Depression and Suicide in Children and Adolescents
Laura M. Prager
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Depression and Suicide in Children and Adolescents

Laura M. Prager, MD*

Author Disclosure
Dr Prager has disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Objectives
After completing this article, readers should be able to:

1. Discuss the clinical presentation and diagnostic criteria of depression.
2. Describe clinical management strategies for depression.
4. Understand how to assess and treat the suicidal patient.

Introduction
Depressive disorders in children and adolescents are common and often disabling. They can interfere with normal growth and development, academic performance, and interpersonal relationships, and they are a significant risk factor for suicide. These disorders fall on a spectrum that ranges from mild symptoms of depressed mood, which might occur in response to an acute stressor, to pervasive sad or irritable mood accompanied by problems with sleep, appetite, social isolation, and sometimes, suicidal ideas, plans, and intent. Prevalence rates for depression range from 1% to 2% of prepubertal children to 3% to 8% of adolescents. Depression in prepubertal children and bipolar disorder in any age group are equally common in both sexes. However, unipolar depressive disorders in adolescents are more common in girls than in boys (ratio of 3:1), and early onset of puberty in girls increases the risk for depression. (1)

Clinical Manifestations
Depressed children and adolescents manifest a variety of signs and symptoms. They can be sad, irritable, or angry and may present with school or behavioral problems. They can demonstrate somatic complaints (eg, headache, stomachache, muscle weakness), decreased or increased appetite, fatigue, insomnia, hypersomnia, or disturbed sleep-wake cycles. Some children and adolescents develop psychotic features consistent with their mood symptoms, such as paranoid delusions or auditory hallucinations with self-deprecatory content. Some develop self-injurious behaviors or suicidal ideation, plan, and intent. Anxiety symptoms may be present and may predate the development of depressive symptoms. Behavioral problems ranging from oppositional defiance to frank conduct disorder may occur in conjunction with an underlying mood disorder.

Depressive disorders vary in degree of severity as well as in intensity and duration of symptoms. Adjustment disorders accompanied by depressed mood can be acute but severe; major depression (with or without psychotic features) can be classified as mild, moderate, or severe. Diagnostic criteria for depressive disorders are specific and detailed and can be found in the latest American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders.

Risk Factors
Potential risk factors for depression are many, ranging from genetic loading to tumultuous life events. However, it is the interaction between biologic vulnerability and environmental stress that takes center stage. Environmental risk factors include abuse or neglect; parental substance abuse; marital problems; low socioeconomic status and education level; loss of parent, sibling, or close friend; and stress related to adolescent

Abbreviations

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
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<tr>
<td>ADHD</td>
<td>attention-deficit/hyperactivity disorder</td>
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<tr>
<td>CBT</td>
<td>cognitive behavioral therapy</td>
</tr>
<tr>
<td>FDA</td>
<td>United States Food and Drug Adminstration</td>
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<tr>
<td>IPT</td>
<td>interpersonal therapy</td>
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<tr>
<td>SSRI</td>
<td>selective serotonin reuptake inhibitor</td>
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<tr>
<td>TADS</td>
<td>Treatment for Adolescent Depression Study</td>
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*Assistant Professor, Child Psychiatry, Massachusetts General Hospital, Boston, Mass.
developmental or issues of sexuality (e.g., homosexuality). Genetic risk factors seem to play a greater role in adolescent depression than in prepubertal depression, with the most potent risk factor being parental depression. The depressed parent contributes both genetic vulnerability and emotional unavailability that can contribute to family dishression and instability. Newer research suggests that the combination of adverse life events and the presence of the shorter allelic form of the serotonin transporter gene results in early-onset depression. (2)

Functional neuroimaging studies in children and adolescents reflect many of the same findings seen in similar studies of adults. The details of such adult studies are beyond the scope of this review, but most have found smaller prefrontal cortex and basal ganglia in depressed individuals. Less work has been done in this area with children and adolescents because of the higher risks associated with radiation exposure. Early, preliminary studies suggest that such structural differences may be transmitted genetically and serve as a marker of inherited risk for depression. (3)

The nature of the relationship between neuroendocrine changes and depressive disorders in children and adolescents is not well understood. Abnormalities in the hypothalamic-pituitary axis, as detected by the dexamethasone suppression test, may reflect a similar risk for depressive disorders in children and adolescents as for adults. Studies of growth hormone secretion theorize that a blunted response to growth hormone may represent vulnerability for early-onset depression in children and adolescents. Similarly, response patterns of depressed children and nondepressed children who have family histories of affective illness may be associated with an increased risk of depression as well as aggressive and suicidal behavior in children and adolescents. (4)

Other risk factors for depressive disorders include certain types of medications (glucocorticoids, immunosuppressives, isotretinoin, antiviral agents) and any chronic illness such as cystic fibrosis, juvenile diabetes, epilepsy, inflammatory bowel disease, sickle cell anemia, organ transplantation, and cancer.

