Generalized Anxiety Disorder in Adults

Case Study and Commentary, *Raushanah Hud-Aleem, DO, and Darnell Ladson, DO*

CME jointly sponsored by Wayne State University School of Medicine and JCOM

This article has a companion CME exam that follows the article. To earn credit, read the article and complete the CME evaluation on pages 362 and 363. Estimated time to complete this activity is 1 hour. Release date: 15 July 2008; valid for credit through 30 July 2009.

Program Audience

Primary care physicians.

Educational Needs Addressed

Generalized anxiety disorder (GAD) is a common psychiatric disorder associated with signficant impairment, including loss of productivity, high utilization of health care resources, and reduced quality of life. Patients typically present with vague somatic compliants rather than psychological symptoms, making diagnosis challenging. Optimal recognition and use of effective therapy are critical skills for the physician and should improve the patient's prognosis for recovery and reduce unnecessary suffering.

Educational Objectives

After participating in this CME activity, primary care physicians should be able to

1. Describe the epidemiology of GAD
2. Know the diagnositic criteria for GAD
3. Describe key components of a historical and physical assessment in patients with anxiety
4. Identify effective treatments for GAD

Generalized anxiety disorder (GAD) is one of the most common psychiatric disorders encountered in the primary care setting. Lifetime prevalence of GAD is approximately 5% in the U.S. adult population [1,2]; prevalence in the primary care setting has been estimated at 8% [3,4]. GAD usually has a chronic course that is associated with significant psychosocial impairment, disability, decreased quality of life, and increased use of health care resources [5–8]. In spite of the high prevalence of GAD, it is frequently overlooked and undertreated. Only 30% of GAD patients who present to primary care are diagnosed [7]. Increasing the awareness of GAD among patients and physicians may lead to improved recognition and appropriate intervention, thereby reducing disability and improving quality of life.

CASE STUDY

Initial Presentation

A 26-year-old graduate student presents to her primary care physician complaining of difficulty with sleep, fatigue, and diarrhea with mucus. She is worried that she may have "colitis."

History

The patient says that she has difficulty falling asleep. Her nights are not restful and she has fatigue throughout the day. She has been experiencing the diarrhea off and on for the past year. She feels it might be related to "stress." Associated abdominal discomfort is usually relieved with defecation.

Upon further questioning, the patient acknowledges that she is a "worry wort" and has been this way as long as she can remember. She often worries about her family, school, and finances and fears that one day she will get mugged or have a car wreck.

She complains that she is constantly on edge and has a very difficult time not worrying about things. She says she tends to worry about insignificant things and often tries to anticipate the outcome of events: "I can't turn my mind off. Even when there's nothing to worry about, I'll find something." The worrying makes it difficult for her to focus on her school work. She says her mind frequently goes blank and she feels like she is not retaining her study materials.

She denies ever being attacked or involved in an auto accident. She does not drink or use illicit drugs. She takes no medications and has no known medical conditions. She denies fever, vomiting, weight loss, bloody stool, joint pain, and skin rash. There is no family history of Crohn's disease or ulcerative colitis.

The patient denies suicidal ideation as well as panic attacks, depression, obsessive-compulsive disorder, social phobia, and eating disorder. There have not been any recent stressors.

From the Department of Psychiatry, Wright State University, Dayton, OH.

Table 1. Symptoms and Behaviors Associated with Generalized Anxiety Disorder

Excessive physiologic arousal
Muscle tension
Irritability
Fatigue
Restlessness
Insomnia
Distorted cognitive processes
Poor concentration
Unrealistic assessment of problems
Worries
Poor coping strategies
Avoidance
Procrastination
Poor problem-solving skills

Adapted from Gliatto MF. Generalized anxiety disorder. Am Fam Physician 2000;62:1591–600, 1602.

Physical Examination

The patient appears nervous and fidgets during the first half of the interview. Her physical examination and neurologic examination are unremarkable. She appears to calm down during the course of the interview and examination. She eventually expresses relief that she has finally sought help and is pleased to have an unremarkable examination.

- **What is the usual clinical presentation of GAD?**

Patients with GAD typically approach primary care physicians with vague somatic complaints rather than psychological symptoms [5]. Gastrointestinal symptoms [9] are common concerns among patients with GAD, and sleep complaints are frequent. Belanger et al [10] reported that among GAD patients, 48% had difficulties initiating sleep, 64% reported difficulties maintaining sleep, and 57% complained of early awakening. Symptoms and behaviors associated with GAD are shown in **Table 1**.

