Comorbidity

Social anxiety disorder is often comorbid with other anxiety disorders, major depressive disorder, and substance use disorders, and the onset of social anxiety disorder generally precedes that of the other disorders, except for specific phobia and separation anxiety disorder. Chronic social isolation in the course of a social anxiety disorder may result in major depressive disorder. Comorbidity with depression is high also in older adults. Substances may be used as self-medication for social fears, but the symptoms of substance intoxication or withdrawal, such as trembling, may also be a source of (further) social fear. Social anxiety disorder is frequently comorbid with bipolar disorder or body dysmorphic disorder; for example, an individual has body dysmorphic disorder concerning a preoccupation with a slight irregularity of her nose, as well as social anxiety disorder because of a severe fear of sounding unintelligent. The more generalized form of social anxiety disorder, but not social anxiety disorder, performance only, is often comorbid with avoidant personality disorder. In children, comorbidities with high-functioning autism and selective mutism are common.

Panic Disorder

Diagnostic Criteria **300.01 (F41.0)**

A. Recurrent unexpected panic attacks. A panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur:

   Note: The abrupt surge can occur from a calm state or an anxious state.

   1. Palpitations, pounding heart, or accelerated heart rate.
   2. Sweating.
   3. Trembling or shaking.
   4. Sensations of shortness of breath or smothering.
   5. Feelings of choking.
   6. Chest pain or discomfort.
   7. Nausea or abdominal distress.
   8. Feeling dizzy, unsteady, light-headed, or faint.
   9. Chills or heat sensations.
   10. Paresthesias (numbness or tingling sensations).
   11. Derealization (feelings of unreality) or depersonalization (being detached from oneself).
   12. Fear of losing control or "going crazy."
   13. Fear of dying.

   Note: Culture-specific symptoms (e.g., tinnitus, neck soreness, headache, uncontrollable screaming or crying) may be seen. Such symptoms should not count as one of the four required symptoms.

B. At least one of the attacks has been followed by 1 month (or more) of one or both of the following:

   1. Persistent concern or worry about additional panic attacks or their consequences (e.g., losing control, having a heart attack, "going crazy").
   2. A significant maladaptive change in behavior related to the attacks (e.g., behaviors designed to avoid having panic attacks, such as avoidance of exercise or unfamiliar situations).

C. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism, cardiopulmonary disorders).
D. The disturbance is not better explained by another mental disorder (e.g., the panic attacks do not occur only in response to feared social situations, as in social anxiety disorder; in response to circumscribed phobic objects or situations, as in specific phobia; in response to obsessions, as in obsessive-compulsive disorder; in response to reminders of traumatic events, as in posttraumatic stress disorder; or in response to separation from attachment figures, as in separation anxiety disorder).

Diagnostic Features

Panic disorder refers to recurrent unexpected panic attacks (Criterion A). A panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four or more of a list of 13 physical and cognitive symptoms occur. The term *recurrent* literally means more than one unexpected panic attack. The term *unexpected* refers to a panic attack for which there is no obvious cue or trigger at the time of occurrence—that is, the attack appears to occur from out of the blue, such as when the individual is relaxing or emerging from sleep (nocturnal panic attack). In contrast, *expected* panic attacks are attacks for which there is an obvious cue or trigger, such as a situation in which panic attacks typically occur. The determination of whether panic attacks are expected or unexpected is made by the clinician, who makes this judgment based on a combination of careful questioning as to the sequence of events preceding or leading up to the attack and the individual's own judgment of whether or not the attack seemed to occur for no apparent reason. Cultural interpretations may influence the assignment of panic attacks as expected or unexpected (see section "Culture-Related Diagnostic Issues" for this disorder). In the United States and Europe, approximately one-half of individuals with panic disorder have expected panic attacks as well as unexpected panic attacks. Thus, the presence of expected panic attacks does not rule out the diagnosis of panic disorder. For more details regarding expected versus unexpected panic attacks, see the text accompanying panic attacks (pp. 214–217).

The frequency and severity of panic attacks vary widely. In terms of frequency, there may be moderately frequent attacks (e.g., one per week) for months at a time, or short bursts of more frequent attacks (e.g., daily) separated by weeks or months without any attacks or with less frequent attacks (e.g., two per month) over many years. Persons who have infrequent panic attacks resemble persons with more frequent panic attacks in terms of panic attack symptoms, demographic characteristics, comorbidity with other disorders, family history, and biological data. In terms of severity, individuals with panic disorder may have both full-symptom (four or more symptoms) and limited-symptom (fewer than four symptoms) attacks, and the number and type of panic attack symptoms frequently differ from one panic attack to the next. However, more than one unexpected full-symptom panic attack is required for the diagnosis of panic disorder.