**Diagnosis and Assessment**

Diagnosing depressive disorders in children and adolescents can be difficult because the presentation can vary widely, depending on developmental stage. Furthermore, almost all children experience some sadness at times of stress, and normal adolescence can be a time of intense moodiness, impulsivity, and erratic behavior. Nevertheless, the risk for continued morbidity and impairment of social function makes differentiation of children who demonstrate symptoms consistent with significant depression from those who are transiently upset in response to stressful circumstances very important. Such assessment can be difficult because few reliable tests support the differentiation. The clinical history and mental status examination are most important. Such evaluations can be time-consuming and challenging because children and adolescents may not volunteer information about their mood, feelings, and circumstances unless they are asked specific, detailed questions. Furthermore, even if asked, they may not be able to recognize or describe changes in mood. (2)

Pediatricians who evaluate children and adolescents must determine the presence or absence of symptoms of a depressive disorder; the child’s current level of functioning relative to his or her baseline; and the potential for self-injurious behavior, suicidal ideation, or suicide attempt. The evaluation involves obtaining a history from the child as well as from the parent or guardian and other caregivers such as teachers, counselors, or coaches. The family’s cultural background can contribute to the child’s presentation and must be taken into account.

The child may report disturbances in mood, sleep, or appetite or note suicidal thoughts or wishes but may be less likely to comment on changes in peer relationships or school performance. Information about interpersonal interactions should be obtained from collateral sources. Any child affected with a disturbance of mood that is persistent and pervasive and interferes with day-to-day functioning should be assessed for depression. Although some fear that asking children and adolescents questions about their level of psychosocial functioning, their mood, or their risk for self-injury can predispose them to mood disorders or to destructive action, all available evidence suggests the opposite. (5)
Assessment of depressive disorders in children must be viewed through the developmental lens. What may be an acute stressor for an elementary school student may have less affective resonance for a middle or high school student and vice versa. A high school freshman will not expect to make the varsity basketball team, whereas a fifth grader might be devastated if relegated to a “B” team after tryouts. A chronic illness such as cystic fibrosis may be less difficult for an 8-year-old third grader who still can play video games and go out for recess than for a high school student who cannot keep up with the rapid pace of school, sports, and parties, who feels ostracized and isolated, and who understands the concept of terminal illness. The importance of such stressors can be missed if the clinician does not recognize the potential power of a seemingly minor loss or defeat in the life of a child.

Supplementation of the clinical history with self-report questionnaires can be enormously helpful, particularly in the primary care setting. Examples of such instruments include the Children’s Depression Inventory (CDI), (6) which assesses the severity of depression in prepubertal school-age children, and the Beck Depression Inventory (BDI), (7) Reynolds Adolescent Depression Scale (RADS-2), (8) and the Mood and Feelings Questionnaire (MFQ) (9) for older adolescents. The Guidelines for Adolescent Depression in Primary Care (GLAD-PC) Toolkit also has child and parent report measures and scoring instructions on their web site [http://www.thereachinstitute.org/files/documents/GLAD-PCToolkit.pdf]. This user-friendly online resource also includes management flowcharts, scales, and educational materials in English and Spanish, as well as tracking forms and information on billing.

Comorbid disorders in depressed children and adolescents include anxiety disorders, attention-deficit/hyperactivity disorder (ADHD), substance abuse, and conduct disorder. Some disorders, such as ADHD, may be transmitted genetically in families; others likely have a bidirectional causality with, for example, substance abuse (alcohol, recreational drugs, tobacco) as both a potential cause and effect of depression.

Management
Management of child and adolescent depressive disorders in primary care settings is challenging because of time constraints, the paucity of formal clinical guidelines, and lack of access to mental health professionals. Nevertheless, given the morbidity and potential mortality associated with depression in children and adolescents, pediatricians have a responsibility to learn to identify children at risk and ensure appropriate evaluation either by themselves or with consultation or referral.

