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normative development in infants, anxiety disorders in childhood predict a wide range of psychological difficulties in adolescence including additional anxiety disorders, panic attacks, and depressive disorders. Fear is an expected response to real or perceived threat; however, anxiety is the anticipation of future danger. Anxiety disorders are characterized by recurrent emotional and physiological arousal in response to excessive perceptions of perceived threat or danger. Anxiety disorders commonly found in youth include separation anxiety disorder, generalized anxiety disorder, social anxiety disorder, and selective mutism. Anxiety is classified into disorders based on how it is experienced, the situations that trigger it, and the course that it tends to follow. 31.13a Separation Anxiety Disorder, Generalized Anxiety Disorder, and Social Anxiety Disorder (Social Phobia) Separation anxiety disorder, generalized anxiety disorder, and social anxiety disorder in children are often considered together in the evaluation process and differential diagnosis, and in developing treatment strategies, because they are highly comorbid and have overlapping symptoms. A child with separation anxiety disorder, generalized anxiety disorder, or social anxiety disorder has a 60 percent chance of having at least one of the other two disorders as well. Of children with one of the above anxiety disorders, 30 percent have all three of them. Children and adolescents may also have additional comorbid anxiety disorders such as specific phobia or panic disorder. Separation anxiety disorder, generalized anxiety disorder, and social anxiety disorder are

distinguished from each other by the types of situations that elicit the excessive anxiety and avoidance behaviors. SEPARATION ANXIETY DISORDER Separation anxiety is a universal human developmental phenomenon emerging in infants younger than 1 year of age and marking a child's awareness of a separation from his or her mother or primary caregiver. Normative separation anxiety peaks between 9 months and 18 months and diminishes by about 2½ years of age, enabling young children to develop a sense of comfort away from their parents in preschool. Separation anxiety or stranger anxiety most likely evolved as a human response that has survival value. The expression of transient separation anxiety is also normal in young children entering school for the first time. Approximately 15 percent of young children display intense and persistent fear, shyness, and social withdrawal when faced with unfamiliar settings and people. Young children with this pattern of significant behavioral inhibition are at higher risk for the development of separation anxiety disorder, generalized anxiety disorder, and social phobia. Behaviorally inhibited children, as a group, exhibit characteristic physiological traits, including higher than average resting heart rates, higher morning cortisol levels than average, and low heart rate variability. Separation anxiety disorder is diagnosed when developmentally

inappropriate and excessive anxiety emerges related to separation from the major attachment figure. According to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), separation anxiety disorder is characterized by a level of fear or anxiety regarding separation from their parents or primary caregiver, which is beyond developmental expectations. Furthermore, there may be a pervasive worry that harm will come to a parent upon separation, which leads to extreme distress, and sometimes nightmares. The DSM-5 requires the presence of at least three symptoms related to excessive worry about separation from a major attachment figure for a period of at least 4 weeks. The worries often take the form of refusal to go to school, fears and distress on separation, repeated complaints of physical symptoms such as headaches and stomachaches when separation is anticipated, and nightmares related to separation issues. GENERALIZED ANXIETY DISORDER Children with generalized anxiety disorder have significant distress in activities of daily life often focused on the child's fears of incompetence in many areas, including school performance and in social settings. In addition, children with generalized anxiety disorder, according to DSM-5, experience at least one of the following symptoms: restlessness, being easily fatigued, "mind going blank," irritability, muscle tension, or sleep disturbance. Children with generalized anxiety disorder tend to feel fearful in multiple settings and expect more negative outcomes when faced with academic or social challenges, compared with peers. Children and adolescents with generalized anxiety disorder may experience symptoms of autonomic hyperarousal such as tachycardia, shortness of breath, or dizziness, and are more likely than nonanxious youth to experience sweating, nausea, or diarrhea when they become anxious. Children and adolescents with generalized anxiety disorder tend to be overly concerned about potential natural disasters such as earthquakes or floods, and these worries can interfere with their daily activities. Finally, children and adolescents with generalized anxiety disorder are continuously worried about the quality of their performance in academics, sports, and other activities, and often seek excessive reassurance about their performance. SOCIAL ANXIETY DISORDER (SOCIAL PHOBIA) Children who experience intense discomfort and distress in social situations and are impaired by their fear of scrutiny or humiliation are given the diagnosis of social anxiety disorder. Their distress may be expressed in the form of crying, tantrums, avoidance, freezing, or even becoming "mute" in these situations. According to DSM-5, this disorder is characterized by consistent anxiety and distress in almost all social situations. Any situation in

