07 - 9.7 Other Anxiety Disorders

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Practice in Clinical Psychology. Vol 2: Adult Disorders. Hoboken: John Wiley & Sons; 2012:651. Ritter MR, Blackmore MA, Heimberg RG. Generalized anxiety disorder. In: McKay D, Abramowitz JS, Taylor S, eds. Cognitive Behavioral Therapy for Refractory Cases: Turing Failure Into Success. Washington, DC: American Psychological Association; 2010. Uebelacker L, Weisberg R, Millman M, Yen S, Keller M. Prospective study on risk factors for suicidal behavior in individuals with anxiety disorders. Psychol Med. 2013;43:1465. 9.7 Other Anxiety Disorders ANXIETY DISORDER ATTRIBUTABLE TO ANOTHER MEDICAL CONDITION Many medical disorders are associated with anxiety. Symptoms can include panic attacks, generalized anxiety, and other signs of distress. In all cases, the signs and symptoms will be due to the direct physiological effects of the medical condition. Epidemiology The occurrence of anxiety symptoms related to general medical conditions is common, although the incidence of the disorder varies for each specific general medical condition. Etiology A wide range of medical conditions can cause symptoms similar to those of anxiety disorders (Table 9.7-1). Hyperthyroidism, hypothyroidism, hypoparathyroidism, and vitamin B12 deficiency are frequently associated with anxiety symptoms. A pheochromocytoma produces epinephrine, which can cause paroxysmal episodes of anxiety symptoms. Other medical conditions, such as cardiac arrhythmia, can produce physiological symptoms of panic disorder. Hypoglycemia can also mimic the symptoms of an anxiety disorder. The diverse medical conditions that can cause symptoms of anxiety disorder may do so through a common mechanism that involves both the noradrenergic system and the serotonergic system. Each of these conditions is characterized by prominent anxiety that arises as the direct result of some underlying physiological perturbation. Table 9.7-1 Disorders Associated with Anxiety

Diagnosis The diagnosis of anxiety disorder attributable to another medical condition requires the presence of symptoms of an anxiety disorder caused by one or more medical illnesses. The DSM-5 suggests that clinicians to specify whether the disorder is characterized by symptoms of generalized anxiety or panic attacks. Clinicians should have an increased level of suspicion for the diagnosis when chronic or paroxysmal anxiety is associated with a physical disease known to cause such symptoms in some patients. Paroxysmal bouts of hypertension in an anxious patient may indicate that a workup for a pheochromocytoma is appropriate. A general medical workup may reveal diabetes, an adrenal tumor, thyroid disease, or a neurological condition. For example, some patients with complex partial epilepsy have extreme

episodes of anxiety or fear as their only manifestation of the epileptic activity. Clinical Features The symptoms of anxiety disorder due to a general medical condition can be identical to those of the primary anxiety disorders. A syndrome similar to panic disorder is the most common clinical picture, and a syndrome similar to a phobia is the least common. Panic Attacks. Patients who have cardiomyopathy may have the highest incidence of panic disorder secondary to a general medical condition. One study reported that 83 percent of patients with cardiomyopathy awaiting cardiac transplantation had panic disorder symptoms. Increased noradrenergic tone in these patients may be the provoking stimulus for the panic attacks. In some studies, about 25 percent of patients with Parkinson's disease and chronic obstructive pulmonary disease have symptoms of panic disorder. Other medical disorders associated with panic disorder include chronic pain, primary biliary cirrhosis, and epilepsy, particularly when the focus is in the right parahippocampal gyrus. Generalized Anxiety. A high prevalence of generalized anxiety disorder symptoms has been reported in patients with Sjögren's syndrome, and this rate may be related to the effects of Sjögren's syndrome on cortical and subcortical functions and thyroid function. The highest prevalence of generalized anxiety disorder symptoms in a medical disorder seems to be in Graves' disease (hyperthyroidism), in which as many as two-thirds of all patients meet the criteria for generalized anxiety disorder. A 86-year-old retired chemical engineer sought help for the onset of a series of attacks over the preceding 4 months in which he experienced marked apprehension, restlessness, a sense that the "walls were caving in," and the need to "get air" to relieve his sense of discomfort. These events typically occurred during the night and awakened him from sound sleep. To feel better, he would need to stick his head out of an open window, regardless of how cold it was outside. His symptoms would gradually improve over 15 to 20 minutes, but complete resolution of these symptoms took a full day. In response to pointed questioning, the patient reported sweating, dizziness, and shortness of breath during these episodes. He imagined that he would die if he could not open the window. He denied palpitations, choking sensations, paresthesia, and nausea. The patient recalled a similar series of attacks almost 30 years earlier during a period of time in which he frequently needed to travel and hence was away from home because of work obligations. The patient denied depressed mood, anhedonia, recent sleep dysfunctions, change in appetite or weight, decreased energy, and feelings of worthlessness. His medical history was notable for a right basal ganglia stroke 6 months earlier. He had a history of hypertension, borderline diabetes, and benign prostatic hypertrophy. Laboratory study results were unremarkable.

