In the Clinic

Generalized Anxiety Disorder

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CME Objective: To review current evidence for the screening, diagnosis, treatment, and practice improvement of generalized anxiety disorder.

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Annals of Internal Medicine

in the clinic

Anxiety can be an appropriate response to stressful situations but is considered a pathologic disorder when it is disabling and difficult to control. Generalized anxiety disorder (GAD) is the most common anxiety disorder seen in primary care, affecting approximately 3% of adults in the United States (1, 2). This disorder is characterized by at least 6 months of pervasive and excessive anxiety; recurring worry about common events; and physical symptoms, such as muscle tension, insomnia, and fatigue (3). The disorder is associated with reduced global life satisfaction, decreased work productivity, lower health-related quality of life (4), and greater health care use and medical costs (4, 5). Primary care physicians can effectively evaluate, diagnosis, and manage most patients with GAD.

Screening

Which patients are at elevated risk for generalized anxiety disorder?

GAD is twice as common in women as in men (6). Patients with comorbid psychiatric disorders (7, 8), obesity (9), history of substance abuse (10), history of trauma (11, 12), and family history of GAD (13) are also at increased risk for GAD.

A meta-analysis of family and twin studies of common anxiety disorders showed a significant association between GAD in patients and their first-degree relatives, with an odds ratio of 6.1 (95% CI, 2.5–14.9) (13).

Are preventive measures useful for patients at elevated risk?

Although prevention or early intervention may reduce the excess disability due to mental disorders, currently there is no evidence on the effectiveness of preventive measures for GAD in adults. However, in children who exhibit withdrawn behavior or early signs of anxiety, cognitive behavioral therapy (CBT) and parent education can prevent development of GAD (14, 15), suggesting the possibility of benefit in adults as well.

Should clinicians screen patients for generalized anxiety disorder if they are at increased risk? If so, how?

Although there are no high-quality studies demonstrating a benefit to screening or to early treatment for GAD, the disorder is undertreated: 58% of persons diagnosed with GAD go untreated (16, 17). As seen in depression care, better detection may be the first step in addressing underdiagnosis and undertreatment and in improving patient outcomes (18).

The screening tools to detect GAD vary in length and number of additional disorders included in the tool. Two brief and accurate options may be most feasible in primary care: the Generalized Anxiety Disorder-2 (GAD-2) (see the Box: Screening Questions for Generalized Anxiety Disorder) and the single-item screening question, "Are you bothered by nerves?" In the 2-item GAD-2 tool, the response to each question is given a score of 0, 1, 2, or 3 (for a total score of 0 to 6). A score of 3 or more has a sensitivity of 86% and specificity of 83% for detecting GAD in a primary care setting (19). The single item screening question, "Are you bothered by nerves?" has 100% sensitivity and 59% specificity among average-risk primary care patients (20). Alternatively, the Generalized Anxiety Disorder-7 (GAD-7) scale (21) and the Primary Care Evaluation of Mental Disorders (PRIME-MD) (22) are slightly longer screening tools that include additional questions to assess symptom severity and can thus be used to monitor symptoms. The 4-item Patient Health Questionnaire (PHQ-4) (23) provides an ultrabrief screen for both depression and anxiety.

Screening Questions for Generalized Anxiety Disorder: GAD-2 Screening Instrument

During the past month, have you been bothered a lot by:

1. Nerves or feeling anxious or on edge?
   - 0: Not at all
   - 1: Several days
   - 2: More than half of the days
   - 3: Nearly every day
2. Worrying about a lot of different things?
   - 0: Not at all
   - 1: Several days
   - 2: More than half of the days
   - 3: Nearly every day

The response to each question is given a score of 0, 1, 2, or 3. The best screening cut-off score is a 3 (19).

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Kroenke and colleagues found no significant difference between GAD-7 and GAD-2 when screening for GAD in primary care patients (19).

Patients who screen positive by any tool should be further evaluated to assess whether they meet diagnostic criteria according to the *Diagnostic and Statistical Manual of Mental Disorders, fifth edition* (DSM-V) (see the Box: Diagnostic Criteria for Generalized Anxiety Disorder) (3).

SCREENING... Clinicians might consider screening for GAD among adults who are at increased risk. Multiple screening tools have similar sensitivity and specificity, so a busy clinician might be inclined to use a tool with as few as 1 or 2 questions.

CLINICAL BOTTOM LINE

Diagnosis

What symptoms should prompt clinicians to consider a diagnosis of generalized anxiety disorder?
GAD is characterized by excessive and difficult-to-control worries about everyday events and problems, resulting in distress or marked trouble in performing day-to-day tasks. According to the DSM-V (see the Box), the excessive anxiety and worry of GAD is associated with 3 or more of the following symptoms occurring on more days than not for at least 6 months: restlessness, difficulty concentrating, irritability, muscle tension, or sleep disturbance. Patients must meet all 6 diagnostic criteria.

