 1995; Kutcher, 1997; Kye and Ryan, 1995; Mezzacappa et al., 1998; Wilens et al., 1996).

Integrated Treatments. Critical commentaries on the current state of psychotherapeutic research have noted a disparity between clinical practice and efficacy studies (Kazdin et al., 1990; Russel and Olinsky, 1996; Seligman, 1995). Concerns have been raised regarding the generalizability of the results from manualized efficacy studies to clinical practice. Kazdin (1978) has challenged the traditional outcome measures used in the bulk of efficacy studies. Seligman (1995) has suggested that the efficacy study may be the wrong approach to studying the effectiveness of psychotherapy, since it fails to recognize that patients select psychotherapies that resonate with their belief systems; that there are individual differences regarding the length of treatment necessary to promote change; that patients may have multiple problems and often additional diagnoses; that individuals in clinical practice are motivated to improve general functioning and not to simply reduce specific symptoms associated with a mental disorder; and that in clinical practice, the clinician varies his or her clinical techniques depending on patient response, and thus applies multiple or integrated therapies. With these limitations noted, there is an emerging recognition that the combination or integration of technical variables intrinsic to CBT, IPT, psychodynamic psychotherapy, and other psychotherapies may be brought together in the best interests of the patient.

Continuation Treatment Phase

Given the high rate of relapse and recurrence of depression, continuation therapy is recommended for all patients for at least 6 to 12 months. During the continuation phase, patients typically are seen at least monthly, depending on clinical status, functioning, support systems, environmental stressors, motivation for treatment, and the presence of comorbid psychiatric or medical disorders.

In this phase, psychotherapy can be used not only to consolidate the skills learned during the acute phase and help patients cope with the psychosocial sequelae of the depression, but also to address the antecedents, contextual factors, environmental stressors, and intrapsychic conflicts that may contribute to a relapse, and, if the patient is taking antidepressants, to foster medication compliance. The only continuation study in depressed youth (Kroll et al., 1996) suggests that monthly CBT sessions may be efficacious preventing relapses of depression in adolescents. In adults, both psychotherapy and pharmacotherapy treatments have been found to be helpful to prevent MDD and DD relapse (Prien and Kocsis, 1995; Thase and Kupfer, 1996).

If antidepressants were used to attain remission in the acute phase of treatment, they should be continued at the same dose, unless there are significant side effects or dose-related negative effects on patient compliance (APA, 1993; Depression Guideline Panel, 1993; Prien and Kocsis, 1995). At the end of the continuation phase, if maintenance treatment is not needed, medications should be discontinued over a 6-week period or more to avoid withdrawal effects.

Maintenance Treatment Phase

Once the patient has been asymptomatic for approximately 6 to 12 months, the clinician must decide whether maintenance therapy is indicated, to whom to administer maintenance therapy, which therapy, and for how long. The main goal of the maintenance phase is to foster healthy growth and development and prevent relapse or recurrence. This phase may extend from 1 year to indefinitely, and is typically conducted in at least monthly or quarterly visits, depending on the patients' clinical status, functioning, support systems, environmental stressors, motivation for treatment, and the existence of comorbid psychiatric/medical disorders.

It is important to emphasize that there are no published data regarding maintenance treatment in children and adolescents with MDD. Because depression in youth has similar clinical presentations, sequelae, and natural course as in adults, the guidelines presented below, though based on data collected in studies on adults, also may apply to youth with depression. Further research in this area is warranted.

The recommendation for maintenance therapy considers several factors, including the severity of the present depressive episode (e.g., suicidality, psychosis, functional impairment), number and severity of the prior depressive episodes, chronicity, presence of comorbid disorders, and patient willingness to continue treatment. Environmental factors, such as family stability (e.g., divorce, illness, job loss, or homelessness), family psychopathology, appropriateness of school placement, availability of community support (e.g., youth groups, athletic teams, scouts), and contraindications for treatment, also must be considered.