A diagnosis of anxiety disorder due to stroke, with panic attacks, was made. The patient was prescribed alprazolam (Xanax), 0.5 mg orally twice a day as needed for panic attacks, and started on escitalopram (Lexapro), 10 mg per day. At a follow-up visit, the patient reported complete resolution of his anxiety symptoms. He remained taking the escitalopram but no longer required the alprazolam. (Courtesy of LL Lavery, M.D., and EM Whyte, M.D.) Phobias. Symptoms of phobias appear to be uncommon, although one study reported a 17 percent prevalence of symptoms of social phobia in patients with Parkinson's disease. Older persons with balance difficulties often complain of a fear of falling, which may express itself by their being unwilling or fearful of walking. Laboratory Examination A targeted work-up is required when an anxiety disorder due to another medical condition is being considered as part of the differential diagnosis. If possible, tests should be selected to rule in specific diagnoses suggested by the patient's somatic symptoms (if present). Test to consider include complete book count, electrolytes, glucose, blood urea nitrogen, creatinine, liver function tests, calcium, magnesium, phosphorus, thyroid function tests, and urine

toxicology. Occasionally, additional studies may be indicated to rule out a pheochromocytoma (e.g., urinary catecholamines), a seizure disorder (e.g., EEG), cardiac arrhythmia (e.g., Holter monitoring), and pulmonary disease (pulse oximetry, arterial blood gases). Brain imaging may be useful in ruling out demyelinating disorder, tumor, stroke, or hydrocephalus and is especially important if the anxious individual reports neurological symptoms (e.g., headache, motor or sensory changes, and dizziness), although such complaints may represent somatic manifestations of primary anxiety disorders. Lumbar puncture may be appropriate if an inflammatory or infectious cause is suspected. Differential Diagnosis Anxiety, as a symptom, can be associated with many psychiatric disorders in addition to the anxiety disorders themselves. A mental status examination is necessary to determine the presence of mood symptoms or psychotic symptoms that may suggest another psychiatric diagnosis. For a clinician to conclude that a patient has an anxiety disorder caused by a general medical condition, the patient should clearly have anxiety as the predominant symptom and should have a specific causative nonpsychiatric medical disorder. To ascertain the degree to which a general medical condition is causative for the anxiety, the clinician should evaluate the timeline between the medical condition and the anxiety symptoms, the age of onset (primary anxiety disorders usually have their onset before age 35 years), and the patient's family history of both anxiety disorders and relevant general medical conditions (e.g., hyperthyroidism). A diagnosis

of adjustment disorder with anxiety must also be considered in the differential diagnosis. Course and Prognosis The unremitting experience of anxiety can be disabling and can interfere with every aspect of life, including social, occupational, and psychological functioning. A sudden increase in anxiety level may prompt an affected person to seek medical or psychiatric help more quickly than when the onset is insidious. The treatment or the removal of the primary medical cause of the anxiety usually initiates a clear course of improvement in the anxiety disorder symptoms. In some cases, however, the anxiety disorder symptoms continue even after the primary medical condition is treated (e.g., after an episode of encephalitis). Some symptoms linger for a longer time than other anxiety disorder symptoms. When anxiety disorder symptoms are present for a significant period after the medical disorder has been treated, the remaining symptoms should probably be treated as if they were primary—that is, with psychotherapy, pharmacotherapy, or both. Treatment The primary treatment for anxiety disorder due to a general medical condition is to treat the underlying medical condition. If a patient also has an alcohol or other substance use disorder, this disorder must also be addressed therapeutically to gain control of the anxiety disorder symptoms. If the removal of the primary medical condition does not reverse the anxiety disorder symptoms, treatment of these symptoms should follow the treatment guidelines for the specific mental disorder. In general, behavioral modification techniques, anxiolytic agents, and serotonergic antidepressants have been the most effective treatment modalities. SUBSTANCE-INDUCED ANXIETY DISORDER Substance-induced disorder is the direct result of a toxic substance, including drugs of abuse, medication, poison, and alcohol, among others. Epidemiology Substance-induced anxiety disorder is common, both as the result of the ingestion of socalled recreational drugs and as the result of prescription drug use. Etiology A wide range of substances can cause symptoms of anxiety that can mimic any of the DSM-5 anxiety disorders. Although sympathomimetics, such as amphetamine, cocaine, and caffeine, have been most associated with the production of anxiety disorder symptoms, many serotonergic drugs (e.g., LSD and MDMA) can also cause both acute and chronic anxiety syndromes in users. A wide range of prescription medications is also associated with the production of anxiety disorder symptoms in susceptible persons.