The worries about panic attacks or their consequences usually pertain to physical concerns, such as worry that panic attacks reflect the presence of life-threatening illnesses (e.g., cardiac disease, seizure disorder); social concerns, such as embarrassment or fear of being judged negatively by others because of visible panic symptoms; and concerns about mental functioning, such as "going crazy" or losing control (Criterion B). The maladaptive changes in behavior represent attempts to minimize or avoid panic attacks or their consequences. Examples include avoiding physical exertion, reorganizing daily life to ensure that help is available in the event of a panic attack, restricting usual daily activities, and avoiding agoraphobia-type situations, such as leaving home, using public transportation, or shopping. If agoraphobia is present, a separate diagnosis of agoraphobia is given.

Associated Features Supporting Diagnosis

One type of unexpected panic attack is a *nocturnal* panic attack (i.e., waking from sleep in a state of panic, which differs from panicking after fully waking from sleep). In the United States, this type of panic attack has been estimated to occur at least one time in roughly one-quarter to one-third of individuals with panic disorder, of whom the majority also have daytime panic attacks. In addition to worry about panic attacks and their consequences, many individuals with panic disorder report constant or intermittent feelings of anxiety that are more broadly related to health and mental health concerns. For example, individuals with panic disorder often anticipate a catastrophic outcome from a mild physical symptom or medication side effect (e.g., thinking that they may have heart disease or that a headache means presence of a brain tumor). Such individuals often are relatively intolerant of medication side effects. In addition, there may be pervasive concerns about abilities to complete daily tasks or withstand daily stressors, excessive use of drugs (e.g., alcohol, prescribed medications or illicit drugs) to control panic attacks, or extreme behaviors aimed at controlling panic attacks (e.g., severe restrictions on food intake or avoidance of specific foods or medications because of concerns about physical symptoms that provoke panic attacks).

Prevalence

In the general population, the 12-month prevalence estimate for panic disorder across the United States and several European countries is about 2%–3% in adults and adolescents. In the United States, significantly lower rates of panic disorder are reported among Latinos, African Americans, Caribbean blacks, and Asian Americans, compared with non-Latino whites; American Indians, by contrast, have significantly higher rates. Lower estimates have been reported for Asian, African, and Latin American countries, ranging from 0.1% to 0.8%. Females are more frequently affected than males, at a rate of approximately 2:1. The gender differentiation occurs in adolescence and is already observable before age 14 years. Although panic attacks occur in children, the overall prevalence of panic disorder is low before age 14 years (<0.4%). The rates of panic disorder show a gradual increase during adolescence, particularly in females, and possibly following the onset of puberty, and peak during adulthood. The prevalence rates decline in older individuals (i.e., 0.7% in adults over the age of 64), possibly reflecting diminishing severity to subclinical levels.

Development and Course

The median age at onset for panic disorder in the United States is 20–24 years. A small number of cases begin in childhood, and onset after age 45 years is unusual but can occur. The usual course, if the disorder is untreated, is chronic but waxing and waning. Some individuals may have episodic outbreaks with years of remission in between, and others may have continuous severe symptomatology. Only a minority of individuals have full remission without subsequent relapse within a few years. The course of panic disorder typically is complicated by a range of other disorders, in particular other anxiety disorders, depressive disorders, and substance use disorders (see section "Comorbidity" for this disorder).

Although panic disorder is very rare in childhood, first occurrence of "fearful spells" is often dated retrospectively back to childhood. As in adults, panic disorder in adolescents tends to have a chronic course and is frequently comorbid with other anxiety, depressive, and bipolar disorders. To date, no differences in the clinical presentation between adolescents and adults have been found. However, adolescents may be less worried about additional panic attacks than are young adults. Lower prevalence of panic disorder in older adults appears to be attributable to age-related "dampening" of the autonomic nervous system response. Many older individuals with "panicky feelings" are observed to have a "hybrid" of limited-symptom panic attacks and generalized anxiety. Also, older adults

tend to attribute their panic attacks to certain stressful situations, such as a medical procedure or social setting. Older individuals may retrospectively endorse explanations for the panic attack (which would preclude the diagnosis of panic disorder), even if an attack might actually have been unexpected in the moment (and thus qualify as the basis for a panic disorder diagnosis). This may result in under-endorsement of unexpected panic attacks in older individuals. Thus, careful questioning of older adults is required to assess whether panic attacks were expected before entering the situation, so that unexpected panic attacks and the diagnosis of panic disorder are not overlooked.