which the child feels exposed to possible scrutiny by others can provoke fear or anxiety, and the child will often try to avoid these feared social situations. Children must experience the anxiety in the presence of peers, not only with adults, in order to receive the diagnosis. A child or adolescent with social anxiety

disorder may exhibit the performance only type, which targets a specific type of performing, such as fear of public speaking. The performance only type typically manifests in school or academic settings in which public presentations must be performed, such as in front of classmates in school. Social anxiety disorder has significant implications for future accomplishments, since it is associated with lower levels of satisfaction in leisure activities, increased rates of school dropout, less productivity in the workplace as adults, and increased rates of remaining single. Despite the significant impairment caused by social anxiety disorder, up to half of individuals with the disorder do not receive treatment. EPIDEMIOLOGY The prevalence of anxiety disorders has varied with the age group of the children surveyed and the diagnostic instruments used. Lifetime prevalence of any anxiety disorder in children and adolescents ranges from 10 percent to 27 percent. Anxiety disorders are common in preschoolers as well, and follow a similar epidemiologic profile as in older children. An epidemiologic survey using the Preschool Age Psychiatric Assessment (PAPA) found that 9.5 percent of preschoolers met criteria for any anxiety disorder, with 6.5 percent exhibiting generalized anxiety disorder, 2.4 percent meeting criteria for separation anxiety disorder, and 2.2 percent meeting criteria for social phobia. Separation anxiety disorder is estimated to be about 4 percent in children and young adolescents. Separation anxiety disorder is more common in young children than in adolescents and has been reported to occur equally in boys and girls. The onset may occur during preschool years, but is most common in children 7 to 8 years of age. The rate of generalized anxiety disorder in school-age children is estimated to be approximately 3 percent, the rate of social phobia is 1 percent, and the rate of simple phobias is 2.4 percent. In adolescents, lifetime prevalence for panic disorder was found to be 0.6 percent; the prevalence for generalized anxiety disorder was 3.7 percent. ETIOLOGY Biopsychosocial Factors Evidence for the influences of parental psychopathology and parenting styles on the emergence of anxiety disorders in childhood has been found in multiple investigations. Longitudinal studies have found that parental overprotection has been associated with an increased risk of the development of anxiety disorders in children, and insecure parent–child attachment is associated with higher than expected rates of anxiety disorders in childhood. It is also well known that maternal depression and anxiety have led to an increased risk for anxiety and depression in children. Psychosocial factors in conjunction with a child’s temperament influences the degree of separation anxiety evoked in situations of brief separation and exposure to unfamiliar environments. The temperamental trait of shyness and withdrawal in unfamiliar situations has been shown to be associated with a higher risk of developing separation anxiety disorder,

generalized anxiety disorder, social anxiety disorder, or all three during childhood and adolescence. External life stresses often coincide with development of the disorder. The death of a relative, a child’s illness, a change in a child’s environment, or a move to a new neighborhood or school is frequently noted in the histories of children with separation anxiety disorder. In a vulnerable child, these changes probably intensify anxiety. Neurophysiological correlations are found with behavioral inhibition (extreme shyness); children with this constellation are shown to have a higher resting heart rate and an acceleration of heart rate with tasks requiring cognitive concentration. Additional physiological correlates of behavioral inhibition include elevated salivary

cortisol levels, elevated urinary catecholamine levels, and greater papillary dilation during cognitive tasks. Neuroimaging studies of adolescents with anxiety show an increased activation of the amygdala compared to non-anxious adolescents when presented with anxiety-provoking stimuli. Furthermore, anxious adolescents maintain the hyperactivation of the amygdala over time, rather than showing an attenuation of the effect as in nonanxious adolescents. Structural studies of the amygdala in adolescents with anxiety have led to conflicting results, some studies finding increased amygdala volumes, whereas other studies finding decreased amygdala volumes. Social Learning Factors Fear, in response to a variety of unfamiliar or unexpected situations, may be unwittingly communicated from parents to children by direct modeling. If a parent is fearful, the child will probably have a phobic adaptation to new situations, especially to a school environment. There are much data to suggest that overprotective parenting promotes increased interpersonal sensitivity in healthy children, and increases the risk of social anxiety disorder in children with behavioral inhibition or other anxiety disorders such as separation anxiety disorder. Some parents appear to teach their children to be anxious by overprotecting them from expected dangers or by exaggerating the dangers. For example, a parent who cringes in a room during a lightning storm teaches a child to do the same. A parent who is afraid of mice or insects conveys the affect of fright to a child. Conversely, a parent who becomes angry with a child when the child expresses fear of a given situation, for example, when exposed to animals, may promote a phobic concern in the child by exposing the child to the intensity of the anger expressed by the parent. Social learning factors in the development of anxiety reactions are magnified when parents have anxiety disorders themselves. These factors may be pertinent in the development of separation anxiety disorder as well as in generalized anxiety disorder and social phobia. A recent study found no association between psychosocial hardships, such as ongoing family conflict, and behavioral inhibition among young children. It appears that temperamental predisposition to anxiety disorders emerges as a highly heritable constellation of traits, and is not created by psychosocial stressor.