- **How is the diagnosis of GAD established?**
- **What are key components of the assessment?**

The DSM-IV-TR diagnostic criteria for GAD are listed in **Table 2**. As patients may not report anxiety symptoms directly, the physician may need to obtain additional clinical history to confirm the diagnosis. To help physicians screen for GAD, Bohn [11] developed the mnemonic device "Does Mr. Fisc worry excessively about minor matters?" Initially, the clinician asks "Do you worry excessively about minor matters?" If endorsed by the patient, the clinician uses the mnemonic "Mr. Fisc" to determine if 3 or more of the associated motor tension and hypervigilance criteria included in the DSM-IV-TR are present. Each letter of "Mr. Fisc" stands for 1 of the associated symptoms: M = muscle tension, R = restlessness, F = fatigue, I = irritability, S = sleep (difficulty falling asleep), and C = concentration (difficulty concentrating).

Table 2. DSM-IV-TR Diagnostic Criteria for Generalized Anxiety Disorder

A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of different events or activities (eg, work, school performance, and leisure activity)
B. The person finds it difficult to control the worry
C. The anxiety and worry are associated with 3 (or more) of the following 6 symptoms (with at least some symptoms being present for more days than not during a 6-month period)
   1. Restlessness, feeling keyed up or on edge
   2. Being easily fatigued
   3. Difficulty concentrating or mind going blank
   4. Irritability
   5. Muscle tension
   6. Sleep disturbance
D. The focus of the worry is not confined to features of an Axis I disorder: the worry is not about having a panic attack (as in panic disorder), being embarrassed in public (as in social phobia), gaining weight (as in anorexia nervosa), being contaminated (as in obsessive-compulsive disorder), or having a serious illness (as in hypochondriasis)
E. The worry and physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
F. The symptoms are not due to a substance or a medical condition (eg, hyperthyroidism) and does not occur exclusively during exacerbations of an Axis I disorder (eg, mood disorder or psychotic disorder)

Adapted with permission from American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed., text revision. Washington (DC): The Association; 2000:476. Copyright 2000, American Psychiatric Association.

Measures of Anxiety

There are a number of clinical measures available that can aid in diagnosis of GAD as well as symptom monitoring. The GAD-7 (**Figure**) is a brief, self-administered, validated screening tool that evaluates for the presence and severity of GAD in clinical practice [12]. Using a cut-off score of 10 or greater, sensitivity and specificity exceed 0.80 and sensitivity is nearly

GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

Total score ____ = Add columns ____ + ____ + ____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all ❑ Somewhat difficult ❑ Very difficult ❑ Extremely difficult ❑

Figure. Generalized anxiety disorder 7-item (GAD-7) scale.

maximized. A score of 15 or greater maximizes specificity and approximates prevalence (9%) more in line with current estimates, but sensitivity is low.

The Hamilton Anxiety Rating Scale (HAM-A) [13,14] is an interview scale that measures the severity of a patient's anxiety based on 14 parameters, including anxious mood, tension, fears, insomnia, somatic complaints, and behavior at the interview. It was created prior to the current GAD definition but covers many of the features of GAD and is helpful in assessing its severity. It takes approximately 20 minutes to complete the interview and score the responses.

The Beck Anxiety inventory (BAI) [15] is a self-report measurement of anxiety. The BAI is biased toward somatic and panic-like symptoms of anxiety, which have been shown to be less characteristic of GAD [16].

The Penn State Worry Questionnaire (PSWQ) [17] measures a general trait-like tendency to worry excessively and has been found to be especially useful in assessing the severity of pathological worry characteristic of GAD. Evidence suggests that it can discriminate among the anxiety disorders; individuals with GAD usually score higher on the PSWQ than individuals in other anxiety disorder groups. Additionally, it has been shown to be sensitive to change in studies of cognitive behavioral therapy for GAD [18].

Differential Diagnosis

GAD can be difficult to distinguish from other mood and anxiety disorders, with which it shares many symptoms. Anxiety symptoms may be seen in several other anxiety spectrum disorders such as panic disorder, social phobia, obsessive-compulsive disorder, and posttraumatic stress disorder. The core features of these disorders are presented in **Table 3**. It is the chronic, nonspecific, excessive nature of the worry that distinguishes GAD from other anxiety disorders.

Certain medications and substances of abuse can cause anxiety (**Table 4**), as can withdrawal from chronically abused substances. Physicians should ask about the use of alcohol, caffeine, and nicotine and inquire about use of any over-the-counter drugs or herbal products. A physical and neurologic examination can help exclude medical entities that can present with anxiety symptoms (**Table 5**). Laboratory studies that should be considered include complete blood count (CBC), calcium level, electrolytes, drug screen, fasting blood glucose, hepatic function test, renal function test, thyroid function test, and urinalysis. Depending on the patient's presentation, other tests such as electrocardiogram and pulmonary function tests may be considered.