Diagnosis The diagnostic criteria for substance-induced anxiety disorder require the presence of prominent anxiety or panic attacks. The DSM-5 guidelines state that the symptoms should have developed during the use of the substance or within 1 month of the cessation of substance use; however, clinicians may have difficulty determining the relation between substance exposure and anxiety symptoms. The structure of the diagnosis includes specification of (1) the substance (e.g., cocaine), (2) the appropriate state during the onset (e.g., intoxication), and (3) the specific symptom pattern (e.g., panic attacks). Clinical Features The associated clinical features of substance-induced anxiety disorder vary with the particular substance involved. Even infrequent use of psychostimulants can result in anxiety disorder symptoms in some persons. Cognitive impairments in comprehension, calculation, and memory can be associated with anxiety disorder symptoms. These cognitive deficits are usually reversible when the substance use is stopped. Virtually everyone who drinks alcohol, on at least a few occasions, has used it to reduce anxiety, most often social anxiety. In contrast, carefully controlled studies have found that the effects of alcohol on anxiety are variable and can be significantly affected by gender, the amount of alcohol ingested, and cultural attitudes. Nevertheless, alcohol use disorders and other substance-related disorders are commonly associated with anxiety disorders. Alcohol use disorders are about four times more common among patients with panic disorder than among the general population and about two and a half times more common among patients with phobias. Several studies have reported data indicating that genetic diatheses for both anxiety disorders and alcohol use disorders can exist in some families. Differential Diagnosis The differential diagnosis for substance-induced anxiety disorder includes the primary anxiety disorders; anxiety disorder due to a general medical condition (for which the patient may be receiving an implicated drug); and mood disorders, which are frequently accompanied by symptoms of anxiety disorders. Personality disorders and malingering must be considered in the differential diagnosis, particularly in some urban emergency departments. Course and Prognosis The course and prognosis generally depend on removal of the causally involved substance and the long-term ability of the affected person to limit use of the substance. The anxiogenic effects of most drugs are reversible. When the anxiety does not reverse with cessation of the drug, clinicians should reconsider the diagnosis of substance-

induced anxiety disorder or consider the possibility that the substance caused irreversible brain damage. Treatment The primary treatment for substance-induced anxiety disorder is the removal of the causally involved substance. Treatment then must focus on finding an alternative treatment if the substance was a medically indicated drug, on limiting the patient’s exposure if the substance was introduced through environmental exposure, or on treating the underlying substance-related disorder. If anxiety disorder symptoms continue even after stopping substance use, treatment of the anxiety disorder symptoms with appropriate psychotherapeutic or pharmacotherapeutic modalities may be appropriate. MIXED ANXIETY-DEPRESSIVE DISORDER Mixed anxiety-depressive disorder describes patients with both anxiety and depressive symptoms who do not meet the diagnostic criteria for either an anxiety disorder or a mood disorder. The combination of depressive and anxiety symptoms results in significant functional impairment for the affected person. The condition may be particularly prevalent in primary care practices and outpatient mental health clinics. Opponents have argued that the availability of the diagnosis may discourage clinicians from taking the necessary time to obtain a complete psychiatric history to differentiate true depressive disorders from true anxiety disorders. In Europe and especially in China, many of these patients are given a diagnosis of neurasthenia. Epidemiology The coexistence of major depressive disorder and panic disorder is common. As many as two-thirds of all patients with depressive symptoms have

prominent anxiety symptoms, and one-third may meet the diagnostic criteria for panic disorder. Researchers have reported that 20 to 90 percent of all patients with panic disorder have episodes of major depressive disorder. These data suggest that the coexistence of depressive and anxiety symptoms, neither of which meets the diagnostic criteria for other depressive or anxiety disorders, may be common. Presently, however, formal epidemiological data on mixed anxiety-depressive disorder are not available. Nevertheless, some clinicians and researchers have estimated that the prevalence of the disorder in the general population is as high as 10 percent and as high as 50 percent in primary care clinics, although conservative estimates suggest a prevalence of about 1 percent in the general population. Etiology Four principal lines of evidence suggest that anxiety symptoms and depressive symptoms are causally linked in some affected patients. First, several investigators have