While the low rate of panic disorder in children could relate to difficulties in symptom reporting, this seems unlikely given that children are capable of reporting intense fear or panic in relation to separation and to phobic objects or phobic situations. Adolescents might be less willing than adults to openly discuss panic attacks. Therefore, clinicians should be aware that unexpected panic attacks do occur in adolescents, much as they do in adults, and be attuned to this possibility when encountering adolescents presenting with episodes of intense fear or distress.

Risk and Prognostic Factors

Temperamental. Negative affectivity (neuroticism) (i.e., proneness to experiencing negative emotions) and anxiety sensitivity (i.e., the disposition to believe that symptoms of anxiety are harmful) are risk factors for the onset of panic attacks and, separately, for worry about panic, although their risk status for the diagnosis of panic disorder is unknown. History of "fearful spells" (i.e., limited-symptom attacks that do not meet full criteria for a panic attack) may be a risk factor for later panic attacks and panic disorder. Although separation anxiety in childhood, especially when severe, may precede the later development of panic disorder, it is not a consistent risk factor.

Environmental. Reports of childhood experiences of sexual and physical abuse are more common in panic disorder than in certain other anxiety disorders. Smoking is a risk factor for panic attacks and panic disorder. Most individuals report identifiable stressors in the months before their first panic attack (e.g., interpersonal stressors and stressors related to physical well-being, such as negative experiences with illicit or prescription drugs, disease, or death in the family).

Genetic and physiological. It is believed that multiple genes confer vulnerability to panic disorder. However, the exact genes, gene products, or functions related to the genetic regions implicated remain unknown. Current neural systems models for panic disorder emphasize the amygdala and related structures, much as in other anxiety disorders. There is an increased risk for panic disorder among offspring of parents with anxiety, depressive, and bipolar disorders. Respiratory disturbance, such as asthma, is associated with panic disorder, in terms of past history, comorbidity, and family history.

Culture-Related Diagnostic Issues

The rate of fears about mental and somatic symptoms of anxiety appears to vary across cultures and may influence the rate of panic attacks and panic disorder. Also, cultural expectations may influence the classification of panic attacks as expected or unexpected. For example, a Vietnamese individual who has a panic attack after walking out into a windy environment (*trúng gió;* "hit by the wind") may attribute the panic attack to exposure to wind as a result of the cultural syndrome that links these two experiences, resulting in classification of the panic attack as expected. Various other cultural syndromes are associated with panic disorder, including *ataque de nervios* ("attack of nerves") among Latin Americans and *khyâl* attacks and "soul loss" among Cambodians. *Ataque de nervios* may involve trembling, uncontrollable screaming or crying, aggressive or suicidal behavior, and depersonalization or derealization, which may be experienced longer than the few minutes typical

of panic attacks. Some clinical presentations of *ataque de nervios* fulfill criteria for conditions other than panic attack (e.g., other specified dissociative disorder). These syndromes impact the symptoms and frequency of panic disorder, including the individual's attribution of unexpectedness, as cultural syndromes may create fear of certain situations, ranging from interpersonal arguments (associated with *ataque de nervios*), to types of exertion (associated with *khyâl* attacks), to atmospheric wind (associated with *trúng gió* attacks). Clarification of the details of cultural attributions may aid in distinguishing expected and unexpected panic attacks. For more information regarding cultural syndromes, refer to the "Glossary of Cultural Concepts of Distress" in the Appendix.

The specific worries about panic attacks or their consequences are likely to vary from one culture to another (and across different age groups and gender). For panic disorder, U.S. community samples of non-Latino whites have significantly less functional impairment than African Americans. There are also higher rates of objectively defined severity in non-Latino Caribbean blacks with panic disorder, and lower rates of panic disorder overall in both African American and Afro-Caribbean groups, suggesting that among individuals of African descent, the criteria for panic disorder may be met only when there is substantial severity and impairment.

Gender-Related Diagnostic Issues

The clinical features of panic disorder do not appear to differ between males and females. There is some evidence for sexual dimorphism, with an association between panic disorder and the catechol-O-methyltransferase (COMT) gene in females only.

Diagnostic Markers

Agents with disparate mechanisms of action, such as sodium lactate, caffeine, isoproterenol, yohimbine, carbon dioxide, and cholecystokinin, provoke panic attacks in individuals with panic disorder to a much greater extent than in healthy control subjects (and in some cases, than in individuals with other anxiety, depressive, or bipolar disorders without panic attacks). Also, for a proportion of individuals with panic disorder, panic attacks are related to hypersensitive medullary carbon dioxide detectors, resulting in hypocapnia and other respiratory irregularities. However, none of these laboratory findings are considered diagnostic of panic disorder.