Comorbidity in GAD

GAD is commonly comorbid with other disorders, especially other anxiety disorders and major depression [19]. The National Comorbidity Survey found that 90% of people with lifetime GAD have a lifetime history of at least 1 other psychiatric diagnosis [2]. Major depression is the most common comorbid disorder occurring with GAD; at least one third of GAD patients will experience depression. In addition, 27% will have agoraphobia, 25% will have simple phobia, 23% will have social anxiety disorder, and 23% will have panic disorder [2]. Substance use disorders associated with GAD

Table 3. Core Features of 5 Main Anxiety Disorders

Panic Disorder	Social Anxiety Disorder (Social Phobia)	Obsessive-Compulsive Disorder	Posttraumatic Stress Disorder	Generalized Anxiety Disorder
Recurring and unexpected anxiety attacks Fearful of another attack occurring	Fear of public scrutiny or humiliation	Recurrent or unwanted obsessive thoughts resulting in compulsive rituals to reduce anxiety	Flashbacks, hypervigilance, depression, numbing after a traumatic event	Persistent (6 months), uncontrollable worrying Somatic anxiety (tension, insomnia, hypervigilance)

Adapted with permission from Nutt DJ, Ballenger JC, Sheehan D, Wittchen HU. Generalized anxiety disorder: comorbidity, comparative biology and treatment. Int J Neuropsychopharmacol 2002;5:315–25.

Table 4. Medications and Substances That May Produce Anxiety

Anticonvulsants
Tricyclics
Antihistamines
Antihypertensive agents
Anti-inflammatory agents
Antiparkinsonian agents
Digitalis
Sympathomimetics
Thyroid supplements
Hallucinogens
Stimulants
Caffeine
Cocaine
Amphetamines
Withdrawal syndromes
Alcohol
Narcotics
Sedatives-hypnotics

Adapted with permission from Tasman A, Kay J, Lieberman J, editors. Psychiatry. 2nd ed. London: John Wiley & Sons; 2003:1380–404.

include alcohol dependence and drug dependence, with prevalence rates of 11.2% and 5.1%, respectively. Comorbidity leads to even greater health care use and hospitalization rates and a greater number of sick days. Considering the frequency with which depression and anxiety co-occur, some experts recommend that a search for 1 condition should always be accompanied by an assessment of the other [20].

GAD comorbidity, especially with anxiety and depressive disorders, often increases suicide risk. Patients with psychiatric symptoms should always be screened for risk of suicide.

Case Continued

Laboratory testing, including a CBC, thyroid-stimulating hormone, erythrocyte sedimentation rate, and fasting complete metabolic panel reveals values within normal limits. Stool culture is negative. A diagnosis of GAD is made.

- **What etiologic factors are involved in GAD?**

Clinical data have shown that various neurobiologic irregularities (eg, in the γ-aminobutyric acid [GABA] and serotonin systems) are associated with the development of anxiety. Benzodiazepine receptors are attached to the $GABA_A$ receptor. When benzodiazepine binds to its receptor, it increases the effectiveness and prolongs the effect of GABA by increasing the amount of time the chloride channel is open. This suppresses neuronal activity and regulates the release of other neurotransmitters in GABA-rich areas of the brain, especially in the hippocampus, substantia nigra, cerebellum, and striatum. Altered sensitivity of central benzodiazepine receptors have been suggested. Changes in the peripheral benzodiazepine receptor binding have also been observed. Long-term treatment with benzodiazepines has been shown to increase the benzodiazepine peripheral binding sites to normal levels, which suggests that dysregulation of peripheral benzodiazepine receptors may be involved in the mechanism of GAD [21].

Multiple serotonin mechanisms may be involved in the development of anxiety. Serotonergic neurons, which are primarily located in the dorsal and median raphe nuclei of the brainstem, project through various structures of the limbic system. The amygdala plays a significant role and has been associated with modulating autonomic response to stress. Increasing research demonstrating serotonin's role in mental illness has been inspired by serotonergic medications that reduce symptoms (eg, buspirone). Serotonin has also been shown to interact with the norepinephrine system, particularly on the serotonin receptors localized on the noradrenergic cells of the locus ceruleus.

Noradrenergic projections originate from neurons in the locus ceruleus and usually facilitate sympathetic response to stress or a threat. Therefore, dysfunction of the noradrenergic

system has been suspected in the involvement of anxiety. Increase norepinephrine levels or decrease in alpha 2 receptors has been observed in research [22].

