Guide to family practitioners for the diagnosis and treatment of depression in children and adolescents

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Childhood and adolescent depression is probably more common in the primary care setting than most physicians realize. Because depression can result in suicide, it must be differentially diagnosed from the more common complaints seen in pediatric and adolescent patients. The cause of depression is usually multifactorial and may include psychodynamic, cognitive, behavioral, life stress/socioenvironmental, biologic/biochemical, and genetic components. Depending on the patient's age, depression can present as mood disturbances, and eating and sleeping disturbances, as well as somatic complaints. With no laboratory tests currently available to diagnose depression, physicians must rely on the history and physical examination as the best diagnostic tool. To aid family practitioners, the authors present criteria for diagnosing depression from the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* along with treatment that includes psychotherapy and pharmacotherapy for the best possible outcome.

(Key words: Depression, pediatrics, adolescent medicine, diagnosis, treatment, suicide, primary care)

Childhood and adolescent depression is a significant health problem in the United States. Primary care physicians need to be aware of depression as a clinical entity in today's children. The prevalence rate of depression in preschool children is approximately 0.9%; 1% to 8% in prepubertal children; and 4.7% in adolescents.^{1,2}

Depression could be diagnosed in 40% of patients with unexplained headaches in a neurology ward, 7% of general pediatric inpatients, 28% of patients in a child psychiatry clinic, and 59% of psychiatric inpatients. Children

diagnosed with attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), as well as children in the psychiatric clinic reported significantly more depression and anxiety than did children in the community.^{3,4}

Until the late 1970s, depression was not clearly acknowledged as a clinical phenomenon in children and adolescents.^{5,6} The existence of depression in children is still controversial. Because depression is characterized by feelings of hopelessness and helplessness about the future, some researchers think an individual can become depressed only after achieving the ability to put together hypothetical thoughts concerning the future.⁷ Hypothetical thinking may not develop until adolescence; therefore, depression cannot develop until then.⁷ However, with the use of structured interviews and psychologic scales, researchers have demonstrated that prepubertal children

do manifest mood disturbance, anhedonia (insensitivity to pleasure), and vegetative symptoms associated with depression.

Demographic characteristics

There seems to be no gender differences in depression rates in prepubescent children. However, after the age of 15, girls and women are nearly twice as likely to be depressed as boys and men.^{4,8,9} Many of the challenges that are more prevalent in the lives of adolescent girls continue to be prevalent in the lives of adult women.⁸ These include coping with menstruation and behavioral expectations of parents and society at large. In addition, adolescents of both sexes who have long or frequent periods of depression may be at risk for episodes of depression in adulthood. The prevalence of depression also increases with age. Depressed children are likely to be depressed adolescents.⁹

Suicide must always be considered with depression. Suicide is the third leading cause of death among American adolescents, aged 15 to 19 years, with the suicide rates in this age group three times as high today as it was in 1950.^{7,10} As age increases, so does the completed suicide rate: 15 to 19 year-olds are 10 times more likely to commit suicide than are 10 to 14 year olds. Boys younger than 12 years of age are at a higher risk than are girls of developing suicidal behavior, but there are no gender-related differences in the seriousness of expressed suicide tendencies.⁶ Female adolescents *attempt* suicide more often than male adolescents, but male teenagers *complete* suicide more often using more violent means. However, overall most adolescent boys and girls attempt suicide using medication (usually tricyclic antidepressants). Therefore, close monitoring is essential when young patients are following a prescribed drug therapy.

Etiology

Many models exist to explain the cause of depression: psychodynamic, cognitive, behavioral, life stress/socioenvironmental, biologic/biochemical, and genetic. With the psychodynamic model, depression is

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the result of actual—or perceived—loss of a loved object. The cognitive model recognizes when persons cannot influence events in their lives, and an experience or expectation produces depression and results in “learned helplessness.” Stressful life events have also been implicated to cause depression. Neuroendocrine and neurotransmitter abnormalities, along with strong familial links, have been related to the onset of depression as well.

Children and adolescents with depressed parents are up to three times more likely to have depression. The earlier the depression is present in the child’s life, the more severe it will be, and the more likely it will recur.¹¹ Among those psychologic, environmental, and biologic factors that can trigger depression are personal loss, anniversaries of emotional trauma, season of the year, viral illness, and chemicals, including drugs and alcohol.