What physical examination findings indicate possible generalized anxiety disorder?
A patient with GAD can appear restless, irritable, or fatigued. In primary care settings, patients with GAD may also have medically unexplained symptoms, such as chest pain and rapid heart rate (18). A thorough physical

Diagnostic Criteria for Generalized Anxiety Disorder

Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).

The individual finds it difficult to control the worry.

The anxiety and worry are associated with 3 (or more) of the following 6 symptoms (with at least some symptoms having been present for more days than not for the past 6 months):

- Restless or feeling keyed up or on edge.
- Being easily fatigued.
- Difficulty concentrating or mind going blank.
- Irritability.
- Muscle tension.
- Sleep disturbances (difficulty falling or staying asleep, or restless, unsatisfying sleep).

The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

The disturbance is not attributable to the physiologic effects of a substance (e.g., drug of abuse, medication) or another medical condition (e.g., hyperthyroidism).

The disturbance is not better explained by another mental disorder (e.g., anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder [social phobia], contamination or other obsessions in obsessive-compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical problems in somatic symptoms disorder, body dysmorphic disorder, having a serious illness in illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder).

Patients must meet all 6 criteria for a diagnosis of generalized anxiety disorder.

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examination is necessary and may uncover an underlying or co-occurring medical condition that requires further evaluation (3).

What laboratory tests should clinicians use?

No laboratory testing is necessary to diagnose GAD. However, clinicians should consider directed laboratory testing to exclude medical conditions suggested by the presenting symptoms as well as physical signs found during the evaluation (24). Among the most useful tests in patients presenting with symptoms of anxiety are thyroid function tests to exclude thyroid disease, hemoglobin measurement to exclude anemia, and a urine drug screen if substance use is a potential concern, but other routine laboratory testing has a low yield. In particular, catecholamine levels to check for pheochromocytoma should primarily be limited to persons with a family history of endocrine disorders or those with episodic hypertension, headaches, and palpitations.

What other diagnoses should clinicians consider?

Several physical and mental disorders can mimic or co-occur with GAD (Table 1). In fact, more than half of patients with GAD have comorbid mental illnesses (6). In evaluating patients for GAD, clinicians should consider medical conditions (e.g., cardiac, pulmonary, or endocrine illnesses); mood and other anxiety disorders, such as simple or social phobia, panic disorder, obsessive-compulsive disorder, acute stress disorder, and posttraumatic stress disorder; side effects of prescribed or over-the-counter medications and supplements; and substance misuse and withdrawal. Patients with GAD may use alcohol and benzodiazepines to control anxiety, so clinicians should be vigilant to assess for substance misuse. If symptoms of anxiety persist after appropriate treatment of physical

Differential Diagnosis for Generalized Anxiety Disorder

Disease	*Notes*
Cardiopulmonary disorders (such as asthma, chronic obstructive pulmonary disease, or congestive heart failure)	These disorders can co-occur with generalized anxiety disorder or mimic anxiety symptoms. Medications used to treat these disorders, such as β-agonists, may also cause symptoms mimicking generalized anxiety disorder.
Endocrine disease, including thyroid disorders, diabetes, and hypoglycemia	Many endocrine disorders (most commonly hyperthyroidism, hypoglycemia, or hypothyroidism) can mimic anxiety symptoms. Consider thyroid function tests and blood glucose testing. Consider catecholamine level testing, limited to patients with a family history of endocrine neoplasms or those with episodic headaches, hypertension, and palpitations, for evaluation of pheochromocytoma.
Mood disorders, including major depressive disorder and bipolar disorder	Generalized anxiety disorder and mood disorders frequently co-occur. Symptoms of mood disorders should be treated first. As the depression is treated, symptoms of generalized anxiety disorder may become more apparent.
Other anxiety disorders, including simple or social phobia, panic disorder, obsessive-compulsive disorder, acute stress disorder, and posttraumatic stress disorder	Generalized anxiety disorder can be diagnosed in the presence of any other anxiety disorder if there is disabling, generalized worry in addition to other symptoms.
Prescribed and over-the-counter medications	Corticosteroids, sympathomimetics, and herbal medications (such as ginseng) may mimic symptoms of generalized anxiety disorder.
Misuse of such substances as alcohol, benzodiazepines, caffeine, nicotine, amphetamine, cocaine, and other stimulants	Stimulant (nicotine, caffeine, amphetamines, cocaine, and various "party pills") intoxication can cause anxiety and mimic generalized anxiety disorder. Anxiety is also a symptom of alcohol and benzodiazepine withdrawal. Consider ordering a drug screen and taking a detailed history if substance use is suspected.

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and other mental disorders, clinicians should consider screening for GAD.

Epidemiologic data indicate that 69%–95% of patients with GAD have a co-occurring psychiatric disorder. Between 45% and 70% of GAD patients had a comorbid mood disorder, mainly depression, and 38% to 56% had another anxiety disorder, such as panic disorder, social anxiety disorder, and posttraumatic stress disorder (6).

When should clinicians consider consulting with a psychologist, psychiatrist, or other specialist?

