# ANXIETY AND STRESS DISORDERS: COURSE OVER THE LIFETIME

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This chapter traces the course and trajectory of anxiety disorders across the life span. The chapter discusses these disorders in three age groups: (a) childhood, (b) young adulthood to middle age, and (c) older adulthood.

### ANXIETY AND STRESS DISORDERS IN CHILDHOOD

## Temperamental and Environmental Precursors

There are a number of factors that relate to the development of anxiety in general. Although this remains a controversial area, current evidence suggests that anxiety does not appear to be specifically heritable; what clusters in families is a more general predisposition to mood or anxiety disorders. Evidence of this comes from twin studies (1) as well as from studies of the incidence of disorders in the families of anxious patients (2). Specific phobia, however, may be an exception to this general heritability; family members with specific phobias tend to be associated with increased risk only for specific phobias (3).

Any biological predisposition is likely moderated by environmental factors. For example, Beidel and Turner (2) found that parental psychopathology was a risk factor for the development of disorder only among the lower socioeconomic status (STS) portion of their sample. It has been suggested that environmental factors play a significant role in the manifestation of specific psychopathology (1). Anxiety in particular is believed to be related to a combination of negative affect, a sense of lack of control over situations or environments, and attentional self-focus. Early experiences of being unable to influence or control situations, therefore, may lead to the development of anxiety (4).

Specific patterns within the family may lead to increased

risk of development of childhood anxiety. Expressed emotion (EE), which is an interactional style composed of emotional overinvolvement and high levels of criticism, has been associated with an increased likelihood of childhood anxiety disorders (5) and with long-term functioning in those with anxiety disorders (6). Parents may also influence a child's anxiety by providing positive (e.g., the child gets attention) or negative (e.g., the child is allowed to avoid anxiety-provoking situations) reinforcement for expressions of anxiety, by providing inadequate affection and by excessive control/overprotection (4).

Can it be said that some people are born anxious? The answer is a qualified yes. The last decade or so of research by Jerome Kagan and colleagues has led to the identification of a temperament, "behavioral inhibition" (BI), that appears to be related to the subsequent onset of anxiety disorders. BI involves reacting to unfamiliar or novel situations with behavioral restraint and physiologic arousal (5). When confronted with an unfamiliar person or object, a BI child will withdraw, cling, be reluctant to interact, show emotional distress, and stop other activities. BI has also been associated with physiologic differences, such as high and stable heart rate, increased salivary cortisol and urinary catecholamines, pupillary dilation, and laryngeal muscle tension (7). These findings have led to the hypothesis that BI is related to a low threshold for arousal in the amygdala and hypothalamus (8). This characteristic, which appears to be present in 10% to 15% of children, has been identified in children as young as 14 months, has been shown to persist throughout childhood (9), and is more commonly found in offspring of anxious parents (8). The inhibited temperament has been associated with risk of developing an anxiety disorder, most commonly social phobia (10).

Some have suggested that childhood anxiety and depression are so closely related that they are best considered as part of the same construct, often referred to as internalizing disorder. This lack of differentiation appears to be characteristic of younger children, with increased specificity developing over time (11,12). At least by middle childhood, there is support for the set of anxiety-related diagnoses in the

Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV). Spence (12) conducted a confirmatory factor analysis with data from children of 8 to 12 years. The best model included six correlated factors—panic-agoraphobia, social phobia, separation anxiety, obsessive-compulsive problems, generalized anxiety, and fear of physical injury (including dogs, dentists, heights, doctors)—and a single higher-order factor reflecting overall anxiety.

There is a clear need for further research in childhood anxiety. Estimates of prevalence and recovery vary widely because of a lack of standardization of criteria, assessment instruments, and methodology (e.g., clinician rating vs. selfreport, child vs. parent or teacher report). A few general conclusions can be drawn about childhood internalizing disorders. Internalizing symptoms appear to remain fairly stable over time (13,14). Among boys, internalizing symptoms are not only predictive of later internalizing symptoms but also of subsequent externalizing problems (15). Although there may be high rates of recovery associated with a particular anxiety disorder, children who recover are at increased risk of developing other psychiatric diagnoses, most commonly other anxiety disorders or depressive disorders (16). Similarly, the presence of an anxiety or depressive disorder [overanxious disorder (OAD)/generalized anxiety disorder (GAD), panic, major depression] in adolescence is nonspecifically predictive of anxious or depressive disorders in adulthood (17).