Other factors involved in the etiology of GAD include genetics and psychosocial and/or environmental factors, such as childhood trauma or stressors.

- **What is the natural history and course of GAD?**

GAD usually presents during the third decade of life for women and the fourth decade for men but may begin as early as childhood and late teens. The Harvard/Brown Anxiety Research Program (HARP) data showed that GAD has an episodic pattern in which periods of remission and recurrences are evident for many years [23]. Several studies have shown that symptoms may wax and wane for up to 20 years [24]. Acute exacerbation of anxiety may last days to weeks. Although many patients will respond to treatment, only about one third will achieve full remission. In the HARP study, patients were followed at 6-month intervals for 2 years, and it was noted that only 15% had a full remission of 2 months or longer at any time in the first year after baseline, while only 25% had a full remission in the 2 years after baseline [25].

- **What is acute treatment of GAD?**

Patients with GAD may benefit from cognitive behavioral therapy (CBT), pharmacotherapy, or a combination of both. It is important to outline a clear treatment plan and to let the patient know that recovery is often gradual and variable.

Nonpharmacologic Treatments

Patients with mild GAD may respond to simple psychological interventions such as supportive psychotherapy [26,27]. Mild anxiety symptoms may improve with supportive techniques such as empathic listening, reassurance, suggestions, teaching, and reinforcing desired behaviors. The goal is to strengthen defense mechanisms and to alleviate anxiety symptoms.

CBT is an effective intervention for GAD [28–30] and has been shown to be more effective in treating GAD than supportive therapy or behavioral therapy alone. CBT should focus on identifying the mechanisms that lead to the anxiety with an attempt to cognitively restructure the patients' thoughts. During treatment, patients are exposed to anxiety-provoking conditions and through deconditioning strategies and relaxation techniques (progressive muscle relaxation), anxiety is controlled.

Table 5. Medical Conditions That May Cause Anxiety

Endocrine
Addison's disease
Cushing's syndrome
Hyperparathyroidism
Hyperthyroidism
Hypothyroidism
Carcinoid
Pheochromocytoma
Metabolic
Acidosis
Porphyria (acute intermittent)
Electrolyte abnormalities
Hypoglycemia
Cardiovascular
Congestive heart failure
Coronary insufficiency
Dysrhythmia
Hypovolemia
Myocardial infarction
Respiratory
Asthma
Chronic obstructive pulmonary disease
Pulmonary embolism
Pulmonary edema
Immunologic
Systemic lupus erythematosus
Temporal arteritis
Neurologic
Brain tumor
Cerebral syphilis
Cerebrovascular disorders
Encephalopathies
Epilepsy (expecially temporal lobe)
Postconcussive syndrome
Vertigo
Akathisia
Hematologic
Anemia
Gastrointestinal
Peptic ulcer disease
Infectious
Miscellaneous viral and bacterial infections

Adapted with permission from Tasman A, Kay J, Lieberman J, editors. Psychiatry. 2nd ed. London: John Wiley & Sons; 2003: 1380–404.

Although there are no controlled studies of psychodynamic psychotherapy, it also is used to treat GAD. In the psychoanalytic model, the psychiatrist attempts to uncover unconscious conflicts that are central to the genesis of these feelings. The

Table 6. Pharmacologic Interventions for Generalized Anxiety Disorder (GAD)

Medication	Initial Dose (mg/d)	Dose Range (mg/d)	Advantages	Disadvantages
Benzodiazepines			Rapid onset of action; favorable side effects	Sedation; multiple doses for shorter-acting agents; physical dependence; limited antidepressant effect; sexual side effects
Alprazolam	1	2–10		
Lorazepam	0.75	3–10		
Diazepam	4	4–40		
Clonazepam	0.25	1–5		
Antidepressants				
TCAs			Once-daily dosing; effective treating comorbid depression	Delayed onset; need for titration; activation; anticholinergic effects; orthostatic hypotension; weight gain; toxicity in overdose; sexual side effects
Clomipramine	25	25–250		
Desipramine	10	150–300		
Nortriptyline	10	75–150		
Imipramine	75	50–200		
SSRIs			Effective in GAD and comorbid depression; favorable side effects when compared with TCAs; easy dosing	Gastrointestinal side effects; delayed onset; sexual side effects
Paroxetine	10	20–40		
Escitalopram	10	10–20		
Fluoxetine	5–10	10–80		
Sertraline	25	25–200		
Citalopram	10	20–60		
Fluvoxamine	25	25–300		
SNRIs	10	20–40	Effective in GAD, depression, and pain	May elevate blood pressure; nausea, vomiting, dizziness, sweating; sexual side effects
Venlafaxine XR	37.5	75–300		
Duloxetine	30	60		
Atypicals			Effective for treating comorbid depression; low anticholinergic effects	Delayed onset; orthostatic hypotension; weight gain; sexual side effects; priapism; sedation; nefazodone can cause liver failure
Nefazodone	100	300–600		
Mirtazapine	15	15–45		
$5HT_{1A}$ partial agonists				
Buspirone	15	30–60	No physical/ psychological dependence	Nausea, drowsiness, dizziness, headache; not as useful in patients with previous exposure to benzodiazepines

SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant. (Modified from Tasman A, Kay J, Liberman J, editors. Psychiatry. 2nd ed. London: John Wiley & Sons; 2003:1380–1404 and Goodman W. Selecting pharmacotherapy for generalized anxiety disorder. J Clin Psychiatry 2004;65[Suppl 13]:8–13.)

mutative effect of dynamic psychotherapy occurs when the patient understands the reason for the conflict.

Biofeedback and relaxation techniques are nonpharmacologic treatments occasionally used to treat GAD. They have been used to treat anxiety because of commonly associated autonomic symptoms. The effectiveness of biofeedback is unknown. Applied relaxation therapy appears to be helpful in some patients. However, there are no head-to-head studies comparing relaxation with other therapies [31].

Pharmacotherapy

Antidepressants

A number of antidepressants have been shown to be effective in the treatment of GAD and are considered first-line pharmacotherapy agents (**Table 6**). The most commonly used agents are selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs). Antidepressant doses should be optimized before changing or augmenting. If there is an inadequate response to a first-line agent following a fair trial (8–12 weeks), then another first-line medication should be tried. For example, if the first medication used was an SSRI, then switch to a different SSRI or a SNRI. Depending on symptom severity, physicians may elect to use benzodiazepines on a short-term basis until the antidepressant takes effect. However, before using a benzodiazepine, risk for abuse and suicidality should be assessed.

Tricyclic antidepressants. Tricyclic antidepressants are effective

for treating GAD. Imipramine, trazodone, and diazepam were compared with placebo in a study by Rickels and colleagues [32] in GAD patients. Diazepam was effective for 2 weeks before it plateaud and all 3 were found to be more effective than placebo. Imipramine was found to be the most effective of the 3. Despite being effective, tricyclic antidepressants are not often used because of their safety and side effect profile.

SSRIs. SSRIs are considered first-line therapy for GAD. Rocca and colleagues [33] performed the first controlled study examining the efficacy of SSRIs in treating GAD. The 8-week double-blind trial comparing paroxetine, imipramine, and 2′-chlordesmethyldiazepam demonstrated that paroxetine and imipramine were more effective than benzodiazepines in reducing of psychic symptoms. Even though only paroxetine and escitalopram are currently approved by the U.S. Food and Drug Administration (FDA) for the treatment of GAD, other SSRIs may be useful.

SNRIs. Venlafaxine extended-release is approved by the FDA for the treatment of GAD. Several studies have demonstrated that venlafaxine extended-release is more effective than placebo and that it reduces both psychic and somatic symptoms due to GAD [34–37]. Venlafaxine extended-release has been shown to be efficacious as an antidepressant and as a long- and short-term anxiolytic and effective for improving social functioning [34,36,37].

Benzodiazepines

In the past, benzodiazepines were the treatments of choice for GAD because of the many studies that have shown their efficacy. According to Dubovsky [38], approximately 75% of patients either have a marked or moderate response to treatment. Benzodiazepines usually work rapidly, providing some early symptomatic relief to GAD patients within the first few weeks. Benzodiazepines, however, may lose their effectiveness during long-term treatment, therefore eventually requiring an increased dose and/or adjunctive treatment.

Benzodiazepines have been shown to cause sedation, muscle relaxation, anxiety reduction, and decreased arousal (eg, palpitations) (Table 6). Insomnia associated with GAD can be treated with benzodiazepines, which shorten latency to sleep, lengthens sleep, and reduces the number of night time awakenings. They are helpful in improving hypervigilance and somatic symptoms associated with GAD but less effective in improving psychological symptoms such as ruminative worry and irritability. In fact, some benzodiazepines can exacerbate irritability and depression.

Despite the benefits of benzodiazepines, there are some potential risks involved with their use such as daytime sedation, disinhibitions, dependence, and withdrawal and rebound anxiety. It is suggested that they be used for a brief time or intermittently if possible. Reemergence of anxiety is often associated discontinuation of benzodiazepines and should be distinguished from withdrawal.