For adults, there is consensus that patients who have only a single uncomplicated episode of depression, mild episodes, or a lengthy interval between episodes (e.g., 5 years) probably should not receive maintenance treatment (Prien and Kocsis, 1995). Also there is consensus that patients with 3 or more episodes, especially if they occur within a short period of time and have deleterious consequences, and chronic depressions should receive maintenance treatment (APA, 1993; Depression Guidelines Panel, 1993). Maintenance therapy also has been considered for depressed adults with two episodes who meet one or more of the following criteria (Depression Guideline Panel, 1993): a family history of bipolar disorder or recurrent depression; onset of the first depressive episode before age 20; and severe or life threatening episodes that occurred during the past 3 years.

Unless there is a contraindication, the psychotherapeutic or pharmacologic treatments that were efficacious to induce the remission of the acute episode should be used for maintenance therapy. It is recommended, however, that patients who are maintained only on medications also should be offered psychotherapy, to help them cope with the psychosocial sequelae of the depression. Furthermore, since many depressed youth live in stressful environments and their parents may have psychiatric disorders, maintenance treatments, especially multimodal, may be critical to prevent relapse and/or development or exacerbation of comorbid disorders.

There are no maintenance studies for children and adolescents with DD. In contrast, maintenance adult studies have shown that "full-dose" antidepressants (mainly TCAs and possibly SSRIs) and psychotherapy (CBT, IPT) alone or in combination are efficacious to prevent recurrences of depression (Frank et al., 1990, 1993; Prien and Kocsis, 1995).

Although controversy exists, it appears that lithium, and other mood stabilizers, are useful for maintenance treatment of patients with recurrent unipolar depression (Schou, 1997).

It is important to note that the long-term effects of antidepressant medications on the maturation and development of children have not been studied. The clinician and the patient's

family should weigh the risks and benefits of maintenance antidepressants against the possible consequences of relapses of MDD or DD.

In the absence of studies with children and adolescents, and considering the existing adult literature, it is recommended that youth with two or three episodes of MDD receive maintenance treatment for at least 1 to 3 years. Patients with second episodes accompanied by psychosis, severe impairment, severe suicidality, and treatment-resistance, as well as patients with more than 3 episodes, should be considered for longer treatment.

Treatment of variants of MDD

Suicidal Ideation and/or Suicide Attempts. In general, the treatment of suicidal youth is similar to that for non-suicidal youth, except for additional focus on assessment, monitoring, and amelioration of suicidality. Assessment of suicide risk considers functional impairment, degree of hopelessness, presence of psychosis, stability of family environment, presence and availability of support, and availability of method. If the risk of suicide is high, then treatment in a more restrictive setting, such as an inpatient or partial hospital unit, may be required. When an adequate safety plan is developed, outpatient treatment may be an appropriate option (Brent, et al., 1997; Pfeffer et al., 1993).

All lethal agents, especially firearms and toxic medications, should be removed from the patient's home. Consequently, because of the increased risk of death after an overdose, TCAs should not be given as a first-line treatment for severely suicidal patients (Kapur et al., 1992). Because family conflict, hopelessness, and cognitive distortions frequently are present in suicidal adolescents, early treatment should include family therapy and education and other psychosocial interventions (Brent et al., 1997). SSRIs may be prescribed if there is significant impairment that reduces the patient's capacity to benefit from psychotherapy, or if the patient worsens or fails to improve with psychotherapy alone. It is critical to assess for physical and sexual abuse because of their strong association with suicidal behavior (Ferguson et al., 1996). Comorbidity with substance use, disruptive, and personality disorders, as well as poor parent-child communication, school problems, maltreatment, and negative life events, are frequently found in suicidal adolescents (Gould et al., 1996; Lewinsohn et al., 1993b). Thus, these conditions should be assessed for and, if present, targeted in treatment.

Psychotic Depression. Consistent with the adult literature (Coryell, 1998), a small study in adolescents suggested that the combination of antidepressants with antipsychotics may be helpful for patients with psychotic depression (Geller et al., 1985). Given the risk of tardive dyskinesia, neuroleptics should be tapered after remission of the psychotic symptoms. The atypical antipsychotic medications, such as risperidone, olanzapine, and clozapine, may be useful alternatives to neuroleptics and deserve further investigation. However, it is important to note that fatty liver secondary to extreme weight gain has been reported in four children on risperidone (Kumra et al., 1997). Furthermore, the long-term side effects of these medications on youth have not been evaluated.