The remainder of this section discusses disorder-specific information, including clinical manifestations, prevalence, and course.

#### **Generalized Anxiety Disorder (GAD)**

GAD is characterized by excessive anxiety or worry, which is difficult to control and is accompanied by symptoms of tension and physiologic arousal (18). The GAD diagnosis is currently used in place of overanxious disorder (OAD), which was eliminated with the publication of the DSM-IV. Children and adolescents with GAD most frequently worry about future events, personal safety, and social evaluation, and often present with multiple somatic complaints, such as headaches and stomachaches (19).

There is little information about the prevalence of GAD in children and adolescents because the diagnosis of OAD was used previously. Prevalence estimates of OAD tended to be quite variable, 2% to 19% (19), and often very high, partially because functional impairment was not necessary for the diagnosis (20). Recent estimates of the prevalence of GAD are in the range of 2.1% to 10.8% (21). It appears to be more prevalent in older children and in girls (19). Onset typically falls between 10.8 and 13.4 years of age (4).

Information about course is not yet available for the GAD diagnosis, but some extrapolation from OAD is possible. Cohen et al. (22) looked at three different statistical measures of persistence. They found that OAD was very

stable in a subset of children and younger adolescents (ages 11 to 16), but that there was a substantial amount of new onset among older adolescents (ages 17 to 19). Their conclusion was that the disorder may be trait-like for those who exhibit symptoms early and that the development of the disorder in others may be triggered in adolescence. Cantwell and Baker (23) also found considerable stability; 25% of children who had been diagnosed with OAD approximately 4 years earlier had recovered (although the group size, eight, limits the usefulness of this estimate). In contrast, Last et al. (16) reported that 80% of their OAD sample had recovered 3 to 4 years later; however, 25% had developed another anxiety disorder and 25% had developed a depressive disorder.

GAD/OAD is a frequently co-occurring disorder. Of those with a primary diagnosis of OAD, there is often an additional diagnosis of separation anxiety disorder (37% to 44%), social phobia (4% to 57%), simple phobia (9% to 43%) or a depressive disorder (1% to 69%) (24). There are a number of potential reasons for the high rates of comorbidity, including true covariation of distinct disorders, the presence of a single underlying construct, overlap of diagnostic categories, and measurement error (12,25).

#### **Obsessive-Compulsive Disorder (OCD)**

OCD is recognizable by the presence of obsessions and compulsions, which are distressing or cause marked interference in one's life (18). Among young children, the disorder often presents with excessive and rigid ritualized behavior. For children in general, compulsions alone are more common than obsessions alone (26). The most common compulsions include washing/cleaning, repeating/redoing, and checking, and the most common obsessions include germs/contaminants and fear of harm to the self or to another (26). OCD symptoms change over time in 90% of children (4).

OCD is relatively uncommon, with estimated prevalences of approximately 0.3% for children and 0.35% to 1.9% for adolescents (27,28). Mean age of onset is approximately 10 years. Information about the course of OCD is variable and may be best described as chronic but fluctuating (4). Leonard et al. (6) followed children and adolescents who had been part of National Institute of Mental Health (NIMH) treatment studies. During the 2- to 7-year followup period, the patients on average received two different modalities of treatment (medication, behavioral therapy, other individual therapy, and family therapy), with 96% having had additional psychopharmacologic treatment and 46% some form of behavioral therapy. In spite of ongoing treatment, at follow-up 43% met the criteria for OCD, 18% had subclinical OCD, and 28% had OC features. Of the 11% who were symptom-free, only three (of 54) patients had no symptoms and were not on current medications. However, treatment was associated with decreased functional impairment. Last et al. (16), on the other hand, found

a 75% recovery rate in their sample. Other estimates of continued OCD at follow-up (1.5 to 7 years) range from 31% to 68% (16).