Buspirone

There have been several double-blind, placebo-controlled trials comparing buspirone with benzodiazepines and placebo. Most studies demonstrated that buspirone was better than placebo but not better than benzodiazepines. It appears that previous benzodiazepine treatment is a predictor of poor response to buspirone treatment. Thus, buspirone may be best suited for patients who have never been on benzodiazepines or who have not been on benzodiazepines in a long time [39].

Advantages of buspirone are the absence of addiction, sedation, cognitive impairment, and adverse interactions with alcohol. Another important feature is that it does not decrease respiratory function like benzodiazepines, making it a reasonable alternative in patients with GAD and pulmonary disease. Disadvantages of buspirone include much slower onset than benzodiazepines, often requiring 7 to 10 days or more to have a clinical effect. Because buspirone is not a sedative, hypnotic, or muscle relaxant, it does not help associated insomnia or muscle tension in the GAD patient.

Case Continued

The patient wants to try medication and is prescribed escitalopram 10 mg daily. She says she will consider psychotherapy later during her summer break.

- **What is long-term management of GAD?**

Once a reasonable acute treatment plan has been established, a long-term treatment plan and goal should be formulated. The goal of long-term treatment should be remission and return of function. Remission is considered a HAM-A score of 7 or less, or greater than 70% improvement. Unfortunately, remission may not occur for many; 60% to 70% of GAD patients report moderate to marked improvement after 8 weeks of acute therapy and only 35% to 40% of these patients will achieve full remission [39]. Functional improvement may take some time, and it is recommended that an objective measure of the patient's progress be used to assess the degree of improvement. Once full functional capacity is achieved, long-term maintenance or discontinuation of medications should be considered [40]. The most common recommendation is to continue pharmacotherapy for at least 6 to 12 months before tapering off. In general, comorbid psychiatric disorders are usually more resistant to

treatment. Primary care physicians should refer patients to psychiatrist when GAD is complicated (ie, bipolar) or if the patient has failed 2 or more first-line agents.

CONCLUSION

GAD is a common psychiatric illness that is often overlooked. Patients can present with varying degrees of psychic and somatic symptoms, often with another comorbid illness, which can complicate the presentation. Despite the high prevalence of GAD, only 30% of sufferers are diagnosed. Increasing the awareness of GAD among patients and physicians could lead to early detection and treatment that reduces the severity of impairment and improves quality of life.

Corresponding author: Raushanah Hud-Aleem, DO, Dept. of Psychiatry, Wright State University, 627 S. Edwin C. Moses Blvd., Dayton, OH 45401.