Genetic Factors Genetic studies suggest that genes account for at least one third of the variance in the development of anxiety disorders. Heritability for anxiety disorders in children and adolescents ranges from 36 percent to 65 percent, with the highest estimates found in younger children with anxiety disorders. Two heritable characteristics—behavioral inhibition (the tendency toward fear and withdrawal in new situations) and physiological hyperarousal—have both been found to impart significant risk factors for future development of an anxiety disorder. However, although the temperamental constellation of behavioral inhibition, excessive shyness, the tendency to withdraw from unfamiliar situations, and the eventual emergence of anxiety disorders have a genetic contribution, one third to two thirds of young children with behavioral inhibition do not appear to go on to develop anxiety disorders. Family studies have shown that the offspring of adults with anxiety disorders are at an increased risk of having an anxiety disorder themselves. Separation anxiety disorder and depression in children overlap, and the presence of an anxiety disorder increases the risk of a future episode of a depressive disorder. Current consensus on the genetics of anxiety disorders suggests that what is inherited is a general predisposition toward anxiety, causing heightened levels of arousal, emotional reactivity, and increased negative affect, all of which increase the risk of developing separation anxiety disorder, generalized anxiety disorder, and social phobia. DIAGNOSIS AND CLINICAL FEATURES Separation anxiety disorder, generalized anxiety disorder, and social phobia are highly related in children and adolescence because, in most children, overlapping symptoms as well as comorbid disorders emerge. Generalized anxiety disorder is the most common anxiety disorder among youth, more common in adolescents than in

younger children; in almost one third of these cases, a child with generalized anxiety disorder also exhibits separation anxiety disorder and social anxiety disorder. Diagnostic criteria for separation anxiety disorder, according to the DSM-5, include three of the following symptoms for at least 4 weeks: persistent and excessive worry about losing, or possible harm befalling, major attachment figures; persistent and excessive worry that an untoward event can lead to separation from a major attachment figure; persistent reluctance or refusal to go to school or elsewhere because of fear of separation; persistent and excessive fear or reluctance to be alone or without major attachment figures at home or without significant adults in other settings; persistent reluctance or refusal to go to sleep without being near a major attachment figure or to sleep away from home; repeated nightmares involving the theme of separation; repeated complaints of physical symptoms, including headaches and stomachaches, when separation from major attachment figures is anticipated; and recurrent excessive distress when separation from home or major attachment figures is anticipated or involved. The following case history demonstrates separation anxiety disorder along