In adults, electroconvulsive therapy (ECT) is particularly effective for this subtype of depression (Coryell, 1998). Anecdotal reports suggest that ECT also may be efficacious for depressed psychotic adolescents (Moise and Petrides, 1996; Rey and Walter, 1997).

Atypical Depression. Psychotherapy and pharmacotherapy are used frequently, although no psychotherapy or pharmacotherapy studies on atypical depression in children and adolescents have been published. In adults, SSRIs and MAOIs have been found to be helpful (Stewart et al., 1997).

Seasonal Affective Disorder. The few studies published regarding youth with SAD have shown that bright light therapy is efficacious (Papatheodorou and Kutcher, 1995; Swedo et al., 1997). The most widely used protocol is a light box with 10,000 lux at 1-foot distance from the face of the patient for 30 to 45 minutes. Treatment can be extended to 1 hour in cases of partial response. It appears that patients may respond better during the morning hours, but morning hours may be difficult on school days and for youth who refuse to wake-up early in the morning. Data on light-visors and other head-mounted devices are controversial. Bright light therapy has been associated with some side effects, such as headaches and eyestrain. Some authors have recommended an ophthalmological evaluation before initiating light therapy, but this practice has been frequently questioned unless patients have a history of eye illness. Treatment with light may induce episodes of hypomania or mania in vulnerable patients.

Bipolar Disorder. Most youth referred for depression usually are experiencing their first depressive episode. Because the symptoms of unipolar and bipolar depression are similar, if the patient requires medication treatment it is difficult to determine whether a patient needs only an antidepressant or concomitant use of mood stabilizers. As noted above, some signs and symptoms such as psychosis, psychomotor retardation, or family history of bipolar disorder may warn the clinician about the possibility that the child is at risk to develop a manic or hypomanic episode. If indicators are present, the clinician should discuss with the patient and family the pros and cons of initiating a prophylactic mood-stabilizing agent. (American Academy of Child and Adolescent Psychiatry 1997d).

There is only one pharmacological study in youth with bipolar depression. In this study, Geller et al. (1997) reported that lithium was not found to be superior to placebo for 30 prepubertal children with MDD and risk factors for development of bipolar disorder.

Given that antidepressants may induce mania, it has been recommended that clinicians start first with a mood stabilizer, such as lithium carbonate, valproate, or carbamazepine (APA, 1994). In adults, mood stabilizers reduce the risk of cycling and have modest antidepressant effects (30% to 50%) (APA, 1994). For patients with bipolar depression who do not respond to mood stabilizers alone, an antidepressant may be added to the treatment. In particular, bupropion, SSRIs, and MAOIs (Haykal and Akiskal, 1990; Himmelhoch et al., 1991) may be useful adjuncts.

Although no randomized controlled studies have been published, patients with bipolar II disorder, especially with sporadic periods of hypomania, may respond to bupropion, MAOIs, or SSRIs without mood stabilizers. Clinicians should note, however, that antidepressants may induce rapid cycling in adult bipolar patients, particularly women with bipolar II disorder (Coryell et al., 1992).

For patients presenting with mixed episodes, the use of anticonvulsants, such as valproate, should be considered instead of lithium (Swann et al., 1997).

Depression in Medically Ill Youth. There are few published studies examining the efficacy of psychopharmacological or psychotherapeutic treatments for depression in medically ill children and adolescents. Studies are necessary, however, because diagnosable depression may occur frequently in children and adolescents with medical diseases, and medical illness may change the natural course of depression (Lewinsohn et al., 1996). Furthermore, the pharmacokinetics, pharmacodynamics, and side effects of the antidepressants may be affected by both the medical illnesses and medications used to treat these illnesses. Psychotherapy is useful not only for treating depression in these children, but for helping them and their families cope with the medical illness (Kovacs et al., 1996).