Environment

Children and adolescents are greatly affected by parental losses in the form of death and divorce, as well as other stressors, such as trauma and abuse. However, it is often difficult to distinguish bereavement from depression. In one study,¹² recently bereaved children exhibited many depressive symptoms. Yet, the depressed children studied were found to have more depressive symptoms on average than those children who were merely bereaved.

Biology

Evidence exists of biologic dysregulation in adults with depression. However, biologic markers for depression in adolescents and children are inconclusive. Adults tend to secrete more cortisol when depressed, whereas depressed children and adolescents tend to secrete less cortisol.¹³ An imbalance in norepinephrine may contribute to the fatigue associated with depression. Biogenic amines (norepinephrine and serotonin), believed to be essential for transmission of positive-effect stimuli in the central nervous system, are found in low levels in depressed and suicidal adolescents.¹⁰ Irritability and

anxiety associated with depression may be caused by an imbalance in serotonin.¹⁴ Biologic changes of puberty, along with the social changes that come with advancing from elementary to secondary school, can increase the risk of depression. Puberty affects the body and self-image, as well as how the adolescent peer group interaction occurs.

Illness

Childhood disorders may be major stressors that precipitate depression in children who are vulnerable because of life events, family dysfunction, or a predisposition to affective illness.¹⁵ Acute and chronic medical conditions can lead to changes in appetite, weight loss, decreased energy, or irritable mood, but do not meet the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* criteria of Major Depressive Disorder (MDD).⁴

History and physical assessment

A thorough history and physical examination should always be performed. A history that includes such risk factors as verbal, physical, or sexual abuse; frequent separation from, or loss of, a loved one; family (particularly parental) history of depression; incarceration; pregnancy; lower socioeconomic status; homosexuality; mental retardation; ADD/ADHD; hyperactivity; chronic illness; and drug/medication use/abuse plays a significant role in the diagnosis of depression.

The clinician should obtain a careful description of the problem as seen by the child or adolescent and parent(s). Besides the standard history and physical examination, special emphasis should be placed on the patient’s appetite, sleep patterns, bladder and bowel control, and menstrual history.⁶

Clinical presentation Infants and preschoolers

The clinical presentation of depression varies; biologic, psychologic, and cognitive differences should be considered. Separation of infants (age 6 to 7 months) from a primary caregiver leads to anacletic (dependent) depression in infancy.

Signs include protest in the form of crying, panic-like behavior, and hypermobility of both arms and legs. The infant turns away from everyone, searching for his caregiver. If the caregiver is not found, the infant will become hypotonic and inactive and exhibit obvious sad facial expression, silently cry, and stare into space.^{2,6,7}

The onset of depression or mood disturbance is insidious in older infants and preschoolers, and it tends to be chronic. Most such children demonstrate apathy, withdrawn behavior, difficulty sleeping, and weight loss. Nonverbal signs of depression are important at this age, because most infants and preschoolers lack well-developed verbal and cognitive skills. Furthermore, interpreting children’s answers to questions about their feelings can be unreliable. Few children will admit they are sad when asked.⁶

Elementary-school children

As children learn language skills in school, they are better able to describe their feelings. School teachers can also assist by observing children’s behavior.² Among those signs teachers should watch for are sad facial expressions, crying, irritable behavior, slow movements, withdrawal from otherwise pleasurable interests, eating/sleeping disturbances, and a monotone voice.⁷ Such children are apt to describe themselves as “dumb” or “bad.” “Nobody loves me” is a commonly expressed sentiment.²

Academic performance deteriorates, and children drop out of their favorite extracurricular activities, often having somatic complaints (headaches and stomachaches).

Teenagers

As children grow older, low self-esteem, disappointment with self, anxiety, and decreased ability to concentrate may ensue. Suicide ideation and self-endangering, reckless behavior may also occur. Psychotically depressed adolescents frequently have hallucinations and delusions; however, psychotically depressed children do not. Similarly, depressed adolescents often express hopelessness while children do not.

Depressed adolescents also possess a preoccupation with death, exhibit uncharacteristic emotional or rebellious outbursts, and pay little or no attention to their physical appearance. Increased substance abuse, rapidly falling grades, and hostile attitudes may signal depression as well, particularly in male teens. Boredom, proclivity to accidents, and eating and sleeping disorders are other traits associated with depression in male adolescents as well. Self-destructive, rather than anti-social, behavior is more likely to be demonstrated in female adolescents. They tend to run away from home, become pregnant, or use drugs.