Comorbidity is a frequent problem with OCD. The most common co-occurring conditions include other anxiety disorders (38%), tic disorders (24% to 30%), mood disorders (26% to 29%), and specific developmental disabilities (24%) (26). Leonard et al. (6) found that both a lifetime history of tic disorder and current affective disorder at baseline were associated with poorer outcome.

# Panic Disorder (with and without Agoraphobia) (PD)

PD involves recurrent and unexpected panic attacks, which cause significant distress for the affected individual. This frequently leads to avoidance of various situations for fear of developing symptoms and being unable to escape (18). Young children tend to articulate their panic-related fears in a different way than do adolescents or adults by virtue of their developmental level; they are more likely to express concerns about sudden somatic symptoms and less likely to describe fears of dying, losing control, or going crazy (4).

PD is uncommonly reported in children, to the point that there has been some debate as to whether it exists before puberty. Evidence of the existence of PD in children comes from both retrospective reports of adults with PD and from case reports (29). There is no epidemiologic study to date, and it is likely that many cases go undetected because of the predominance of somatic symptoms in presentation. Prevalence of PD in adolescents is low, 0.7% girls and 0.4% boys (0.6 overall) according to one large high school sample (28). The rate of panic attacks is expectedly higher, 11.6% for at least one full attack and an additional 3.2% for at least one limited symptom attack (30). PD appears to be two to three times more common in females (29). Hayward et al. (31) examined the relationship between the occurrence of panic attacks and sexual development in girls and found a positive relationship. There were no reported panic attacks among the least sexually mature girls, and a rate of 8% among those who were most developed. The authors proposed a number of theories for this association, including hormonal changes, psychosocial factors, and emergence of the ability to think abstractly, but further work is necessary to draw any definitive conclusions.

In the one study of the course of early PD, 30% continued to have PD and 30% had another psychiatric disorder 3 to 4 years later, but the generalizability of this result is questionable because of the small size of the study population (ten) (16). Retrospective reports suggest that earlier onset is associated with poorer outcomes, including greater functional impairment and increased incidence of alcohol abuse and suicidality (32). Available information suggests that there is a high rate of comorbidity in adolescents with PD, particularly with affective disorders; again, this should

be interpreted with caution because it is based on a single, small (N = 28) study of adolescents (33).

#### **Posttraumatic Stress Disorder (PTSD)**

To meet the criteria for a diagnosis of PTSD, a person must have been exposed to a traumatic event and as a result is exhibiting symptoms of reexperiencing, numbing/avoidance, and arousal (18). A recent confirmatory factor analytic study supported the presence of these three basic clusters of symptoms in children and adolescents, although it found that arousal is often manifested as general somatic complaints (34). PTSD presentations that are specific to children include reenactment of the trauma in play, physical attempts (e.g., covering eyes or ears) to avoid memories of the trauma, reduced interest in activities, behavioral regression (e.g., thumb-sucking, enuresis), and sleep disturbance (35).

Diagnosis of PTSD depends on exposure to a traumatic stressor. Each year, 6% to 7% of Americans are exposed to traumatic events (36), but the incidence is much greater in certain subpopulations. For example, studies of urban youth report exposure rates of up to 75% (37). Not everyone who is exposed to trauma goes on to develop PTSD. Estimates vary tremendously depending on the type of trauma and the elapsed time between the event and assessment. In Saigh et al.'s (37) review of the literature, they found PTSD prevalence among exposed youth to be 0% to 70.8% for crimerelated events, 8.3% to 75% for war, and 0% to 95% for disasters. Overall, it appears that exposed children may be somewhat more likely to develop PTSD than are exposed adults (36). PTSD is more common in those who have been exposed to more severe trauma (34).

The course of PTSD in children over the short- or longterm has not been well studied, but it appears that prognostically important factors are whether the trauma involves a single occurrence or is repeated, and whether it involves abuse. Although the evidence is not entirely consistent, it appears that a single exposure is less likely to lead to longterm symptomatology (36).

Comorbidity is generally high, particularly with other anxiety disorders (7.7% to 41.6%) and affective disorders (16.7% to 85%), but there is also substantial co-occurrence of attention-deficit/hyperactivity disorder (5.8% to 34.6%), conduct disorder (0% to 26.9%), and oppositional defiant disorder (25%) (37). Additional disorders may be integrally related to the trauma, such as fears about safety of the self or loved ones or grief about loss (35). Other psychopathology may also be a function of other factors, such as a disrupted or disorganized childhood or engagement in risky behaviors, which increase the risk for both psychopathology and traumatic exposure (38).