with autonomic arousal symptoms. Jake was a 9-year-old boy who was referred for outpatient evaluation by his family physician. He refused to sleep in his room alone at night and exhibited violent tantrums each morning in order to avoid going to school. Jake expressed recurrent fears that something bad would happen to his mother. He worried that she would get into a car accident or that there would be a fire at home and his mother would be killed. Developmental history revealed that Jake was anxious and irritable as an infant and toddler. He had trouble adjusting to babysitters in the preschool years. There was a history of panic disorder, with agoraphobia in the mother and major depression in his father. Jake became more concerned and territorial over his mother when his father left the family, and his mother became depressed. Jake always kept track of his mother’s whereabouts and insisted that she stay at home. Nighttime was a particularly difficult time at home. When Jake’s mother tried to get Jake to remain in his room, Jake would whine and cry and insist that his mother lie in bed with him until he fell asleep. He also expected his mother to be in the master bedroom across the hall from his room throughout the evening. Jake’s mother reported that that each evening her son would get up and peek through the crack in the master bedroom door, as frequently as every 10 minutes, to be certain that she was still there. Jake reported frequent nightmares that his mother was killed and that monsters prevented him from rescuing his mother, taking him away from his family forever. During the daytime, Jake would shadow his mother around the house. Jake would agree to play a game with his sister in the lower level of the house only if his mother was close by. When Jake’s mother went upstairs, he would interrupt the game and follow her upstairs. He refused to sleep at a friend’s house. Frequently, at home as the evening progressed, Jake described a queasy sensation in his stomach mixed with feelings of sadness. On school days, Jake usually complained of stomachaches and tried to stay home. Jake appeared distressed and panicky and would become violent when his mother attempted to drop him off at school. Once at school, he seemed calmer and less distressed, but frequently was seen in the nurse’s office, complaining of nausea and seeking to be sent home. (Adapted from case material from Gail A. Bernstein, M.D. and Anne E. Layne, Ph.D.) The essential feature of separation anxiety disorder is extreme anxiety precipitated by separation from parents, home, or other familiar surroundings, whereas in generalized anxiety disorder, fears are extended to negative outcomes for all kinds of events, including academic, peer relationship, and family activities. In generalized anxiety disorder, a child or adolescent experiences at least one recurrent physiological symptom, such as restlessness, poor concentration, irritability, or muscle tension. In

social phobia, the child’s fears peak during performance situations involving exposure to unfamiliar

people or situations. Children and adolescents with social phobia have extreme concerns about being embarrassed, humiliated, or negatively judged. In each of the preceding anxiety disorders, the child’s experience can approach terror or panic. The distress is greater than that normally expected for the child’s developmental level and cannot be explained by any other disorder. Morbid fears, preoccupations, and ruminations characterize separation anxiety disorder. Children with anxiety disorders overestimate the probability of danger and the likelihood of negative outcome. Children with separation anxiety disorder and generalized anxiety disorder become overly fearful that someone close to them will be hurt or that something terrible will happen to them or their families, especially when they are away from important caring figures. Many children with anxiety disorders are preoccupied with health and worry that their families or friends will become ill. Fears of getting lost, being kidnapped, and losing the ability to be in contact with their families is predominant among children with separation anxiety disorder. Adolescents with anxiety disorders may not directly express their worries; however, their behavior patterns often reflect either separation anxiety or other anxiety if they exhibit discomfort about leaving home, engage in solitary activities because of fears about how they will perform in front of peers, or have distress when away from their families. Separation anxiety disorder in children is often manifested at the thought of travel or in the course of travel away from home. Children may refuse to go to camp, a new school, or even a friend’s house. Frequently, a continuum exists between mild anticipatory anxiety before separation from an important figure and pervasive anxiety after the separation has occurred. Premonitory signs include irritability, difficulty eating, whining, staying in a room alone, clinging to parents, and following a parent everywhere. Often, when a family moves, a child displays separation anxiety by intense clinging to the mother figure. Sometimes, geographical relocation anxiety is expressed in feelings of acute homesickness or psychophysiological symptoms that break out when the child is away from home or is going to a new country. The child yearns to return home and becomes preoccupied with fantasies of how much better the old home was. Integration into the new life situation may become extremely difficult. Children with anxiety disorders may retreat from social or group activities and express feelings of loneliness because of their self-imposed isolation. Sleep difficulties are frequent in children and adolescents with any anxiety disorder or in severe separation anxiety; a child or adolescent may require having someone remain with him or her until he or she falls asleep. An anxious child may awaken and go to a parent’s bed or even sleep at the parents’ door in an effort to diminish anxiety. Nightmares and morbid fears may be expressions of anxiety (Fig. 31.13a-1).

FIGURE 31.13a-1 This surrealistic photograph symbolically represents the anxiety in a childhood nightmare. (Courtesy of Arthur Tress for Magnum Photos, Inc.) Associated features of most anxiety disorders include fear of the dark and imaginary worries. Children may have the feeling that eyes are staring at them and monsters are reaching out for them in their bedrooms. Children with separation anxiety disorder, generalized anxiety disorder, and social anxiety disorder often complain of somatic symptoms and may be more sensitive to changes in their bodies compared to youth without anxiety disorders. Children with separation anxiety disorder, generalized anxiety disorder, or social anxiety disorder are often more emotionally sensitive than peers and more easily brought to tears. Frequent somatic complaints accompanying anxiety disorders include gastrointestinal symptoms, nausea, vomiting, and stomachaches; unexplained pain in various parts of the body; sore throats; and flu-like symptoms. Older children and adolescents typically complain

of somatic experiences classically reported by adults with anxiety, such as cardiovascular and respiratory symptoms—palpitations, dizziness, faintness, and feelings of strangulation. Physiological signs of anxiety are a part of the diagnostic criteria for generalized anxiety disorder, but they are more often also experienced by children with separation anxiety and social phobia than the general population. The following case history demonstrates a young adolescent with generalized anxiety disorder.