Although many of these signs and symptoms (lethargy, loss of interest, sleep disturbances, feelings of worthlessness) can occur as part of the normal mood swings characteristic of adolescence, symptoms associated with depression are *not* short-lived and are generally more severe.

In some ways, symptoms of adolescent depression mimic those in adult depression: crying spells (or inability to cry); feelings of discouragement; negative expectations of oneself; and isolation.¹⁶ As adolescents grow into adults, they are less likely to appear depressed (disheveled) or have somatic complaints, psychomotor agitation, separation anxiety, and phobia(s) (fear of being left alone, for example). However, an *increase* in anhedonia, hopelessness, psychomotor retardation, delusions, hypersomnia, and weight changes are likely as adolescents mature. Because this age group tends to "treat" themselves with alcohol and drugs, evaluation for depression is complicated.

Teenagers not able to tolerate the feelings of sadness may present with recurrent or persistent psychosomatic complaints (abdominal pain, chest pain, headache, dizziness, syncope, and other nonspecific symptoms).¹⁶ Defying authority, running away from home, vandalizing property, acting out sexually, and behaving in an overall delinquent manner may signal the presence of depression as well. And while low self-esteem may be present, it is not a necessary trait for the diagnosis of depression.

Depression can develop over a peri-

od of days to weeks, but can occur suddenly if precipitated by a stressful event, such as the loss of a close friend. Symptoms can last up to 6 months, and if left untreated, may persist for 2 to 3 years.⁷ Depressed children and adolescents are at risk for having depression develop as adults.

An increased risk of having depression develop exists with a family history of a major depressive disorder. This risk is especially prevalent if the history includes a suicide attempt.

A depressed parent (whether dysthymic [defined as having a depressed mood—not depression—that occur for most of the day, more days than not for at least 2 years] or depressed) can make evaluating the child more difficult. Such parents may overreport problems in their children, because the parents view everything in a negative fashion. Conversely, depressed parents may also underreport depressive symptoms in their child because these parents are preoccupied with themselves. Often, children report feelings of sadness, suicidal thoughts, and sleep disturbances of which their parents are unaware. However, parents *do* tend to report changes in their child's behavior demonstrating irritability, moodiness, whinniness, and anhedonia. To get a clearer picture, the clinician should separately interview both the child and parent.²

Suicide signals

If the clinician suspects a child or adolescent is depressed, the potential for suicide should also be weighed. One way to begin may be with the question, "If you did have suicidal thoughts, would you be able to tell me about them?" Ask the patient if he or she has ever felt so sad that death seems preferable to living. ("Have things been so bad that you've thought you'd be better off dead?" or "Has it gotten to the point where you may have had some thought about taking your own life?")¹⁸ If so, the physician should inquire about the patient's intent, plan, and access to the means for suicide. An immediate referral to a psychiatrist or an admittance to the proper healthcare facility is warranted.

Other "red flags" include the loss of a friend or family member, especially by suicide. An increased risk of suicide exists if there is a personal or family history of substance abuse.

Although suicide is uncommon in children younger than 12 years of age, its possibility in this age group should not be ignored. Usually, the means by which children commit suicide—running in front of a car, jumping out of a window, stabbing themselves, ingesting pills—are mistaken for accidents. Other more obvious means include carbon monoxide poisoning from automobile exhaust, drug/alcohol ingestion, shooting, and hanging.

In suicidal children and adolescents, depressive and aggressive symptoms coexist in a greater frequency than among suicidal adults.⁶ These may include tearfulness and irritability (depressive symptoms) and combative behavior (aggressive symptoms).

Disciplinary cries, that is punishment by the parent, and the disruption of a relationship with another adolescent often precipitate a suicide. Of those suicides reported, 25% met the criteria for Major Depressive Disorder (*Figure*); 40% to 50% exhibited antisocial behavior; 40% had been drunk at least 3 times a week, were abusing other drugs, and had gotten into trouble at school or had been pressured by relatives or friends to cut down on their alcohol use.⁶ Of those who actually committed suicide, 50% had had a brother, sister, or parent who attempted—or committed—suicide.