#### **Separation Anxiety Disorder (SAD)**

SAD is the only current anxiety disorder that is uniquely diagnosed in children and adolescents. The hallmark feature

of this disorder is excessive concern about separation from attachment figures. This is frequently manifested as distress at separation and excessive worry that harm will befall the attachment figure or that some negative event will lead to separation (18). These children frequently avoid going to school, fear being left alone or sleeping alone, and exhibit a panic-like physiologic response to separation (32).

Prevalence estimates for SAD are 2.0% to 5.4% for children and 1.3% to 4.6% for adolescents, with some evidence of higher rates in girls, those of lower SES, and those with less educated parents (21,32). The onset of SAD is usually early and associated with a major stressor (4). Of nine children with SAD followed by Cantwell and Baker (23), only one was still diagnosable 4 to 5 years later; this was the highest rate of recovery of any of the disorders that they followed. Similarly, Last et al. (16) found an approximately 96% recovery rate among their 24 children and adolescents with SAD, although 25% had developed another disorder, most commonly depressive, 3 to 4 years later. SAD frequently co-occurs with other disorders, most often other anxiety disorders (OAD, 23% to 33%; specific phobias, 12.5% to 27%; social phobia, 8%) (24) or a depressive disorder (approximately one-third) (32).

SAD has been suggested to be a childhood manifestation of PD. Evidence that has been cited in support of this idea includes the symptomatic similarity between a panic attack and the response to separation in a child with SAD; the frequency of a history of SAD in panic patients; the clustering of SAD, PD, and depressive disorders in families; and the similarities in effective pharmacologic treatments for the two conditions (39–41). Documented cases of panic episodes unrelated to separation, however, argue against this hypothesis (29). Nonetheless, SAD appears to be a risk factor for the later development of PD, at least among females (4).

#### **Specific Phobia**

A specific phobia is diagnosed if a child consistently displays significant and excessive fear in response to a specific object or situation (18). The most common fears among children are heights, small animals, doctors/dentists, dark, loud noises, and thunder/lightening (19). The prevalence of this disorder is in the range of 0.3% to 9.1%, with somewhat higher rates in girls and younger children (19,21,42).

Unlike the other anxiety disorders reviewed here, children with specific phobias remain a fairly distinct group. Last et al. (16) found that those with specific phobias were least likely to recover within 3 to 4 years (69.2%) but also were least likely to show onset of a different disorder within the follow-up period. Similarly, Pine et al. (17) found that simple phobias in adolescence were related only to adult simple phobias.

#### **Social Phobia**

Social phobia involves "marked and persistent fear of one or more performance or social situations in which the person is exposed to unfamiliar people or to possible scrutiny by others" (18). The anxious response in such situations is associated with cognitions involving concerns about being humiliated or embarrassed. Childhood social phobia is associated with significant impairment and distress, and frequently leads to extensive phobic avoidance and deficient social skill development (43).

Although there are few good epidemiologic studies of social phobia in childhood, data from community studies in adolescents suggest that it is quite common (1% to 2%), with a noticeable jump in prevalence rates sometime between ages 12 to 13 and ages 14 to 17 (44). One longitudinal study suggested that many cases of social phobia in childhood remit within 3 to 4 years (86.4%) (16). However, when social phobia is present in adolescence, it is a strong predictor of social phobia in adulthood (17). These data, taken together, suggest that social phobia in childhood may be a more transitory phenomenon than social phobia in adolescence. If these findings are confirmed in future studies, they may suggest critical developmental time frames during which preventative efforts may be applied.

## ANXIETY AND STRESS DISORDERS IN YOUNG TO MIDDLE-AGE ADULTS

#### **Epidemiology**

Several epidemiologic studies have documented the high rate of anxiety disorders among adults in the general population. In reports from the Epidemiologic Catchment Area (ECA) Study, anxiety disorders were found to occur as a lifetime diagnosis in 14.6% of the adult U.S. population aged 18 years or older (45). More recently, the National Comorbidity Survey (NCS) found that 24.9% of adults in the age group 15 to 54 years had a lifetime anxiety disorder diagnosis (46). The two studies used somewhat different sampling methods, and different diagnostic interviews, probably therein explaining at least some of the variance in rates between studies (47).