Rachel was a 13-year-old girl referred for an evaluation by her pediatrician based on her chronic gastrointestinal complaints without any organic illness. On interview, Rachel appeared withdrawn and meek but responsive to questions. She endorsed a number of worries that included concerns about her health, her parents' safety, her school performance, and her peer relationships. Rachel's greatest worries were related to her health and safety. Rachel's mother reported that Julie had recently been very reluctant to play outside, because she feared she would contract Lyme disease from a tick bite or West Nile virus from a mosquito bite. Rachel was also very distressed by news reports about catastrophic events locally and around the world (e.g., kidnapping, crime, terrorism). Rachel was described by her family and teachers as overly conscientious about her schoolwork and as often being concerned about adult matters (e.g., finances, parents' job security). Symptoms that accompanied Rachel's worries primarily involved stomach pain and problems falling asleep. Rachel tended to be quite perseverative; repetitively verbalizing her worries even after reassurance was given. Rachel admitted that she worried for hours each day and could not "turn off" her worried thoughts. Rachel was the product of a normal pregnancy and delivery. Her medical history was unremarkable, with the exception of frequent gastrointestinal pain since kindergarten. Julie was described as irritable and difficult to soothe as an infant. Developmental milestones were met within normal limits. She was described as very obedient and had no history of externalizing behavior problems. She was very concerned about her academic performance from an early age and earned A's with an occasional B. Rachel was somewhat shy in social situations but well-liked by her peers. Family history included depression in her maternal grandmother and a maternal history of generalized anxiety disorder, social anxiety, and separation anxiety disorder as a child. Rachel had two younger siblings who were high achievers and without notable problems. (Adapted from case material from Gail A. Bernstein, M.D., and Ann E. Layne, Ph.D.) The next case history demonstrates an adolescent with multiple anxiety and depressive disorders. Kate is a 15-year-old 10th grader who lives with her biological parents and two sisters, age 9 and 14 years. Kate is a very articulate teen who has always been a good student, although she never volunteers answers in school unless she is called on by her teachers. She gets along well with her sisters when at home, but ever since she entered high school in the 9th grade year, she declines invitations to go to friends' homes, has turned down opportunities to go to parties, and has even stopped going on outings with her sisters to the neighborhood mall and the movies. Kate reports that she gets too nervous, and blushes when she is with friends outside of the classroom at school because she can't think of anything to say to them. She reports that she is embarrassed

to go shopping or to the movies with her sisters because they often run into neighborhood peers along the way, stop to chat, and this makes her feel "stupid," because even though she is the oldest, she does not say anything, and believes that her sisters' friends will laugh at her shyness. Recently, one of her former best friends confronted her about why she had stopped "hanging out" with her friends. Kate had stopped eating lunch with her friends in school because she felt humiliated when they would talk about their weekend plans and even when they invited her to join,