References

1. Robins LN, Regier DA, editors. Psychiatric disorders in America: the epidemiologic catchment area study. New York: Free Press; 1991.
2. Wittchen HU, Zhao S, Kessler RC, Eaton WW. DSM-III-R generalized anxiety disorder in the National Comorbidity Survey. Arch Gen Psychiatry 1994;51:355–64.
3. Sartorius N, Ustun TB, Lecrubier Y, Wittchen HU. Depression comorbid with anxiety: results from the WHO study on psychological disorders in primary health care. Br J Psychiatry Suppl 1996;(30):38–43.
4. Maier W, Gansicke M, Freyberger HJ, et al. Generalized anxiety disorder (ICD-10) in primary care from a cross-cultural perspective: a valid diagnostic entity? Acta Psychiatr Scand 2000;101:29–36.
5. Wittchen HU, Kessler R, Beesdo K, et al. Generalized anxiety and depression in primary care: prevalence, recognition, and management. J Clin Psychiatry 2002;63 Suppl 8:24–34.
6. Stein MB. Public health perspectives on generalized anxiety disorder. J Clin Psychiatry 2004;65 Suppl 13:3–7.
7. Schweizer E. Generalized anxiety disorder. Longitudinal course and pharmacologic treatment. Psychiatr Clin North Am 1995;18:843–57.
8. Belanger L, Ladouceur R, Morin CM. Generalized anxiety disorder and health care use. Can Fam Physician 2005;51:1362–3.
9. Mussell M, Kroenke K, Spitzer RL, et al. Gastrointestinal symptoms in primary care: prevalence and association with depression and anxiety. J Psychosom Res 2008;64:605–12.
10. Belanger L, Morin CM, Langlois F, Ladouceur R. Insomnia and generalized anxiety disorder: effects of cognitive behavior therapy for GAD on insomnia symptoms. J Anxiety Disord 2004; 18:561–71.
11. Bohn P. Mnemonic screening device for generalized anxiety disorder [letter]. Am J Psychiatry 2000;157:837.
12. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166:1092–7.
13. Shear MK, Vander Bilt J, Rucci P, et al. Reliability and validity of a structured interview guide for the Hamilton anxiety rating scale (SIGH-A). Depress Anxiety 2001;13:166–78.
14. Doyle AC, Pollack MH. Establishment of remission criteria for anxiety disorders. J Clin Psychiatry 2003;64 Suppl 15:40–5.
15. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol 1988;56:893–7.
16. Belzer KD, Schneier FR. Tools for assessing generalized anxiety disorder. Psychiatric Times [serial online] 2006;23. Available at www.psychiatrictimes.com/display/article/10168/46946. Accessed 10 Jun 2008.
17. Brown TA, Antony MM, Barlow DH. Psychometric properties of the Penn State Worry Questionnaire in a clinical anxiety disorders sample. Behav Res Ther 1992;30:33–7.
18. Stober J, Bittencourt J. Weekly assessment of worry: an adaptation of the Penn State Worry Questionnaire for monitoring changes during treatment. Behav Res Ther 1998;36:645–56.
19. Nutt D, Argyropoulos S, Hood S, Potokar J. Generalized anxiety disorder: a comorbid disease. Eur Neuropsychopharmocol 2006;16 Suppl 2:S109–18.
20. Kroenke K, Spitzer RL, Williams JB, et al. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Ann Intern Med 2007;146:317–25.
21. Nutt DJ, Ballenger JC, Sheehan D, Wittchen HU. Generalized anxiety disorder: comorbidity comparative biology and treatment. Int J Neuropsychopharmacol 2002;5:315–25.
22. Sevy S, Papadimitriou GN, Surmont DW, et al. Noradrenergic function in generalized anxiety disorder, major depressive disorder, and healthy subjects. Biol Psychiatry 1989;25:141–52.
23. Yonkers KA, Warshaw MG, Massion AO, Keller MB. Phenomenology and course of generalised anxiety disorder. Br J Psychiatry 1996;168:308–13.
24. Brawman-Mintzer O, Lydiard RB. Generalized anxiety disorder: issues in epidemiology. J Clin Psychiatry 1996;57 Suppl 7: 3–8.
25. Kessler RC, Wittchen HU. Patterns and correlates of generalized anxiety disorder in community samples. J Clin Psychiatry 2002;63 Suppl 8:4–10.
26. Catalan J, Gath D, Edmonds G, Ennis J. The effects of non-prescribing of anxiolytics in general practice. I. Controlled evaluation of psychiatric and social outcome. Br J Psychiatry 1984;144:593–602.
27. Gath D, Catalan J. Evaluation of the outcome of brief psychological treatments in primary care. Presented at The Treatment of Mental Disorders in General Health Care Settings: A Research Conference; 1988 Jun 15–17; Pittsburgh, PA.
28. Linden M, Zubraegel D, Baer T, et al. Efficacy of cognitive behaviour therapy in generalized anxiety disorders. Results of a controlled clinical trial (Berlin CBT-GAD Study). Psychother Psychosom 2005;74:36–42.
29. Hunot V, Churchill R, Silva de Lima M, Teixeira V. Psychological therapies for generalised anxiety disorder. Cochrane Database Syst Rev 2007;(1):CD001848.
30. Covin R, Ouimet AJ, Seeds PM, Dozois DJ. A meta-analysis of CBT for pathological worry among clients with GAD. J Anxiety Disord 2008;22:108–16.

31. Fisher PL, Durham RC. Recovery rates in generalized anxiety disorder following psychological therapy: an analysis of clinically significant change in the STAI-T across outcome studies since 1990. Psychol Med 1999;29:1425–34.
32. Rickels K, Downing R, Schweizer E, Hassman H. Antidepressants for the treatment of generalized anxiety disorder. A placebo-controlled comparison of imipramine, trazodone, and diazepam. Arch Gen Psychiatry 1993;50:884–95.
33. Rocca P, Fonzo V, Scotta M, et al. Paroxetine efficacy in the treatment of generalized anxiety disorder. Acta Psychiatr Scand 1997; 95:444–50.
34. Allgulander C, Hackett D, Salinas E. Venlafaxine extended release (ER) in the treatment of generalized anxiety disorder: twenty-four-week placebo-controlled dose-ranging study. Br J Psychiatry 2001;179:15–22.
35. Davidson JR, DuPont RL, Hedges D, Haskins JT. Efficacy, safety, and tolerability of venlafaxine extended release and buspirone in outpatients with generalized anxiety disorder. J Clin Psychiatry 1999;60:528–35.
36. Gelenberg AJ, Lydiard RB, Rudolph RL, et al. Efficacy of venlafaxine extended-release capsules in nondepressed outpatients with generalized anxiety disorder: a 6-month controlled trial. JAMA 2000;283:3082–8.
37. Rickels K, Pollack MH, Sheehan DV, Haskins JT. Efficacy of extended-release venlafaxine in nondepressed outpatients with generalized anxiety disorder. Am J Psychiatry 2000; 157:968–74.
38. Dubovsky SL. Generalized anxiety disorder: new concepts and psychopharmacologic therapies. J Clin Psychiatry 1990;51 Suppl:3–10.
39. Rickels K, Rynn M. Pharmacotherapy of generalized anxiety disorder. J Clin Psychiatry 2002;63 Suppl 14:9–16.
40. Culpepper L. Use of algorithms to treat anxiety in primary care. J Clin Psychiatry 2003;64 Suppl 2:30–3.