An attempt should be made to rule out medical conditions that may produce psychologic symptoms (infections, neurologic disorders, tumors, endocrine defects, and side effects from medications and drug use).² Depression may masquerade as abdominal pain, headache, eating disorders, and weight loss, all which can confound the diagnosis.¹⁹

Tests and laboratory assessment

Psychiatric assessment consists of clinical interviews, standardized structured interviews, questionnaires, rating scales, and standardized tests, including psycholog-

ic, developmental, neurologic, educational, and linguistic tests and biologic studies.⁶

Structured interviews, questionnaires, and laboratory tests to measure physiologic and neuroendocrine dysfunctions can also aid in the diagnosis of depression. Questionnaires, such as the Children's Depression Inventory, Children's Depression Scale, Depression Self-Rating Scale, Center for Epidemiological Studies Depression Scale for Children, Reynolds Children Depression Scale, Reynolds Adolescent Depression Scale, and the Beck Depression Index have been used to help diagnose depression in children and adolescents.

No laboratory test exists that can be used to specifically diagnose depression in children and adolescents. Children have been shown to hyposecrete growth hormone in response to insulin-induced hypoglycemia during depression. Some depressed children produce peak hormone growth levels during sleep.^{7,10} Results from electroencephalograms taken while the patient was sleeping have been inconclusive in diagnosing depression in children and adolescents.²

Laboratory tests can be run to rule out organic causes, such as leukemia and central nervous system and gastrointestinal malignancies, as well as drug abuse and toxins.⁴ Routine laboratory studies should be done to determine complete blood cell count (CBC) with differential, sedimentation rate, urinalysis, serum electrolytes, blood urea nitrogen (BUN), serum calcium, thyroxine, thyroid-stimulating hormone levels, presence of syphilis (via Venereal Disease Research Laboratory test or rapid plasma reagent test), and liver enzymes.

Diagnosis

The *Figure* presents the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* criteria for diagnosing depression.

Treatment

Psychotherapy

Antidepressant medication and psychologic therapy make up the treatment program for children and adolescents. Vig-

orous treatment of symptoms is required to prevent relapse, recurrence, and resistance to the psychologic therapy and the drugs. It is best to begin psychotherapy before starting the young patient on a trial of antidepressants. Although intervention by a psychiatrist or psychologist proves helpful, a clinical social worker or family therapist may be particularly useful if the clinician thinks the depression is related to familial or environmental stress. In milder forms of major depression and dysthymia, vigorous psychotherapeutic intervention should be the first step.⁹

Psychotherapy is an important treatment modality, especially for children and adolescents who have other disorders, such as anxiety and behavioral problems. Play therapy has been used successfully to treat young patients with depression.⁷

When a young person is depressed, family members may feel guilty, believing that they were inadequate parents which caused their child's depression. Parents should be reassured that depression is *not* the result of poor parenting. Rather, parents should be asked to participate in their child's treatment. Such participation often enhances treatment outcomes.

Pharmacotherapy

Tricyclic antidepressants (TCAs), such as amitriptyline, desipramine, and nortriptyline, have been used to improve symptoms. Serotonin reuptake inhibitors (fluoxetine, sertraline, paroxetine) are also effective and have fewer side effects than TCAs.^{7,10,16}

The TCAs have not been conclusively shown to be effective in treating childhood depression. Adolescents seem to respond even less favorably.⁶ A median of 75% of children with depression (range 46% to 100%) treated with TCAs show a good response, but these results are based primarily on open trials.^{2,6,10} With such a variable response rate, plasma drug monitoring should be performed regularly during treatment to monitor the effectiveness of the drug.

Results from double-blind, placebo-controlled studies in prepubertal chil-

dren^{6,9,10,20,21} have shown no significant difference between placebo and imipramine. However, when plasma levels were considered, children with higher imipramine plasma levels were found to respond well to this pharmacotherapy.⁶ Comparatively, 69% of those on placebo therapy had a recurrence within 30 days of discontinuing the placebo, according to one study.⁶ Furthermore, when the imipramine level was maintained at 150 ng/mL to 300 ng/mL, a better response resulted in the children.⁵

Pharmacotherapy in adolescents has not been shown to be efficacious.¹³ In this patient population, open trials have shown improvement rates of less than 50%.^{13,20,21} Few placebo-controlled studies of TCAs in adolescents have been conducted.⁶ A 44% response rate to a TCA was found in an open study² of depressed adolescents. This rate is lower than that for prepubescent children. Bipolar disorders must also be considered with depression and so should the use of lithium.