#### Comorbidity

Comorbidity among the anxiety, mood, and substance use disorders is extensive (47). For example, two-thirds of persons in the community with generalized anxiety disorder in a 12-month period also had major depressive disorder during that time frame (48). In a clinical sample of 85 patients with major depression, 29% met criteria for a current anxiety disorder and 34% had at least one anxiety disorder during their lives (49).

What is particularly noteworthy about this relationship

is the temporal sequencing of disorders. Certain anxiety disorders, social phobia in particular (which has a median onset of between 13 and 15 years of age), almost inevitably begin prior to the onset of the mood or substance use disorder (50,51). In one study of depressed patients, social phobia was the most common lifetime anxiety disorder (occurring in 15% of cases) followed closely by panic disorder with agoraphobia (in 12%) (49). Social phobia occurred on average 2 years prior to the onset of major depressive disorder in these patients. Similar findings have emerged from community studies (52), suggesting that particular anxiety disorders such as social phobia may be considered risk factors for the subsequent development of major depression. It remains to be established what the mechanisms might be for this observed relationship. Does being socially anxious lead to increased isolation or decreased self-worth, thereby leading to an increase in subsequent major depression? Is social phobia merely the earliest manifestation of an anxiety-mood disorder diathesis? These questions will only be answered with future research that focuses broadly on psychosocial and biological vulnerabilities for anxiety and mood disorders.

Another interesting aspect of the anxiety-depression link lies in the relationship between major depressive disorder (MDD) and PTSD. Extensive comorbidity between PTSD and MDD is the norm in studies of various traumatized groups, including persons exposed to combat (53,54), disasters (55), and intimate partner violence (56). Community studies also demonstrate strong ties between these two disorders, with approximately 35% to 50% of cases of PTSD in the general population being comorbid with MDD (57).

Studies that have examined the temporal association between major depression and PTSD have posited several causal pathways. It has been observed that preexisting major depressive disorder increases an individual's risk for PTSD following exposure to traumatic events (58,59). The converse has also been observed, namely that preexisting PTSD is a risk factor for the later development of MDD (58,60). The mechanisms for this apparent reciprocal risk have yet to be explained, but might involve a general vulnerability to stress that can result in major depression (61) or PTSD in susceptible individuals.

# Functioning, Quality of Life, and Cost to Society

Data have been collected in the past several years that highlight the disability and reduced quality of life associated with anxiety disorders in young and middle-aged adults. Studies in clinical samples of patients with PD, PTSD, OCD, and social phobia all depict these as serious conditions that rob individuals of enjoyment and pleasure and impair functioning in multiple domains (62). Epidemiologic studies, where the range of severity is expected to be wider and where many milder cases are expected to be seen,

also provide persuasive evidence of the seriousness of anxiety disorders (52,63,64). The annual cost of anxiety disorders in the United States was estimated at \$42.3 billion in 1990, or \$1,542 per sufferer (65). Other than simple phobia, all anxiety disorders analyzed were associated with impairment in workplace performance. These observations, gleaned from a variety of clinical and nonclinical perspectives, portray anxiety disorders in adults as serious mental disorders worthy (and in need) of greater societal willingness to develop and apply better interventions to prevent or mitigate their impact on the lives of individuals.

### ANXIETY AND STRESS DISORDERS IN OLDER ADULTS

Although anxiety is among the most prevalent of psychiatric disorders in the elderly, research in this area has lagged far behind that of depression and dementia (66). But in the past few years, several important studies have been conducted that provide novel information about the prevalence, features, and course of anxiety disorders in older adults.

#### **Epidemiology**

Whereas it had previously been believed that anxiety disorders decline in prevalence with age, several possible explanations for this finding have been put forward. It has been suggested that this might be an artifact of measurement error, owing to differences in the way older individuals report anxiety (67). Previous epidemiologic studies may also have underestimated the prevalence of anxiety disorders in the elderly by limiting participation to community-dwelling older adults, who may have lower rates of anxiety disorder than those living in institutions (68).