For children and adolescents who have mild depressive symptoms, supportive counseling, problem-solving discussions, and education of family members may suffice. However, for more severe symptoms, other interventions may be necessary. Approaches for treatment of moderate and severe depression include the prescribing of medication, either alone or with other interpersonal therapies. Three types of treatments are validated empirically: 1) psychopharmacologic intervention, specifically selective serotonin uptake inhibitors (SSRIs), either alone or in combination with psychotherapy; 2) cognitive behavioral therapy (CBT); and 3) interpersonal therapy (IPT).

Psychopharmacologic Agents
Antidepressant medications, specifically the SSRIs, have demonstrated efficacy in the treatment of depression in adults, children, and adolescents. Currently, fluoxetine is the only antidepressant approved by the United States Food and Drug Administration (FDA) for treatment of children and adolescents, although research studies have demonstrated efficacy of other drugs such as citalopram, paroxetine, and sertraline. The 2006 FDA meta-analysis of children and adolescents taking SSRIs for the treatment of depression found an increased risk of suicidality in those patients treated with drugs versus those given placebo. Subsequent meta-analysis, using additional studies not included in the FDA report, revealed that those who benefited from SSRI treatment outnumbered those who became suicidal during SSRI treatment by a ratio of 14:1. Some suggest that the temporal relationship between the decrease in prescribing practices after implementation of the FDA black box warning and the recent increase in adolescent suicide attempts provides evidence that SSRI treatment of depression can be life-saving. (10)

Because the most evidence for efficacy and safety exists for fluoxetine, many suggest that it should be the first choice for medication management of depressive symptoms. The success of treatment can be reassessed after a 6- to 8-week trial, unless adverse effects or a worsening clinical picture dictate earlier intervention. Common adverse effects from fluoxetine include nausea and vomiting, sleep disturbance with vivid dreams, and agitation. Dosage can start as low as 2.5 mg/day for prepubertal children and 10 mg/day for older adolescents, with increases based on clinical response at 2-week intervals according to the pharmacokinetic profile of the
medication. Most patients respond to fluoxetine at doses ranging from 20 to 80 mg/day.

For vulnerable patients, any antidepressant can precipitate agitation and secondary mania and, therefore, should be used with caution. The FDA suggests careful monitoring of medication response, with weekly face-to-face meetings between caregiver and patient or patient’s family for the first month, although no evidence supports such management, and it is likely that weekly consultation by phone could be sufficient. The interval between visits can be lengthened to biweekly for the next 4 weeks and subsequently reduced further, based on the clinical situation. Consideration of a trial of other antidepressants in children and adolescents, either SSRIs or other classes, should prompt consultation with a child and adolescent psychiatrist prior to initiation. Studies regarding clinical efficacy and response of childhood depression to treatment with tricyclic antidepressants and the serotonin norepinephrine reuptake inhibitor venlafaxine have been inconclusive.

Most unipolar, untreated depressive disorders in children and adolescents last between 3 and 12 months. The risk of recurrence ranges from 34% to 50% within the first year after discontinuation of treatment; 50% to 75% of affected children have a relapse within 8 years following the initial episode. (11) Comorbid disorders such as anxiety or substance abuse, presence of suicidal ideation, recurrent episodes of parental depression, and family chaos predispose to a longer duration of active symptoms.

Depression in children and adolescents should be conceptualized as a chronic illness. Clinicians should treat the acute episode until the patient’s symptoms are in remission. Additional treatment should focus on prevention. In general, if the symptoms have not improved or remitted after a 6- to 8-week trial on medication or if the patient has developed intolerable adverse effects, the clinician should change medication. If the response to treatment has been partial, the clinician might consider increasing the dose of the current medication, adding another agent, or suggesting other types of therapy. Of note, treatment failure in adolescents might be due to noncompliance rather than refractory symptoms. If the patient’s depression has gone into remission, therapy to prevent recurrence should continue for another 6 to 9 months. More than 90% of children and adolescent outpatients who have depressive disorder recover within 1 to 2 years. Because no data are available on the long-term effects of medication on children or adolescents, it is difficult to justify indefinite continuation of treatment. However, given the risks for recurrence and relapse, it is prudent to monitor children and adolescents closely, even after treatment.