Suicide Risk

Panic attacks and a diagnosis of panic disorder in the past 12 months are related to a higher rate of suicide attempts and suicidal ideation in the past 12 months even when comorbidity and a history of childhood abuse and other suicide risk factors are taken into account.

Functional Consequences of Panic Disorder

Panic disorder is associated with high levels of social, occupational, and physical disability; considerable economic costs; and the highest number of medical visits among the anxiety disorders, although the effects are strongest with the presence of agoraphobia. Individuals with panic disorder may be frequently absent from work or school for doctor and emergency room visits, which can lead to unemployment or dropping out of school. In older adults, impairment may be seen in caregiving duties or volunteer activities. Full-symptom panic attacks typically are associated with greater morbidity (e.g., greater health care utilization, more disability, poorer quality of life) than limited-symptom attacks.

Differential Diagnosis

Other specified anxiety disorder or unspecified anxiety disorder. Panic disorder should not be diagnosed if full-symptom (unexpected) panic attacks have never been experienced. In

the case of only limited-symptom unexpected panic attacks, an other specified anxiety disorder or unspecified anxiety disorder diagnosis should be considered.

Anxiety disorder due to another medical condition. Panic disorder is not diagnosed if the panic attacks are judged to be a direct physiological consequence of another medical condition. Examples of medical conditions that can cause panic attacks include hyperthyroidism, hyperparathyroidism, pheochromocytoma, vestibular dysfunctions, seizure disorders, and cardiopulmonary conditions (e.g., arrhythmias, supraventricular tachycardia, asthma, chronic obstructive pulmonary disease [COPD]). Appropriate laboratory tests (e.g., serum calcium levels for hyperparathyroidism; Holter monitor for arrhythmias) or physical examinations (e.g., for cardiac conditions) may be helpful in determining the etiological role of another medical condition.

Substance/medication-induced anxiety disorder. Panic disorder is not diagnosed if the panic attacks are judged to be a direct physiological consequence of a substance. Intoxication with central nervous system stimulants (e.g., cocaine, amphetamines, caffeine) or cannabis and withdrawal from central nervous system depressants (e.g., alcohol, barbiturates) can precipitate a panic attack. However, if panic attacks continue to occur outside of the context of substance use (e.g., long after the effects of intoxication or withdrawal have ended), a diagnosis of panic disorder should be considered. In addition, because panic disorder may precede substance use in some individuals and may be associated with increased substance use, especially for purposes of self-medication, a detailed history should be taken to determine if the individual had panic attacks prior to excessive substance use. If this is the case, a diagnosis of panic disorder should be considered in addition to a diagnosis of substance use disorder. Features such as onset after age 45 years or the presence of atypical symptoms during a panic attack (e.g., vertigo, loss of consciousness, loss of bladder or bowel control, slurred speech, amnesia) suggest the possibility that another medical condition or a substance may be causing the panic attack symptoms.

Other mental disorders with panic attacks as an associated feature (e.g., other anxiety disorders and psychotic disorders). Panic attacks that occur as a symptom of other anxiety disorders are expected (e.g., triggered by social situations in social anxiety disorder, by phobic objects or situations in specific phobia or agoraphobia, by worry in generalized anxiety disorder, by separation from home or attachment figures in separation anxiety disorder) and thus would not meet criteria for panic disorder. (**Note:** Sometimes an unexpected panic attack is associated with the onset of another anxiety disorder, but then the attacks become expected, whereas panic disorder is characterized by recurrent unexpected panic attacks.) If the panic attacks occur only in response to specific triggers, then only the relevant anxiety disorder is assigned. However, if the individual experiences unexpected panic attacks as well and shows persistent concern and worry or behavioral change because of the attacks, then an additional diagnosis of panic disorder should be considered.

Comorbidity

Panic disorder infrequently occurs in clinical settings in the absence of other psychopathology. The prevalence of panic disorder is elevated in individuals with other disorders, particularly other anxiety disorders (and especially agoraphobia), major depression, bipolar disorder, and possibly mild alcohol use disorder. While panic disorder often has an earlier age at onset than the comorbid disorder(s), onset sometimes occurs after the comorbid disorder and may be seen as a severity marker of the comorbid illness.