she would just look the other way and ignore the conversation. Kate had become isolated, even in school, and admitted to her sister that she was lonely. Kate was brought for an evaluation after her younger sister commented to her mother that Kate spent all of her time alone whenever her sisters saw their friends, and that she looked sad and stressed out whenever she was around peers. Kate was down, always in poor spirits and had stopped interacting with her sisters even at home, and her sisters were often out with their own friends. On rare occasions Kate's younger sister had invited Kate to parties or to friend's homes, but Kate had declined and burst into tears. Kate was evaluated by a child psychiatrist who made the diagnoses of social anxiety disorder, generalized anxiety disorder, and major depression and recommended a combination of treatment options, including cognitive-behavioral therapy (CBT) and a trial of a selective serotonin reuptake inhibitor (SSRI), fluoxetine. Kate and her family decided to try the medication first. Kate was started on 10 mg of fluoxetine and over the next month was titrated to a dose of 20 mg. By the third week of the medication trial, Kate was noticeably less resistant to going out with her sisters to places where they were likely to encounter peers. Her sisters noticed that she did not seem as stressed and started to occasionally sit with peers at lunch in the school cafeteria. She stated that she did not feel as self-conscious as she used to in class and was willing to go to a friend's house. She still declined to go to a birthday party of a peer that she didn't know very well. Kate continued on the same medication and within 2 months, she was significantly less anxious in social situations. She complained occasionally of a stomachache, but tolerated the medication well. Her family was impressed when she requested they plan a birthday party for her 16th birthday and decided to invite 10 friends. Pathology and Laboratory Examination No specific laboratory measures help in the diagnosis of separation anxiety disorder, generalized anxiety disorder, or social anxiety disorder. DIFFERENTIAL DIAGNOSIS The presence of separation anxiety is a developmentally expected feature in a young child and often does not represent an impairing condition, thus clinical judgment must be used in distinguishing normal anxiety from separation anxiety disorder in this age group. In older school-age children, a child experiencing more than normal distress is

apparent when school is refused on a regular basis. For children who resist school, it is important to distinguish whether fear of separation, general worry about performance, or more specific fears of humiliation in front of peers or the teacher are driving the resistance. In many cases in which anxiety is the primary symptom, all three of the above-feared scenarios come into play. In generalized anxiety disorder, anxiety is not primarily focused on separation. When depressive disorders occur in children, possible comorbidities such as separation anxiety disorder should be evaluated as well. A comorbid diagnosis of separation anxiety disorder and depressive disorder should be made when the criteria for both disorders are met; the two diagnoses often coexist. Panic disorder with agoraphobia is uncommon before 18 years of age; the fear is of being incapacitated by a panic attack rather than of separation from parental figures. School refusal is a frequent symptom in separation anxiety disorder, but is not pathognomonic of it. Children with other diagnoses, such as specific phobias, or social anxiety disorder, or fear of failure in school because of learning disorder, may also lead to school refusal. When school refusal occurs in an adolescent, the severity of the dysfunction is generally greater than when it emerges in a young child. Similar and distinguishing characteristics of childhood separation anxiety disorder, generalized anxiety disorder, and social anxiety disorder are presented in Table 31.13a-1. Table 31.13a-1 Common Characteristics in Childhood Anxiety Disorders COURSE AND PROGNOSIS The course and the prognosis of separation anxiety disorder, generalized anxiety disorder, and social anxiety disorder are varied and are related to the age of onset, the duration of the symptoms, and

the development of comorbid anxiety and depressive

disorders. Young children who can maintain attendance in school, after-school activities, and peer relationships generally have a better prognosis than children or adolescents who refuse to attend school and withdraw from social activities. The large multisite randomized clinical trial Child/Adolescent Anxiety Multimodal Study (CAMS) provided acute treatment for children and adolescents with one or more anxiety disorders with sertraline medication alone, cognitive-behavior therapy (CBT) alone, or both together, and found that predictors of future remission included younger age of initiation of treatment, lower severity of anxiety, absence of a comorbid depressive or anxiety disorder, and the absence of social anxiety disorder as the primary anxiety disorder being treated. A follow-up study of children and adolescents with mixed anxiety disorders over a 3-year period reported that up to 82 percent no longer met criteria for the anxiety disorder at follow-up. Of the group followed, 96 percent of those with separation anxiety disorder were remitted at follow-up. Most children who recovered did so within the first year. Early age of onset and later age at diagnosis were factors in this study that predicted slower recovery. Close to one third of the group studied, however, had developed another psychiatric disorder within the follow-up period, and 50 percent of these children developed another anxiety disorder. Studies have shown a significant overlap between separation anxiety disorder and depressive disorders. In cases with multiple comorbidities, the prognosis is more guarded. Longitudinal data indicate that some children with severe school refusal continue to resist attending school into adolescence and remain impaired for many years. TREATMENT The treatment of child and adolescent separation anxiety disorder, generalized anxiety disorder, and social anxiety disorder are often considered together, given the frequent comorbidity and overlapping symptomatology of these disorders. A multimodal comprehensive treatment approach usually includes psychotherapy, most often CBT, family education, family psychosocial intervention, and pharmacological interventions, such as SSRIs. The best evidence-based treatments for childhood anxiety disorders include CBT and SSRIs. The comparative efficacy of CBT, SSRI medication, and their combination (CBT + SSRI) in the treatment of childhood anxiety disorders was investigated in the National Institute of Mental Health (NIMH)–funded Child/Adolescent Anxiety Multimodal Study (CAMS). This double-blind, placebo-controlled, multi-site study included 488 children and adolescents with separation anxiety disorder, generalized anxiety disorder, or social anxiety disorder, who were randomly assigned to be treated with either CBT alone, SSRI medication (sertraline) alone, both CBT and sertraline, or placebo. After an acute treatment phase of 12 weeks, those in the combined CBT + sertraline group had an 80.7 percent response rate of much or very much improved on the clinical global improvement (CGI) rating. Response rates for the CBT–only and sertraline-only groups were 59.7 percent and 54.9 percent, respectively. Placebo response was 23.7 percent. Over time, during open follow-up, the combination of CBT plus sertraline continued to provide the most efficacy. All three treatments—