Cognitive Behavioral Therapy

CBT is the best studied nonpharmacologic intervention for the treatment of depression in children and adolescents. The theoretical underpinning of this therapy posulates that depressed children and adolescents have distortions in their thought processes that cause them to focus on the negative rather than the positive aspects of any given situation. Stressful events serve to accentuate the negative ideation and precipitate depressive episodes, which then may cause counterproductive or maladaptive behaviors. A common therapeutic format includes: psychoeducation; behavioral modification involving active scheduling of enjoyable activities; cognitive restructuring to reframe distortions and allow for new, more rational thoughts; and learning self-relaxation techniques. Most studies of CBT have suggested that it is an extremely effective intervention for depressive disorders in children and adolescents.

The Treatment for Adolescent Depression Study (TADS), published in 2004, evaluated fluoxetine, CBT, and the combination of the two in terms of relative efficacy in the treatment of adolescent depression versus placebo. (12) In this well-powered study, fluoxetine and CBT together and fluoxetine alone were superior to CBT alone and to placebo. CBT alone failed to demonstrate the same efficacy found in earlier studies, perhaps because the patients in TADS were extremely ill and presented with more comorbid conditions. It also is possible that the CBT treatment package used in TADS employed too many different techniques to allow any one technique enough time to succeed.

Interpersonal Therapy

IPT centers on the problems in the patient’s interpersonal interactions, seeking to change conflicted, hostile relationships into supportive, meaningful, and satisfying ones. The focus of the therapy usually is on development of social skills and investigation of the effect of shifting roles within family or peer groups, including adjustment to such events as parental divorce or remarriage. In IPT, the patient looks at his or her place within a larger social context. In contrast, CBT focuses on the patient’s internal thought processes and how they influence perspective and behavioral patterns.

Summary

Any one of the three previously noted approaches is a reasonable first choice in the treatment of children and
adolescents whose symptoms are moderate. Medication likely is the best choice for those who have more severe symptoms, coupled with CBT or supportive counseling, depending on available resources. Evidence suggests that the relationship and degree of trust between child and therapist is a good predictor of the efficacy of therapy. Children and adolescents who fail to respond to initial interventions within 6 to 8 weeks and those who have very severe mood disorders and accompanying significant impairment in psychosocial functioning or suicidal ideation, plan, or intent should be referred to a child psychiatrist or mental health specialist, if possible (Table 1). Most children and adolescents who have depressive disorders can be managed as outpatients. However, those who are actively suicidal, homicidal, or psychotic should be hospitalized.

### Suicide and Suicidal Behavior

#### Epidemiology

According to the Centers for Disease Control and Prevention, (13) suicide is the third leading cause of death in the United States among adolescents and young adults ages 10 to 24 years. From 1990 to 2003, suicide rates in that age group declined from 9.48 to 6.78 per 100,000. However, from 2003 to 2004 (the most recent year for which data are available), the rate increased to 7.32 per 100,000. This increase reflects upward trends in three groups: females ages 10 to 14 years and 15 to 19 years and males ages 15 to 19 years. Hanging/suffocation was the most common cause of death in females in all age groups and firearms the most common method used by males. There are ethnic disparities within these age groups: Native American/Alaskan Native youth and Hispanic females have a higher percentage of suicide attempts than their peers. Few prepubertal children successfully commit suicide (suicide rate 0.6 per 100,000 for ages 5 to 14 years), but these children are at high risk for suicide attempts in their adolescence and young adulthood.

Suicidal ideation and gestures also are increasing in frequency. Although there is no national registry for such behaviors, data from the Youth Risk Behavior Surveillance System, 2005, a survey of high school students across the United States, reveal that 16.9% considered suicide and 8.4% had attempted suicide within the past year. Both mood and anxiety disorders increase the likelihood of suicidal ideation. In prepubertal children, suicidal ideation can be associated with disruptive disorders. In adolescents, substance abuse and separation anxiety may predispose to such ideation.

These statistics are sobering and argue for vigorous efforts at early identification of children and adolescents at risk as well as aggressive prevention and intervention. One instrument used to screen adolescents for psychiatric illness is the Teen-Screen, a school-based program that screened 55,000 students in 2005. The screening has two parts: a self-report questionnaire and an open-ended interview by a skilled mental health professional. The combination of the questionnaire and interview ensures that a positive result on the self-report also is reflected in the clinical history. The program is voluntary but requires consent of the student’s parent or guardian. If the student’s questionnaire and interview suggest the presence of psychiatric illness, he or she is referred for additional psychiatric evaluation. The Teen-Screen is controversial because many feel that it violates parental rights and that the high false-positive rate invalidates the testing. Although the “screen” has a high sensitivity but low specificity, the risk of overlooking a truly suicidal adolescent seems greater than the risk of misdiagnosing (and potentially stigmatizing) a normal teenager.