Fortunately, data have recently become available from a new community survey that provides a more accurate and detailed perspective on anxiety disorders in older adults (69). The Longitudinal Aging Study Amsterdam (LASA) is based on a random sample of 3,107 older adults (ages 55 to 85), stratified for age and sex. The overall prevalence of anxiety disorders in the community was estimated at 10.2%. GAD was most common in a 6-month time period (7.3%), followed by social phobia (3.1%), PD (1.0%), and OCD (0.6%). For comparison purposes, it is noteworthy that the 6-month prevalence of major depression in the same study was 2.0%. Thus, anxiety disorders were far more common than depressive disorders in the elderly, underscoring the point made earlier that it is surprising that the elderly have received so little attention in the clinical and research literature to date.

This study also examined vulnerability factors for anxiety disorders in older adults (69). Many of the vulnerability factors for anxiety disorders in younger adults are common to older adults (e.g., female sex, lower levels of education),

but several unique risk factors were also encountered (e.g., having suffered extreme experiences during World War II). These investigators were also able to show that current stresses commonly experienced by older people (e.g., recent losses in the family and chronic physical illness) also played a part in the onset or exacerbation of anxiety disorders. Current life stresses, then, should be evaluated as possible contributors not only to depression, but also to anxiety in the elderly.

#### Comorbidity

Comorbidity patterns of older adults with anxiety disorders are remarkably similar to those of younger adults. In the LASA, 48% of those with MDD also met criteria for anxiety disorders, whereas 26% of those with anxiety disorders also met criteria for MDD (70).

The entity known as "anxious depression" warrants special mention in this context. Although definitions vary, anxious depression usually refers to MDD with accompanying anxiety. Anxious depression is a particularly common presentation in the elderly (66). Although anxious depression is frequently severe and impairing, its outcome is no worse than nonanxious depression when treated appropriately (71).

# Special Features of Anxiety Disorders in the Elderly

The fact that medical illness becomes more common with increasing age can put a special twist on the presentation and origins of certain anxiety disorders in the elderly. First and foremost, it must be recognized that many medical illnesses (e.g., thyroid disease, chronic obstructive pulmonary disease, and stroke, to name just a few) may be associated with *de novo* anxiety symptoms or with the exacerbation of a preexisting anxiety disorder (66). Most "new" anxiety disorders in older life are either GAD or agoraphobia, whereas most other anxiety syndromes seen in the elderly (e.g., PD and OCD) reflect recurrence or worsening of an anxiety disorder that had its onset earlier in life (72).

Agoraphobia in older adults is usually a different phenomenon, with different etiology, from agoraphobia in younger adults. In younger adults, agoraphobia is almost always a complication of PD (73)—the individual comes to avoid situations that are associated with the possible occurrence of panic or difficulty escaping should a panic attack occur. In the elderly, the new onset of agoraphobia is rarely associated with spontaneous panic attacks, but instead is a maladaptive reaction to some form of medical illness experience that renders the individual fearful of being unable to function safely away from home (66). An example is an elderly woman who breaks her hip, and even after it has satisfactorily healed, is afraid to maneuver without help and therefore avoids leaving the house alone.

#### **SUMMARY**

Anxiety disorders span the full range of human existence from childhood to old age, though symptoms may vary considerably owing to developmental differences and related factors. Anxiety disorders in children are often transitory phenomena, with the majority showing remission by adolescence or early adulthood. Yet, in a minority, extremely shy and fearful temperament in childhood can merge almost imperceptibly into social phobic and panic disorders in adolescence. Anxiety disorders in youth appear to be a risk factor for the subsequent development of major depression (and, although less certain, possibly also substance use disorders) in late adolescence and young adulthood. By adulthood, comorbidity is the rule, with most individuals experiencing multiple anxiety disorders, or concurrent mood and anxiety disorders. For the most part, anxiety disorders are chronic, and these persist from young adulthood into old age. But even in later life, new onset of anxiety disorders can occur, often in the context of medical illness or other sources of life stress.

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