Reported lifetime rates of comorbidity between major depressive disorder and panic disorder vary widely, ranging from 10% to 65% in individuals with panic disorder. In approximately one-third of individuals with both disorders, the depression precedes the onset of panic disorder. In the remaining two-thirds, depression occurs coincident with or following the onset of panic disorder. A subset of individuals with panic disorder develop a substance-related disorder, which for some represents an attempt to treat their anxiety

with alcohol or medications. Comorbidity with other anxiety disorders and illness anxiety disorder is also common.

Panic disorder is significantly comorbid with numerous general medical symptoms and conditions, including, but not limited to, dizziness, cardiac arrhythmias, hyperthyroidism, asthma, COPD, and irritable bowel syndrome. However, the nature of the association (e.g., cause and effect) between panic disorder and these conditions remains unclear. Although mitral valve prolapse and thyroid disease are more common among individuals with panic disorder than in the general population, the differences in prevalence are not consistent.

Panic Attack Specifier

Note: Symptoms are presented for the purpose of identifying a panic attack; however, panic attack is not a mental disorder and cannot be coded. Panic attacks can occur in the context of any anxiety disorder as well as other mental disorders (e.g., depressive disorders, posttraumatic stress disorder, substance use disorders) and some medical conditions (e.g., cardiac, respiratory, vestibular, gastrointestinal). When the presence of a panic attack is identified, it should be noted as a specifier (e.g., "posttraumatic stress disorder with panic attacks"). For panic disorder, the presence of panic attack is contained within the criteria for the disorder and panic attack is not used as a specifier.

An abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur:

Note: The abrupt surge can occur from a calm state or an anxious state.

1. Palpitations, pounding heart, or accelerated heart rate.
2. Sweating.
3. Trembling or shaking.
4. Sensations of shortness of breath or smothering.
5. Feelings of choking.
6. Chest pain or discomfort.
7. Nausea or abdominal distress.
8. Feeling dizzy, unsteady, light-headed, or faint.
9. Chills or heat sensations.
10. Paresthesias (numbness or tingling sensations).
11. Derealization (feelings of unreality) or depersonalization (being detached from oneself).
12. Fear of losing control or "going crazy."
13. Fear of dying.

Note: Culture-specific symptoms (e.g., tinnitus, neck soreness, headache, uncontrollable screaming or crying) may be seen. Such symptoms should not count as one of the four required symptoms.

Features

The essential feature of a panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes and during which time four or more of 13 physical and cognitive symptoms occur. Eleven of these 13 symptoms are physical (e.g., palpitations, sweating), while two are cognitive (i.e., fear of losing control or going crazy, fear of dying). "Fear of going crazy" is a colloquialism often used by individuals with panic attacks and is not intended as a pejorative or diagnostic term. The term *within minutes* means that the time to peak

intensity is literally only a few minutes. A panic attack can arise from either a calm state or an anxious state, and time to peak intensity should be assessed independently of any preceding anxiety. That is, the start of the panic attack is the point at which there is an abrupt increase in discomfort rather than the point at which anxiety first developed. Likewise, a panic attack can return to either an anxious state or a calm state and possibly peak again. A panic attack is distinguished from ongoing anxiety by its time to peak intensity, which occurs within minutes; its discrete nature; and its typically greater severity. Attacks that meet all other criteria but have fewer than four physical and/or cognitive symptoms are referred to as *limited-symptom attacks.*

There are two characteristic types of panic attacks: expected and unexpected. *Expected panic attacks* are attacks for which there is an obvious cue or trigger, such as situations in which panic attacks have typically occurred. *Unexpected panic attacks* are those for which there is no obvious cue or trigger at the time of occurrence (e.g., when relaxing or out of sleep [nocturnal panic attack]). The determination of whether panic attacks are expected or unexpected is made by the clinician, who makes this judgment based on a combination of careful questioning as to the sequence of events preceding or leading up to the attack and the individual's own judgment of whether or not the attack seemed to occur for no apparent reason. Cultural interpretations may influence their determination as expected or unexpected. Culture-specific symptoms (e.g., tinnitus, neck soreness, headache, uncontrollable screaming or crying) may be seen; however, such symptoms should not count as one of the four required symptoms. Panic attacks can occur in the context of any mental disorder (e.g., anxiety disorders, depressive disorders, bipolar disorders, eating disorders, obsessive-compulsive and related disorders, personality disorders, psychotic disorders, substance use disorders) and some medical conditions (e.g., cardiac, respiratory, vestibular, gastrointestinal), with the majority never meeting criteria for panic disorder. Recurrent unexpected panic attacks are required for a diagnosis of panic disorder.