### Risk Assessment and Management

About 70% of adolescents are seen by their primary care physicians at least once a year. The same percentage reports a willingness to talk with their primary care physicians about their mental health. Pediatricians must be trained to detect psychiatric illness that may predispose their patients to self-injurious behaviors. They also must be alert to the risk factors for suicide in children and adolescents: mood disorder, substance abuse, loss of a loved one, family discord, social isolation, family history of suicidal behavior, previous suicide attempt, and availability of firearms.

Any child experiencing a mood disorder or substance abuse should be considered at risk for suicide and evaluated thoroughly. Questions to ask might include those

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**Table 1. When to Refer to a Child Psychiatrist or Mental Health Specialist**

- Moderate or severe depression, with significant impairment in functioning or suicidal ideation, plan, or intent
- Coexisting substance abuse
- Coexisting psychosis
- Patients who fail to respond to initial interventions within 6 to 8 weeks
- Other complicating factors, conditions, or concerns
listed in Table 2. If a child or adolescent is actively suicidal, with plan or intent or both, the clinician should take whatever steps are necessary to ensure the safety of the child.

Suicidal “gestures,” such as superficial cutting or ingestion of a few extra pills, must be taken seriously. Any episode of self-inflicted harm may be a sign of attempted suicide. A child or adolescent might believe that the “gesture” could have caused death or he or she might believe that an overdose of, for example, acetaminophen is safe because it is a drug that can be bought easily at the drugstore. It also is important to review with the child or adolescent what “death” or “killing oneself” means. A child younger than 6 years of age might be unable to appreciate the finality of death.

No evidence suggests that “no suicide contracts” (in which the patient agrees not to harm him- or herself and lists ways to help him- or herself should suicidal feelings arise) are preventive. If the child or adolescent is actively suicidal, it is unlikely that he or she is in any position to understand the contract or to agree to it. Furthermore, once such a contract is signed, parents or guardians charged with helping the child to stay safe might become less vigilant.

For a child or adolescent who has attempted suicide, it is helpful to assess the risk/rescue ratio. This practice assesses the risk of the action in relation to the likelihood of rescue. The child who overdoses on a medication late at night, tells no one, and goes to sleep hoping never to wake up is different from the child who takes a handful of pills while standing in the kitchen arguing with a parent.

In most cases, the legal guardians (parents or other caregivers) must be informed of the results of the assessment; issues of confidentiality become moot in the setting of active suicidal (or homicidal) ideation with intent and plan. Questions regarding availability of and access to firearms and other vectors of harm (including knives, drugs, and poisons) must be discussed, with the goal of removing access to these items in the home or any place where the child or adolescent might go. Usually, it is necessary to hospitalize actively suicidal children and adolescents on psychiatric inpatient units for their immediate safety as well as for containment, stabilization, psychopharmacologic evaluation, and ultimate referral to an outpatient network of care.

One of the most frightening aspects of adolescent suicides is the potential for contagion and cluster formation. Perspectives differ on what constitutes a “cluster,” but for the purposes of this article, it is defined as three or more suicides occurring within the same community that bear a temporal relationship to one another. The etiology of cluster formation is controversial. One theory looks at

**Summary**

- Depressive disorders in children and adolescents fall on a spectrum that ranges from mood changes in response to an acute stressor to pervasive and persistent mood change accompanied by suicidal ideation, plan, or intent.
- Depression likely is caused by interaction between biologic markers (genetic loading) and environmental stressors.
- Assessment is based on the developmental stage of the child, with a focus on clinical history and mental status examination.
- Evidence supports the necessity of asking children and adolescents questions about psychosocial functioning and does not support the concept that such questions influence outcome adversely.
- Comorbid disorders in children and adolescents who have depression include anxiety disorders, attention-deficit disorder, substance abuse, and conduct disorder.
- Empirically validated treatments include psychopharmacologic medication (either alone or in combination with supportive psychotherapy), CBT, and IPT.
- Antidepressant medications have demonstrated efficacy in the treatment of depression in children and adolescents.
- Fluoxetine should be the first choice for medication management of depressive symptoms in children and adolescents.
- According to the Centers for Disease Control and Prevention, suicide is the third leading cause of death in the United States among adolescents and young adults ages 10 to 24 years.

