Generalized Anxiety Disorder in Adults
Case Study and Commentary, Raushanah Hud-Aleem, DO, and Darnell Ladson, DO

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.
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?

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).

- What are key components of the assessment?

The DSM-IV-TR diagnostic criteria for GAD are listed in Table 2. 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, hypothyroidism) and does not occur exclusively during exacerbations of an Axis I disorder (eg, mood disorder or psychotic disorder)


Table 1. Symptoms and Behaviors Associated with Generalized Anxiety Disorder

<table>
<thead>
<tr>
<th>Excessive physiologic arousal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle tension</td>
</tr>
<tr>
<td>Irritability</td>
</tr>
<tr>
<td>Fatigue</td>
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<tr>
<td>Restlessness</td>
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<tr>
<td>Insomnia</td>
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<tr>
<td>Distorted cognitive processes</td>
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<tr>
<td>Poor concentration</td>
</tr>
<tr>
<td>Unrealistic assessment of problems</td>
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<tr>
<td>Worries</td>
</tr>
<tr>
<td>Poor coping strategies</td>
</tr>
<tr>
<td>Avoidance</td>
</tr>
<tr>
<td>Procrastination</td>
</tr>
<tr>
<td>Poor problem-solving skills</td>
</tr>
</tbody>
</table>


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)
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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
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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, hypothyroidism) and does not occur exclusively during exacerbations of an Axis I disorder (eg, mood disorder or psychotic disorder)

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
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
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<sub>A</sub> 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...

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**Table 3. Core Features of 5 Main Anxiety Disorders**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Social Anxiety Disorder (Social Phobia)</th>
<th>Obsessive-Compulsive Disorder</th>
<th>Posttraumatic Stress Disorder</th>
<th>Generalized Anxiety Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panicky Disorder</td>
<td>Fearful of another attack occurring</td>
<td>Persistent (6 months), uncontrollable worrying</td>
<td>Somatic anxiety (tension, insomnia, hypervigilance)</td>
<td></td>
</tr>
</tbody>
</table>


**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

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

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


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
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.

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Dose (mg/d)</th>
<th>Dose Range (mg/d)</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Alprazolam</td>
<td>1</td>
<td>2–10</td>
<td>Rapid onset of action; favorable side effects</td>
<td>Sedation; multiple doses for shorter-acting agents; physical dependence; limited antidepressant effect; sexual side effects</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.75</td>
<td>3–10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>4</td>
<td>4–40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonazepam</td>
<td>0.25</td>
<td>1–5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCAs</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Clomipramine</td>
<td>25</td>
<td>25–250</td>
<td>Once-daily dosing; effective treating comorbid depression</td>
<td>Delayed onset; need for titration; activation; anticholinergic effects; orthostatic hypotension; weight gain; toxicity in overdose; sexual side effects</td>
</tr>
<tr>
<td>Desipramine</td>
<td>10</td>
<td>150–300</td>
<td></td>
<td></td>
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<tr>
<td>Nortriptyline</td>
<td>10</td>
<td>75–150</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imipramine</td>
<td>75</td>
<td>50–200</td>
<td></td>
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<tr>
<td>SSRIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine</td>
<td>10</td>
<td>20–40</td>
<td>Effective in GAD and comorbid depression; favorable side effects when compared with TCAs; easy dosing</td>
<td>Gastrointestinal side effects; delayed onset; sexual side effects</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>10</td>
<td>10–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>5–10</td>
<td>10–80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sertraline</td>
<td>25</td>
<td>25–200</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>10</td>
<td>20–60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>25</td>
<td>25–300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SNRIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine XR</td>
<td>10</td>
<td>20–10</td>
<td>Effective in GAD, depression, and pain</td>
<td>May elevate blood pressure; nausea, vomiting, dizziness, sweating; sexual side effects</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>30</td>
<td>75–300</td>
<td></td>
<td></td>
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<tr>
<td>Atypicals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nefazodone</td>
<td>100</td>
<td>300–600</td>
<td>Effective for treating comorbid depression; low anticholinergic effects</td>
<td>Delayed onset; orthostatic hypotension; weight gain; sexual side effects; priapism; sedation; nefazodone can cause liver failure</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>15</td>
<td>15–45</td>
<td></td>
<td></td>
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<tr>
<td>5HT₁A partial agonists</td>
<td></td>
<td></td>
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<tr>
<td>Buspirone</td>
<td>15</td>
<td>30–60</td>
<td>No physical/ psychological dependence</td>
<td>Nausea, drowsiness, dizziness, headache; not as useful in patients with previous exposure to benzodiazepines</td>
</tr>
</tbody>
</table>

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 plateaued 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 psychiatrists when GAD is complicated (i.e., 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.

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**References**


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
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
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   _ Excellent  _ Good  _ Fair  _ Poor

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