Treatment-Resistant Depression. When managing patients with treatment-resistant depression, the following reasons for treatment failure should be considered: inadequate drug dosage, inadequate length of drug trial, inadequate length of psychotherapy, inadequate fit with, and/or skill level of, psychotherapist, lack of compliance with treatment, comorbidity with other psychiatric disorders (anxiety, dysthymic, substance use, and personality disorders), comorbid medical illnesses, undetected bipolar depression, exposure to chronic or severe life events, such as sexual abuse, that may require different modalities of therapy, misdiagnosis, and mistreatment (Amsterdam and Hornig-Rohan, 1996; Thase and Rush, 1995).

Clinical observation suggests that sometimes after a medication-free period of 4 to 6 weeks, patients may respond to previously unsuccessful antidepressant trials. In addition, psychotherapeutic interventions also appear to be beneficial (Fava et al., 1997; Miller et al., 1985). Several psychopharmacological strategies have been recommended for adults with resistant depression that may be applicable to youth: optimization (extending the initial medication trial and/or adjusting the dose), and switching to another agent in the same or a different class of medications, augmentation or combination (e.g., lithium, T_3) (Amsterdam and Hornig-Rohan, 1996; Depression Guidelines Panel, 1993; Thase and Rush, 1995). Each strategy requires implementation in a systematic fashion, education of the patient and family, and support to reduce the potential for the patient to become hopelessness.

Controlled studies of the efficacy of alternative treatments for patients with treatment-resistant depressions are difficult to pursue for pragmatic reasons (e.g., small sample sizes) as well as ethical concerns about offering placebo to patients with treatment-resistant disorders. Consequently, there are very few randomized controlled treatment trials and few open uncontrolled studies with adults (Thase and Rush, 1995) and youth. One open study in adolescents with treatment-resistant MDD showed significant improvement of depressive symptoms after augmentation of TCAs with lithium (Ryan et al., 1988b). Nevertheless, another open label study, using an historical control group, did not replicate this finding (Strober et al., 1992). Two small open studies found fluoxetine (Boulos et al., 1992) and the MAOI phenelzine (Ryan et al., 1988a) to be efficacious in the treatment of adolescents who did not respond to TCAs. Geller and colleagues (1990), in a group of adolescents with chronic and severe MDD, found that 8% responded to nortriptyline and 21% to placebo. In contrast, Birmaher et al. (1998) found a 70% response to amitriptyline and placebo in a group of adolescents with recurrent, chronic, resistant MDD. Salle et al. (1997) found that intravenous clomipramine was superior to placebo for adolescents with treatment-resistant depression. Finally, anecdotal reports have suggested that adolescents with treatment-resistant depression may respond to ECT (Ghaziuddin et al., 1995; Moise and Petrides, 1996; Rey and Walter, 1997), but further research in this area is needed.

TREATMENT OF DYSTHYMIC DISORDER

The number of children and adolescents with DD, and/or mild to moderate depression, is far greater than the number with MDD. Most of the clinical experience and treatment literature for these youth is based on predominantly traditional psychotherapies, but there have been very few carefully controlled studies. Studies are critically needed on the treatment of children and

adolescents with DD or comorbid MDD and DD (Kovacs and Bastiaens, 1995). In anticipation of further research, interventions described for children and adolescents with MDD are recommended for the treatment of children and adolescents with DD.

Studies in adult dysthymic patients have shown that TCAs, SSRIs, and MAOIs, at the same doses used for the treatment of MDD, are efficacious for the treatment of dysthymia (Kocsis et al., 1997; Thase et al., 1996). In addition, extensive clinical practice and theory support the use of psychodynamic psychotherapies of varying degrees of intensity, including among others psychoanalysis, psychodynamic psychotherapy, CBT, and IBT, to treat DD. These psychotherapies aim to modify maladaptive personality organization that may determine the persistent, long-term change in mood that characterizes DD (McCracken and Cantwell, 1992).

Because of its chronicity, DD may require an intensity of treatment that is often difficult for families to afford because of arbitrary limits on psychotherapy benefits. More research is needed to identify both effective treatment and the long-term consequences of inadequate treatment.