CBT, sertraline, and their combination—were superior to placebo, and thus effective treatments in childhood anxiety, but combined treatment was most likely to help children and adolescents with anxiety disorders. A trial of CBT may be applied first, if available, when a child is able to function sufficiently to engage in daily activities while obtaining this treatment. For a child with severe impairment, however, a combination of treatments is recommended. BT is widely accepted as first-line evidence-based treatment for childhood anxiety disorders. A meta-analysis reviewed 16 randomized controlled trials of CBT for childhood anxiety disorders and found CBT to be consistently superior to a wait-list control group or a psychological placebo group. Exposure-based

CBT has received the most empiric support among psychotherapeutic interventions for anxiety disorders in youth and has been shown to be superior to wait-list control groups in reducing impairment and symptoms of anxiety. Several psychosocial interventions have been designed specifically for anxiety disorders in young children. A randomized clinical trial of CBT for 4- to 7-year-old children was administered via a manualized intervention called “Being Brave: A Program for Coping with Anxiety for Young Children and their Parents.” This manual was loosely modeled after the manualized Coping Cat program. The intervention utilized a combination of parent-only sessions and child-and-parent sessions. Response rate, measured as much or very much improved on the Clinical Global Improvement Scale for Anxiety, was 69 percent among completers versus 32 percent of the wait-list controls. The treated children showed significantly better CGI improvement on social anxiety disorder, separation anxiety disorder, and specific phobia, but not on generalized anxiety disorder. This treatment, a developmentally modified parent–child CBT, shows promise in young children. Coaching Approach behavior and Leading by Modeling (the CALM program) is an intervention aimed at treating anxiety disorders in children younger than 7 years of age, who are too young to effectively engage in traditional CBT. The CALM program draws on previous work with children aged 2 to 7 years through interventions that target a child’s undesired behavior by modifying parents’ behavior, called Parent-Child Interaction Therapy (PCIT). The CALM program is a 12-session manual-based intervention that provides live, individualized coaching via a bug-in-the-ear receiver worn by the parent during sessions. It incorporates exposure tasks and promotes “brave” behavior with parent coaching. A pilot study using the CALM program with nine patients with a mean age of 5.4 years found that all treatment completers (seven patients and families) were rated as global responders, and all but one showed functional improvement. Adapting the PCIT model for anxiety disorders in young children appears to be a promising approach to treating anxiety in early childhood. A meta-analysis of randomized controlled trials of antidepressant agents for childhood anxiety provides evidence that multiple SSRIs, including fluvoxamine (Luvox), fluoxetine (Prozac), sertraline (Zoloft), and paroxetine (Paxil) are efficacious in the treatment of childhood anxiety. Based on this evidence, SSRIs are the first choice of medication in the treatment of anxiety disorders in children and adolescents. A large, multisite investigation by the National Institute of Mental Health (Research