Associated Features

One type of unexpected panic attack is a *nocturnal panic attack* (i.e., waking from sleep in a state of panic), which differs from panicking after fully waking from sleep. Panic attacks are related to a higher rate of suicide attempts and suicidal ideation even when comorbidity and other suicide risk factors are taken into account.

Prevalence

In the general population, 12-month prevalence estimates for panic attacks in the United States is 11.2% in adults. Twelve-month prevalence estimates do not appear to differ significantly among African Americans, Asian Americans, and Latinos. Lower 12-month prevalence estimates for European countries appear to range from 2.7% to 3.3%. Females are more frequently affected than males, although this gender difference is more pronounced for panic disorder. Panic attacks can occur in children but are relatively rare until the age of puberty, when the prevalence rates increase. The prevalence rates decline in older individuals, possibly reflecting diminishing severity to subclinical levels.

Development and Course

The mean age at onset for panic attacks in the United States is approximately 22–23 years among adults. However, the course of panic attacks is likely influenced by the course of any co-occurring mental disorder(s) and stressful life events. Panic attacks are uncommon, and unexpected panic attacks are rare, in preadolescent children. Adolescents might be less willing than adults to openly discuss panic attacks, even though they present with episodes of intense fear or discomfort. Lower prevalence of panic attacks in older individuals may be related to a weaker autonomic response to emotional states relative to younger individuals. Older individuals may be less inclined to use the word "fear" and more inclined

to use the word "discomfort" to describe panic attacks. Older individuals with "panicky feelings" may have a hybrid of limited-symptom attacks and generalized anxiety. In addition, older individuals tend to attribute panic attacks to certain situations that are stressful (e.g., medical procedures, social settings) and may retrospectively endorse explanations for the panic attack even if it was unexpected in the moment. This may result in under-endorsement of unexpected panic attacks in older individuals.

Risk and Prognostic Factors

Temperamental. Negative affectivity (neuroticism) (i.e., proneness to experiencing negative emotions) and anxiety sensitivity (i.e., the disposition to believe that symptoms of anxiety are harmful) are risk factors for the onset of panic attacks. History of "fearful spells" (i.e., limited-symptom attacks that do not meet full criteria for a panic attack) may be a risk factor for later panic attacks.

Environmental. Smoking is a risk factor for panic attacks. Most individuals report identifiable stressors in the months before their first panic attack (e.g., interpersonal stressors and stressors related to physical well-being, such as negative experiences with illicit or prescription drugs, disease, or death in the family).

Culture-Related Diagnostic Issues

Cultural interpretations may influence the determination of panic attacks as expected or unexpected. Culture-specific symptoms (e.g., tinnitus, neck soreness, headache, and uncontrollable screaming or crying) may be seen; however, such symptoms should not count as one of the four required symptoms. Frequency of each of the 13 symptoms varies cross-culturally (e.g., higher rates of paresthesias in African Americans and of dizziness in several Asian groups). Cultural syndromes also influence the cross-cultural presentation of panic attacks, resulting in different symptom profiles across different cultural groups. Examples include *khyâl* (wind) attacks, a Cambodian cultural syndrome involving dizziness, tinnitus, and neck soreness; and *trúng gió* (wind-related) attacks, a Vietnamese cultural syndrome associated with headaches. *Ataque de nervios* (attack of nerves) is a cultural syndrome among Latin Americans that may involve trembling, uncontrollable screaming or crying, aggressive or suicidal behavior, and depersonalization or derealization, and which may be experienced for longer than only a few minutes. Some clinical presentations of *ataque de nervios* fulfill criteria for conditions other than panic attack (e.g., other specified dissociative disorder). Also, cultural expectations may influence the classification of panic attacks as expected or unexpected, as cultural syndromes may create fear of certain situations, ranging from interpersonal arguments (associated with *ataque de nervios*), to types of exertion (associated with *khyâl* attacks), to atmospheric wind (associated with *trúng gió* attacks). Clarification of the details of cultural attributions may aid in distinguishing expected and unexpected panic attacks. For more information about cultural syndromes, see "Glossary of Cultural Concepts of Distress" in the Appendix to this manual.

Gender-Related Diagnostic Issues

Panic attacks are more common in females than in males, but clinical features or symptoms of panic attacks do not differ between males and females.

Diagnostic Markers

Physiological recordings of naturally occurring panic attacks in individuals with panic disorder indicate abrupt surges of arousal, usually of heart rate, that reach a peak within minutes and subside within minutes, and for a proportion of these individuals the panic attack may be preceded by cardiorespiratory instabilities.