TREATMENT OF COMORBID CONDITIONS

It is of prime importance to treat the comorbid conditions that frequently accompany MDD and DD, since comorbidities may influence the initiation, maintenance, and recurrence of depression. Likewise, depressive symptoms also may influence the treatment response of comorbid disorders (Brown, et al. 1996).

The finding that comorbid anxiety or dysthymia predicts poorer response and persists after an episode of MDD (Kovacs et al., 1989) underscores the importance of treating comorbid disorders to ultimate treatment success.

Several psychosocial and pharmacological treatments used to treat depression also may be useful for the treatment of comorbid conditions. For example, cognitive or psychodynamic therapies may be useful for both depressive and anxiety symptoms; SSRIs may help both anxiety disorders and MDD (Birmaher et al., 1994); TCAs and bupropion may help both ADHD and MDD (Barrickman et al., 1995; Findling, 1996); SSRIs may help both bulimia and MDD; clomipramine and the SSRIs may help both MDD and OCD; and SSRIs have been shown to help adult dysthymia and MDD (Kocsis et al., 1997; Thase et al., 1996). Detailed information on the assessment and treatment of ADHD, anxiety disorders, substance use disorders, and OCD is available (American Academy of Child and Adolescent Psychiatry, 1997b,c,f; 1998b).

PREVENTION

Given the prevalence of depressive disorders, prevention is of critical importance, but very few studies have been published in this area. Studies of school-aged children and adolescents with subclinical symptoms of depression have shown that group CBT, together with relaxation training and group problem-solving therapy, may prevent recurrences of depression for up to 9 to 24 months post-treatment (Clarke et al., 1995; Jaycox et al., 1994; Lerner and Clum, 1990). Brief family-based educational interventions also have been shown to be beneficial in decreasing the effects of parental mood disorders on children at high risk for depression, although their impact on ultimate development of mood disorder is yet to be documented (Beardslee et al., 1997a,b).

Children with DD usually have their first episode of MDD 2 to 3 years after the onset of DD, suggesting that DD is a gateway to recurrent mood disorder and indicating the need for preventive interventions targeted at this population (Kovacs et al., 1994b). Preventive interventions also may avert the development of other psychiatric disorders. For example, MDD frequently precedes the onset of substance use disorders, so treatment of depression may prevent the development of substance abuse.

Research on the appropriate targets for prevention (see review by Harrington and Clark, in press), as well as the role of parents and teachers in the detection and prevention of depressive disorders, is needed.

CONFLICT OF INTEREST

As a matter of policy, some of the authors to these practice parameters are in active clinical practice and may have received income related to treatments discussed in these parameters. Some authors may be involved primarily in research or other academic endeavors and also may have received income related to treatments discussed in these parameters. To minimize the potential for these parameters to contain biased recommendations due to conflict of interest, the parameters were reviewed extensively by the Work Group on Quality Issues, consultants, and Academy members. Reviewers were asked to base their recommendations on an objective evaluation of the available evidence. Authors and reviewers who believed that they might have a conflict of interest that would bias, or appear to bias, their work on these parameters were asked to notify the Academy.

SCIENTIFIC DATA AND CLINICAL CONSENSUS

Practice parameters are strategies for patient management, developed to assist clinicians in psychiatric decision-making. These parameters, based on evaluation of the scientific literature and relevant clinical consensus, describe generally accepted approaches to assess and treat specific disorders, or to perform specific medical procedures. The validity of scientific findings was judged by design, sample selection and size, inclusion of comparison groups, generalizability, and agreement with other studies. Clinical consensus was determined through extensive review by the members of the Work Group on Quality Issues, child and adolescent psychiatry consultants with expertise in the content area, the entire Academy membership, and the Academy Assembly and Council.

These parameters are not intended to define the standard of care; nor should they be deemed inclusive of all proper methods of care or exclusive of other methods of care directed at obtaining the desired results. The ultimate judgment regarding the care of a particular patient must be made by the clinician in light of all the circumstances presented by the patient and his or her family, the diagnostic and treatment options available, and available resources. Given inevitable changes in scientific information and technology, these parameters will be reviewed periodically and updated when appropriate.

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