<table>
<thead>
<tr>
<th>Questions To Ask Regarding Suicide Risk</th>
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<tbody>
<tr>
<td>Do you have thoughts of death or dying?</td>
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<tr>
<td>Do you wish you were dead?</td>
</tr>
<tr>
<td>Do you believe that things would be better if you were dead?</td>
</tr>
<tr>
<td>Do you have any intent to kill yourself or any plan to do so?</td>
</tr>
<tr>
<td>If you do have a plan, what is it?</td>
</tr>
<tr>
<td>Do you have the means necessary to carry out your plan?</td>
</tr>
<tr>
<td>Have you ever tried to kill yourself or hurt yourself before?</td>
</tr>
</tbody>
</table>

*Table 2.*
suicide as an infectious disease, as if the impetus to kill oneself is contagious. Another suggests that vulnerable adolescents, particularly those who are depressed, become suicidal in the face of intense loss. Cluster formation can pose a true public health dilemma because too much media coverage (television, Internet) can contribute to the contagious or imitative risk. However, that risk must be balanced with the need for information to be distributed throughout the community as an aid in the process of recovery and healing.

References

Suggested Reading
PIR Quiz

Quiz also available online at pedsinreview.aappublications.org.

1. The antidepressant of choice for the treatment of depression in adolescents is:
   - A. Amitriptyline.
   - B. Citalopram.
   - C. Fluoxetine.
   - D. Paroxetine.
   - E. Venlafaxine.

2. How many weeks after starting treatment for depression with a selective serotonin reuptake inhibitor should the clinician wait to assess treatment success?
   - A. 1 to 2.
   - B. 3 to 4.
   - C. 6 to 8.
   - D. 10 to 12.
   - E. 14 to 16.

3. After 6 months of pharmacotherapy, a 16-year-old girl who has depression is in remission. Her parents ask you how much longer she will require pharmacotherapy. Your best estimate is:
   - A. 1 to 2 months.
   - B. 3 to 4 months.
   - C. 6 to 9 months.
   - D. 12 to 15 months.
   - E. 18 to 24 months.

4. In planning for the treatment of a 15-year-old boy who is depressed, which of the following options is the best evidence-based recommendation?
   - A. Cognitive behavioral therapy alone.
   - B. Cognitive behavioral therapy + fluoxetine.
   - C. Interpersonal therapy alone.
   - D. Interpersonal therapy + fluoxetine.
   - E. Cognitive behavioral therapy + interpersonal therapy.

5. Among the many risk factors for suicide, which of the following is the least concerning?
   - A. Chronic illness.
   - B. Depression.
   - C. Parental suicide.
   - D. Previous attempt.
   - E. Substance abuse.
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PIR Quiz
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10. Which of the following is the primary test used for newborn screening for CF?
   A. DNA testing for CFTR genetic mutation.
   B. Immunoreactive trypsinogen in blood.
   C. Meconium trypsin concentration.
   D. Nasal potential difference.
   E. Sweat chloride concentration.

11. A 2-year-old girl is being evaluated for cough, loose stools, and failure to thrive. Which of the following tests has the highest sensitivity and specificity in establishing the diagnosis of CF in this child?
   A. DNA testing for CFTR genetic mutation.
   B. Immunoreactive trypsinogen in blood.
   C. Meconium trypsin concentration.
   D. Nasal potential difference.
   E. Sweat chloride concentration.

12. A 12-year-old boy who has CF is admitted for worsening cough and difficulty in breathing of 1 month’s duration. Sputum cultures are obtained and intravenous antibiotic therapy begun. Presence of which of the following pathogens in his sputum poses the greatest danger to other patients who have CF with whom he has direct contact?
   A. Burkholderia cepacia.
   B. Klebsiella pneumoniae.
   C. Penicillin-resistant Streptococcus pneumoniae.
   D. Pseudomonas aeruginosa.
   E. Staphylococcus aureus.

13. A 4-year-old girl is being evaluated for cough, loose stools, and poor weight gain of 6 months’ duration. Her parents have noticed that she craves salty foods. Two separate sweat electrolyte tests performed at a CF Foundation-accredited laboratory show chloride values of 70 mEq/L (70 mmol/L) and 64 mEq/L (64 mmol/L), respectively. Which of the following statements is most correct?
   A. A diagnosis of CF should be confirmed by NPD.
   B. The management regimen for CF should begin.
   C. The presence of a single CFTR mutation is required to confirm the diagnosis of CF.
   D. The serum immunoreactive trypsinogen assay should be performed.
   E. The test should be repeated while the girl is eating a low-salt diet.

Clarification