Functional Consequences of Panic Attacks

In the context of co-occurring mental disorders, including anxiety disorders, depressive disorders, bipolar disorder, substance use disorders, psychotic disorders, and personality disorders, panic attacks are associated with increased symptom severity, higher rates of comorbidity and suicidality, and poorer treatment response. Also, full-symptom panic attacks typically are associated with greater morbidity (e.g., greater health care utilization, more disability, poorer quality of life) than limited-symptom attacks.

Differential Diagnosis

Other paroxysmal episodes (e.g., "anger attacks"). Panic attacks should not be diagnosed if the episodes do not involve the essential feature of an abrupt surge of intense fear or intense discomfort, but rather other emotional states (e.g., anger, grief).

Anxiety disorder due to another medical condition. Medical conditions that can cause or be misdiagnosed as panic attacks include hyperthyroidism, hyperparathyroidism, pheochromocytoma, vestibular dysfunctions, seizure disorders, and cardiopulmonary conditions (e.g., arrhythmias, supraventricular tachycardia, asthma, chronic obstructive pulmonary disease). Appropriate laboratory tests (e.g., serum calcium levels for hyperparathyroidism; Holter monitor for arrhythmias) or physical examinations (e.g., for cardiac conditions) may be helpful in determining the etiological role of another medical condition.

Substance/medication-induced anxiety disorder. Intoxication with central nervous system stimulants (e.g., cocaine, amphetamines, caffeine) or cannabis and withdrawal from central nervous system depressants (e.g., alcohol, barbiturates) can precipitate a panic attack. A detailed history should be taken to determine if the individual had panic attacks prior to excessive substance use. Features such as onset after age 45 years or the presence of atypical symptoms during a panic attack (e.g., vertigo, loss of consciousness, loss of bladder or bowel control, slurred speech, or amnesia) suggest the possibility that a medical condition or a substance may be causing the panic attack symptoms.

Panic disorder. Repeated unexpected panic attacks are required but are not sufficient for the diagnosis of panic disorder (i.e., full diagnostic criteria for panic disorder must be met).

Comorbidity

Panic attacks are associated with increased likelihood of various comorbid mental disorders, including anxiety disorders, depressive disorders, bipolar disorders, impulse-control disorders, and substance use disorders. Panic attacks are associated with increased likelihood of later developing anxiety disorders, depressive disorders, bipolar disorders, and possibly other disorders.

Agoraphobia

Diagnostic Criteria **300.22 (F40.00)**

A. Marked fear or anxiety about two (or more) of the following five situations:
   1. Using public transportation (e.g., automobiles, buses, trains, ships, planes).
   2. Being in open spaces (e.g., parking lots, marketplaces, bridges).
   3. Being in enclosed places (e.g., shops, theaters, cinemas).
   4. Standing in line or being in a crowd.
   5. Being outside of the home alone.

B. The individual fears or avoids these situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symp-

toms or other incapacitating or embarrassing symptoms (e.g., fear of falling in the elderly; fear of incontinence).

C. The agoraphobic situations almost always provoke fear or anxiety.
D. The agoraphobic situations are actively avoided, require the presence of a companion, or are endured with intense fear or anxiety.
E. The fear or anxiety is out of proportion to the actual danger posed by the agoraphobic situations and to the sociocultural context.
F. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.
G. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
H. If another medical condition (e.g., inflammatory bowel disease, Parkinson's disease) is present, the fear, anxiety, or avoidance is clearly excessive.
I. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder—for example, the symptoms are not confined to specific phobia, situational type; do not involve only social situations (as in social anxiety disorder); and are not related exclusively to obsessions (as in obsessive-compulsive disorder), perceived defects or flaws in physical appearance (as in body dysmorphic disorder), reminders of traumatic events (as in posttraumatic stress disorder), or fear of separation (as in separation anxiety disorder).

Note: Agoraphobia is diagnosed irrespective of the presence of panic disorder. If an individual's presentation meets criteria for panic disorder and agoraphobia, both diagnoses should be assigned.

Diagnostic Features

The essential feature of agoraphobia is marked, or intense, fear or anxiety triggered by the real or anticipated exposure to a wide range of situations (Criterion A). The diagnosis requires endorsement of symptoms occurring in at least two of the following five situations: 1) using public transporation, such as automobiles, buses, trains, ships, or planes; 2) being in open spaces, such as parking lots, marketplaces, or bridges; 3) being in enclosed spaces, such as shops, theaters, or cinemas; 4) standing in line or being in a crowd; or 5) being outside of the home alone. The examples for each situation are not exhaustive; other situations may be feared. When experiencing fear and anxiety cued by such situations, individuals typically experience thoughts that something terrible might happen (Criterion B). Individuals frequently believe that escape from such situations might be difficult (e.g., "can't get out of here") or that help might be unavailable (e.g., "there is nobody to help me") when panic-like symptoms or other incapacitating or embarrassing symptoms occur. "Panic-like symptoms" refer to any of the 13 symptoms included in the criteria for panic attack, such as dizziness, faintness, and fear of dying. "Other incapacitating or embarrassing symptoms" include symptoms such as vomiting and inflammatory bowel symptoms, as well as, in older adults, a fear of falling or, in children, a sense of disorientation and getting lost.