reported similar neuroendocrine findings in depressive disorders and anxiety disorders, particularly panic disorder, including blunted cortisol response to adrenocorticotropic hormone, blunted growth hormone response to clonidine (Catapres), and blunted thyroid-stimulating hormone and prolactin responses to thyrotropin-releasing hormone. Second, several investigators have reported data indicating that hyperactivity of the noradrenergic system is causally relevant to some patients with depressive disorders and with panic disorder. Specifically, these studies have found elevated concentrations of the norepinephrine metabolite (MHPG) in the urine, the plasma, or the CSF of depressed patients and patients with panic disorder who were actively experiencing a panic attack. As with other anxiety and depressive disorders, serotonin and GABA may also be causally involved in mixed anxiety-depressive disorder. Third, many studies have found that serotonergic drugs, such as fluoxetine (Prozac) and clomipramine (Anafranil), are useful in treating both depressive and anxiety disorders. Fourth, a number of family studies have reported data indicating that anxiety and depressive symptoms are genetically linked in at least some families. Diagnosis The diagnostic criteria for mixed anxiety-depressive disorder require the presence of subsyndromal symptoms of both anxiety and depression and the presence of some autonomic symptoms, such as tremor, palpitations, dry mouth, and the sensation of a churning stomach. Some preliminary studies have indicated that the sensitivity of general practitioners to a syndrome of mixed anxiety-depressive disorder is low, although this lack of recognition may reflect the lack of an appropriate diagnostic label for the patients. Clinical Features The clinical features of mixed anxiety-depressive disorder combine symptoms of anxiety disorders and some symptoms of depressive disorders. In addition, symptoms of autonomic nervous system hyperactivity, such as gastrointestinal complaints, are common and contribute to the high frequency with which the patients are seen in outpatient medical clinics. Differential Diagnosis The differential diagnosis includes other anxiety and depressive disorders and personality disorders. Among the anxiety disorders, generalized anxiety disorder is most likely to overlap with mixed anxiety-depressive disorder. Among the mood disorders, dysthymic disorder and minor depressive disorder are most likely to overlap with mixed anxiety-depressive disorder. Among the personality disorders, avoidant, dependent, and obsessive-compulsive personality disorders may have symptoms that resemble those of mixed anxiety-depressive disorder. A diagnosis of a somatoform disorder should also be considered. Only a psychiatric history, a mental status examination, and a working

knowledge of the specific criteria can help clinicians differentiate among these conditions. The prodromal signs of schizophrenia may show itself as a mixed picture of mounting anxiety and depression with eventual onset of psychotic symptoms. Course and Prognosis On the basis of

clinical data to date, patients seem to be equally likely to have prominent anxiety symptoms, prominent depressive symptoms, or an equal mixture of the two symptoms at onset. During the course of the illness, anxiety or depressive symptoms may alternate in their predominance. The prognosis is not known. Treatment Because adequate studies comparing treatment modalities for mixed anxiety-depressive disorder are not available, clinicians are probably most likely to provide treatment based on the symptoms present, their severity, and the clinician's own level of experience with various treatment modalities. Psychotherapeutic approaches may involve time-limited approaches, such as cognitive therapy or behavior modification, although some clinicians use a less structured psychotherapeutic approach, such as insight-oriented psychotherapy. Pharmacotherapy for mixed anxiety-depressive disorder can include antianxiety drugs, antidepressant drugs, or both. Among the anxiolytic drugs, some data indicate that the use of triazolobenzodiazepines (e.g., alprazolam [Xanax]) may be indicated because of their effectiveness in treating depression associated with anxiety. A drug that affects the serotonin 5-HT1A receptor, such as buspirone (BuSpar), may also be indicated. Among the antidepressants, despite the noradrenergic theories linking anxiety disorders and depressive disorders, the serotonergic antidepressants may be most effective in treating mixed anxiety-depressive disorder. Venlafaxine (Effexor) is an effective antidepressant that has been approved by the FDA for the treatment of depression as well as generalized anxiety disorder and is a drug of choice in the combined disorder. REFERENCES Algeria AA, Hasin DS, Nunes EV, Liu SM, Davies C, Grand BF, Blanco C. Comorbidity of generalized anxiety disorder and substance use disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2010;71:1187. Beard C, Weisberg RB, Keller MB. Health-related quality of life across the anxiety disorders: Findings from a sample of primary care patients. J Anxiety Disord. 2010;24:559. Campbell-Sills L, Stein MB, Sherbourne CD, Craske MG, Sullivan G, Golinelli D, Lang AJ, Chavira DA, Bystritsky A, Rose RD, Welch SS, Kallenberg GA, Roy-Byrne P. Effects of medical comorbidity on anxiety treatment outcomes in primary care. Psychosom Med. 2013; 75:713. Comer JS, Blanco C, Hasin DS, Liu SM, Grant BF, Turner JB, Olfson M. Health-related quality of life across the anxiety disorders. J Clin Psych. 2011;72:43. Galbraith, T., Heimberg, RG, Wang, S., Schneier, FR, & Blanco, C. Comorbidity of social anxiety disorder and antisocial

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