Copyright 2008 by Turner White Communications Inc., Wayne, PA. All rights reserved.

JCOM CME WAYNE STATE UNIVERSITY

CME EVALUATION: Generalized Anxiety Disorder in Adults

DIRECTIONS: Each of the questions below is followed by several possible answers. Select the ONE lettered answer that is BEST in each case and circle the corresponding letter on the answer sheet.

1. All of the following symptoms may be present in generalized anxiety disorder (GAD) EXCEPT
   A. Easily fatigued
   B. Irritability
   C. Mind going blank
   D. Hypersomnia
   E. Initial insomnia

2. What is the prevalence of GAD in primary care settings?
   A. 47%
   B. 20%
   C. 8%
   D. 2%

3. Which of the following is the most common comorbid psychiatric illness associated with GAD?
   A. Bipolar disorder
   B. Major depression
   C. Panic disorder
   D. Substance use disorder

4. Which of the following would be considered first-line pharmacologic treatment for GAD?
   A. Alprazolam
   B. Buspirone
   C. Monoamine oxidase inhibitor
   D. Paroxetine

5. A 30-year-old woman presents to her primary care physician complaining of excessive anxiety and worry about work and family for 6 months. She describes that she is constantly on edge, has difficulty concentrating, and cannot sleep. Results of laboratory testing, including complete blood count, thyroid function tests, and fasting complete metabolic panel, are within normal limits. Urinalysis is unremarkable. A diagnosis of GAD is made. How should this patient be treated?
   A. Initiate a benzodiazepine
   B. Initiate a selective serotonin reuptake inhibitor
   C. Initiate a tricyclic antidepressant
   D. Treatment is not necessary unless symptoms persist for 12 months

WAYNE STATE UNIVERSITY

JCOM CME

EVALUATION FORM: Generalized Anxiety Disorder in Adults

Participants may earn 1 credit by reading the article named above and correctly answering at least 70% of the accompanying test questions. A certificate of credit and the correct answers will be mailed within 6 weeks of receipt of this page to those who successfully complete the test.

Circle your answer to the CME questions below:

1.	A	B	C	D	E
2.	A	B	C	D	
3.	A	B	C	D	
4.	A	B	C	D	
5.	A	B	C	D	

Please answer the following questions:

1. How would you rate this educational activity overall?
   __ Excellent __ Good __ Fair __ Poor

2. This article was fair, balanced, free of commercial bias, and fully supported by scientific evidence.
   __ Yes __ No

3. Please rate the clarity of the material presented in the article.
   __ Very clear __ Somewhat clear __ Not at all clear

4. How helpful to your clinical practice was this article?
   __ Very helpful __ Somewhat helpful __ Not at all helpful

5. What changes will you make in your practice as a result of reading this article?
   _____
   _____
   _____
   _____
   _____
   _____

6. What topics would you like to see presented in the future?
   _____
   _____
   _____
   _____
   _____
   _____

Release date: 15 July 2008
Expiration date: 30 July 2009

Please print clearly:

Name:_____

MD/DO/Other: _____

Address: _____

_____

City: _____

State:_____ Zip:_____

Phone: _____

Fax: _____

E-mail: _____

Are you a health care professional licensed to practice in the US/Canada who can use Category 1 AMA PRA CME credit to fulfill educational requirements? ____ Yes ____ No

Physicians are required to report the actual amount of time spent on the activity, up to the maximum designated 1 hour. The actual time spent reading this article and completing the test was _____.

Please mail or fax this sheet to:

Wayne State University, Division of CME
101 E. Alexandrine, Lower Level
Detroit, MI 48201

FAX: 313-577-7554

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Wayne State University School of Medicine and the *Journal of Clinical Outcomes Management.* Wayne State University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Wayne State University School of Medicine designates this educational activity for a maximum of 1 AMA PRA Category 1 credits. Physicians should only claim credit commensurate with the extent of their participation in the activity.