Units in Pediatric Psychopharmacology [RUPP]) confirmed the safety and efficacy of fluvoxamine in the treatment of childhood separation anxiety disorder, generalized anxiety disorder, and social phobia. This double-blind, placebo controlled study of 128 children and adolescents revealed that 76 percent of children in the group treated with fluvoxamine showed significant improvement compared with 29 percent of those in the placebo group. Response to medication was noticeable after only two weeks of treatment. Fluvoxamine dosages ranged from 50 mg to 250 mg per day in children and up to 300 mg per day in adolescents. Children and adolescents with less comorbid depressive symptoms had the best response. Children and adolescents who responded to this medication were continued on fluvoxamine for a period of 6 months, and almost all of them continued to be responders at the 6-month mark. Several other randomized clinical trials have also supported the efficacy of SSRIs in the treatment of child and adolescent anxiety disorders. A randomized, controlled trial found fluoxetine, at a dose of 20 mg per day, to be safe and effective for children with these disorders, with minor side effects including gastrointestinal distress, headache, and drowsiness. In addition, a randomized clinical trial for the treatment of generalized anxiety disorder in children lends support for the efficacy of sertraline (Zoloft). Finally, a large industry randomized clinical trial of paroxetine (Paxil) in the treatment of children with social

phobia found that paroxetine was associated with response in 78 percent of children treated. Paroxetine was utilized at a dosage range of 10 to 50 mg per day. The Food and Drug Administration (FDA) has placed a “black box” warning on antidepressants, including all of the SSRI agents, used in the treatment of any childhood disorder, because of concerns about increased suicidality; however, no individual childhood anxiety study has found a statistically significant increase in suicidal thoughts or behaviors. Tricyclic drugs are not currently recommended due to their potentially serious cardiac adverse effects. β-Adrenergic receptor antagonists, such as propranolol (Inderal), and buspirone (BuSpar) have been used clinically in children with anxiety disorders, but currently no data support their efficacy. Diphenhydramine (Benadryl) may be used in the short term to control sleep disturbances in children with anxiety disorders. Open trials and one double-blind, placebo-controlled study suggested that alprazolam (Xanax), a benzodiazepine, may help to control anxiety symptoms in separation anxiety disorder. Clonazepam (Klonopin) has been studied in open trials and may be useful in controlling symptoms of panic and other anxiety symptoms. Although SSRIs and CBT alone and in combination have demonstrated efficacy in the treatment of anxiety disorders in youth, approximately 20 to 35 percent of children and adolescents with anxiety disorders do not appear to benefit. Several novel agents have been suggested as potential treatments, some based on their effect on the N-methyl-daspartate (NMDA) system. For example, d-cycloserine (DCS), currently FDA approved in the treatment of pediatric tuberculosis, is a partial receptor agonist of the NMDA system and is hypothesized to augment the benefits of exposure treatment for phobias. Some

evidence suggests that DCS may increase the speed of exposure interventions; however, long-term gains have not been proven. Riluzole is an antiglutamatergic agent that decreases glutamatergic transmission by inhibiting glutamate release and inactivation of sodium channels in cortical neurons, and blocking γ-aminobutyric acid (GABA) reuptake. Due to its antiglutamatergic effects, Riluzole has been postulated to provide augmentation in the treatment of obsessive-compulsive disorder and generalized anxiety disorder. Another agent, memantine, an NMDA receptor antagonist, with FDA approval in the treatment of Alzheimer’s disease, has been hypothesized to decrease anxiety due to its influence on the glutamatergic system. Published case reports have provided mixed results. Although most childhood anxiety disorders wax and wane over time, school refusal associated with separation anxiety disorder can be viewed as a psychiatric emergency. A comprehensive treatment plan involves the child, the parents, and the child’s peers and school. Family interventions are critical in the management of separation anxiety disorder, especially in children who refuse to attend school, so that firm encouragement of school attendance is maintained while appropriate support is also provided. When a return to a full school day is overwhelming, a program should be arranged so the child can progressively increase the time spent at school. Graded contact with an object of anxiety is a form of behavior modification that can be applied to any type of separation anxiety. Some severe cases of school refusal require hospitalization. Cognitivebehavioral modalities include exposure to feared separations and cognitive strategies, such as coping self-statements aimed at increasing a sense of autonomy and mastery. In summary, evidence-based treatments for anxiety disorders have focused SSRIs and CBT. SSRIs have been shown to be both safe and efficacious in the treatment of childhood anxiety disorders; however, in severe disorders, the evidence suggests that optimal treatment is to provide both CBT and SSRI antidepressant agents simultaneously. REFERENCES Bittner A, Egger HL, Erkanli A. What do childhood anxiety disorders predict? J Child Psychol Psychiatry. 2007;48:1174– 1183. Comer JS, Puliafico AC, Ascenbrand SG, McKnight K, Robin JA, Goldfine ME, Albano AM. A pilot feasibility evaluation of the CALM Program for anxiety disorders in early childhood. J Anxiety Disord.

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