The amount of fear experienced may vary with proximity to the feared situation and may occur in anticipation of or in the actual presence of the agoraphobic situation. Also, the fear or anxiety may take the form of a full- or limited-symptom panic attack (i.e., an expected panic attack). Fear or anxiety is evoked nearly every time the individual comes into contact with the feared situation (Criterion C). Thus, an individual who becomes anxious only occasionally in an agoraphobic situation (e.g., becomes anxious when standing in line on only one out of every five occasions) would not be diagnosed with agoraphobia. The individual actively avoids the situation or, if he or she either is unable or decides not to avoid it, the situation evokes intense fear or anxiety (Criterion D). *Active avoidance* means the individual is currently behaving in ways that are intentionally designed to prevent or minimize contact with agoraphobic situations. Avoidance can be behavioral (e.g., changing

daily routines, choosing a job nearby to avoid using public transportation, arranging for food delivery to avoid entering shops and supermarkets) as well as cognitive (e.g., using distraction to get through agoraphobic situations) in nature. The avoidance can become so severe that the person is completely homebound. Often, an individual is better able to confront a feared situation when accompanied by a companion, such as a partner, friend, or health professional.

The fear, anxiety, or avoidance must be out of proportion to the actual danger posed by the agoraphobic situations and to the sociocultural context (Criterion E). Differentiating clinically significant agoraphobic fears from reasonable fears (e.g., leaving the house during a bad storm) or from situations that are deemed dangerous (e.g., walking in a parking lot or using public transportation in a high-crime area) is important for a number of reasons. First, what constitutes avoidance may be difficult to judge across cultures and sociocultural contexts (e.g., it is socioculturally appropriate for orthodox Muslim women in certain parts of the world to avoid leaving the house alone, and thus such avoidance would not be considered indicative of agoraphobia). Second, older adults are likely to overattribute their fears to age-related constraints and are less likely to judge their fears as being out of proportion to the actual risk. Third, individuals with agoraphobia are likely to overestimate danger in relation to panic-like or other bodily symptoms. Agoraphobia should be diagnosed only if the fear, anxiety, or avoidance persists (Criterion F) and if it causes clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion G). The duration of "typically lasting for 6 months or more" is meant to exclude individuals with short-lived, transient problems. However, the duration criterion should be used as a general guide, with allowance for some degree of flexibility.

Associated Features Supporting Diagnosis

In its most severe forms, agoraphobia can cause individuals to become completely homebound, unable to leave their home and dependent on others for services or assistance to provide even for basic needs. Demoralization and depressive symptoms, as well as abuse of alcohol and sedative medication as inappropriate self-medication strategies, are common.

Prevalence

Every year approximately 1.7% of adolescents and adults have a diagnosis of agoraphobia. Females are twice as likely as males to experience agoraphobia. Agoraphobia may occur in childhood, but incidence peaks in late adolescence and early adulthood. Twelve-month prevalence in individuals older than 65 years is 0.4%. Prevalence rates do not appear to vary systematically across cultural/racial groups.

Development and Course

The percentage of individuals with agoraphobia reporting panic attacks or panic disorder preceding the onset of agoraphobia ranges from 30% in community samples to more than 50% in clinic samples. The majority of individuals with panic disorder show signs of anxiety and agoraphobia before the onset of panic disorder.

In two-thirds of all cases of agoraphobia, initial onset is before age 35 years. There is a substantial incidence risk in late adolescence and early adulthood, with indications for a second high incidence risk phase after age 40 years. First onset in childhood is rare. The overall mean age at onset for agoraphobia is 17 years, although the age at onset without preceding panic attacks or panic disorder is 25–29 years.

The course of agoraphobia is typically persistent and chronic. Complete remission is rare (10%), unless the agoraphobia is treated. With more severe agoraphobia, rates of full remission decrease, whereas rates of relapse and chronicity increase. A range of other disorders, in particular other anxiety disorders, depressive disorders, substance use disorders, and personality disorders, may complicate the course of agoraphobia. The long-term