Prepharmacotherapy screening

Before starting children and adolescents on a TCA regimen, several tests should be conducted to determine the following: CBC with differential, electrolytes, thyroid function, BUN, serum creatinine levels, and cardiovascular state (via an electrocardiogram [EKG]). Measuring drug plasma levels throughout treatment ensures patient compliance and helps to avoid excessive drug levels, which could prove toxic to the cardiac and nervous systems.

In particular, children with plasma levels measuring more than 500 ng/mL are at a high risk of having developed increased PR interval and ST segment depression on the standard EKG, as well as increased diastolic blood pressure.^{2,5}

Prolongation of the PR interval on the EKG should not exceed 0.18 seconds to 0.21 seconds. The QRS (principle deflection in an EKG) should not be prolonged by more than 30% of baseline measurement; blood pressure should not exceed 140/90 mm Hg, and the resting pulse rate should not exceed 130 beats per minute.² An increased PR interval

Checklist

DSM-IV Criteria for Diagnosis of Depression*

Diagnostic Criteria for Major Depressive Disorder, Single Episode

■ Presence of a single Major Depressive Episode

■ The Major Depressive Episode is not better accounted for by Schizoaffective Disorder and is not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder not otherwise specified.

■ There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode. **Note:** This exclusion does not apply if all of the manic-like, mixed-like, or hypomanic-like episodes are substance- or treatment-induced or are due to the direct physiological effects of a general medical condition.

Diagnostic Criteria for Major Depressive Disorder, Recurrent

■ Presence of two or more Major Depressive Episodes **Note:** To be considered separate episodes, there must be an interval of at least 2 consecutive months in which criteria are not met for a Major Depressive Episode.

■ The Major Depressive Episodes are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder not otherwise specified.

■ There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode. **Note:** This exclusion does not apply if all of the

manic-like, or hypomanic-like episodes are substance- or treatment-induced or are due to the direct physiological effects of a general medical condition.

Criteria for Major Depressive Episode

Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

■ Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. **Note:** Do not include symptoms that are clearly due to a general medical condition, or mood incongruent delusions or hallucinations.

☐ depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). **Note:** In children and adolescents, can be irritable mood.

☐ markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)

☐ significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. **Note:** In children, consider failure to make expected weight gains.

☐ insomnia or hypersomnia nearly every day

☐ psychomotor agitation or retardation

nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)

☐ fatigue or loss of energy nearly every day

☐ feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)

☐ diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)

☐ recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

■ The symptoms do not meet criteria for a Mixed Episode.

■ The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

■ The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

■ The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

The essential feature of Major Depressive Disorder (MDD) is a clinical course that is characterized by the above criteria.

*(Reprinted with permission from the DSM-IV.)

and ST segment depression are indications that the heart has an electrical disturbance or has decreased blood flow because of drug toxicity. If any of these conditions are exceeded, the antidepressant dosage should be decreased to the previous level.^{2,5,22}

Once a good response rate is obtained, treatment should be continued with TCAs for 4 to 6 months.⁶ Medication should be tapered and eventually stopped when remission is achieved.

Parents should be taught to take their child's resting pulse, and to monitor their child's activity. Such monitoring helps to avoid complications secondary to medication, such as increased PR interval, ST segment depression, and increased pulse rate.

Multidisciplinary approach

The best results in adolescents occur with more than one treatment modality. A biopsychosocial approach that entails cognitive behavioral therapy, psychodynamic-oriented therapy, family therapy, education assessment and planning, social skills training, and supportive group therapy in conjunction with pharmacotherapy offers the best success.¹³

Comment

Primary care practitioners should no longer view depression as being outside their scope of medical practice, particularly with the advent of managed care. With this in mind, primary care physicians need to become aware of the symptoms, diagnostic methodologies, and treatment approaches to child and adolescent depression in children and adolescents, as well as to the possibility of suicide.

It is also imperative that primary care physicians recognize when to refer their young patients for psychiatric evaluation. This referral may pose one of the most challenging aspects of treatment, particularly when the diagnosis of depression is not obvious and, thus, parents resist such action. At this point, it is up to the physician to emphasize to the patient and parents the necessity of such psychologic evaluation. Even after referral, the primary care practitioner should

remain an active participant in their patient's management in conjunction with the psychiatric specialists.

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