Most patients with GAD can be diagnosed by a primary care physician. However, in cases of diagnostic uncertainty clinicians should consider obtaining a second opinion from a psychologist, psychiatrist, or other mental health specialist.

DIAGNOSIS... A thorough history is the foundation of diagnosing GAD. Laboratory testing in patients with GAD can be deferred unless underlying medical disorders are suspected. Comorbid mental illness is common among patients with GAD and should be assessed in each patient. Clinicians should consider consulting a psychiatrist, psychologist, or other mental health specialist if the diagnosis of GAD is uncertain.

CLINICAL BOTTOM LINE

Treatment

What nondrug therapies should clinicians recommend for generalized anxiety disorder?

CBT is the cornerstone of treatment in adults with GAD (Table 2). The primary goal of this therapy is to help patients identify distressing and dysfunctional beliefs and thought patterns, which are often irrational or unrealistic, and replace them with more rational and realistic views (25-29). Clinicians should refer patients to mental health specialists who are specifically trained in CBT. Other nondrug therapies, described in Table 2, can augment or replace CBT if it is not available or is ineffective.

A meta-analysis of 108 controlled trials assessed the effectiveness of CBT alone,

Nondrug Therapies for Patients With Generalized Anxiety Disorder

Nondrug Therapy	*Notes*
Cognitive behavior therapy	Consists of 12–20 sessions, which can involve education, exposure therapy, relaxation training, and problem-solving techniques.
Short-term psychodynamic psychotherapy	Focuses on revealing and resolving unconscious conflicts that are driving anxiety symptoms. Psychodynamic psychotherapy relies on the interpersonal relationship between patient and therapist.
Relaxation training	Various techniques that help a patient to relax and reduce anxiety states. For example, progressive relaxation is a technique taught to patients to systematically identify and relax specific muscle groups.
Self-help and self-examination therapy	Designed to be conducted predominately independently and consists of therapeutic interventions administered through text or audio/video media to mediate anxiety symptoms.
Worry exposure or exposure therapy	The patient stays in an anxiety-provoking or feared situation until the distress or anxiety diminishes. The goal is to learn not react to the situation.

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CBT plus relaxation, CBT plus exposure, CBT plus relaxation and exposure, and relaxation and exposure. All tested therapies improved pre- to posttreatment measures of anxiety in GAD when compared with no treatment. The estimated effect size, from greatest to least magnitude, was 2.08 for relaxation plus CBT, 2.06 for CBT alone, 2.02 for CBT plus exposure, 1.72 for relaxation and exposure, and 1.54 for CBT plus relaxation and exposure (28). A recent meta-analysis failed to show that aerobic exercise had any significant effect on treatment for anxiety disorders (30).

How should clinicians choose and dose drug therapy?

For most adults with GAD, clinicians should offer drug therapy (Table 3) when CBT or other nondrug therapies are not available or are ineffective or if the patient is not interested in nondrug therapy. Second-generation antidepressants,

Drug Treatment for Generalized Anxiety Disorder

Class of Agent	*Specific Agent, Daily Dose*	*Benefits*	*Side Effects and Notes*
First-line medications: second-generation antidepressants		As a class: effective, well tolerated	As a class: nausea, diarrhea, decreased appetite, nervousness, insomnia, somnolence, impaired sexual function, and hyponatremia
	Citalopram, 10–40 mg	Few drug interactions	See class effects
	Escitalopram, 10–20 mg/d	Few drug interactions	See class effects
	Paroxetine, 20–60 mg/d	Long clinical experience	More weight gain and sexual adverse effects; withdrawal syndrome not uncommon.
	Sertraline, 50–200 mg/d	Long clinical experience	Higher incidence of diarrhea
	Duloxetine, 60–120 mg/d	Maybe effective in patients with anxiety and comorbid pain	Agitation, urine retention; withdrawal symptoms
	Venlafaxine, 75–225 mg/d	Similar efficacy to other second–generation antidepressants	May increase blood pressure
Second-line medications			
Azapirones		As a class: lack abuse potential and are not addictive	As a class: dizziness, drowsiness
	Buspirone, 15–30 mg/d	Can be used for augmentation	See class effects
	Gepirone, 10–45 mg/d	See class benefits	Not available in the United States
	Ipsapirone, 10–30 mg/d	See class benefits	Not available in the United States
Benzodiazepines	Alprazolam, 0.5–2 mg/d; diazepam, 2–10 mg/d; chlordiazepoxide, 15–40 mg/d	As a class: very effective, particularly in the short term; faster onset of action than antidepressants	As a class: falls, memory impairment, risk dependence
Third-line medications			Clinicians should consider consulting with a mental health specialist if unfamiliar with these therapies.
Atypical antipsychotics	Olanzapine, 2.5–20 mg/d; risperidone, 0.5 –1.5 mg/d	Should be reserved for treatment-refractory cases	As a class: sedation, extrapyramidal symptoms, tardive dyskinesia, weight gain and metabolic side effects.
Antihistamine	Hydroxyzine 50–100 mg 4 times/d	Potentially useful for treating insomnia associated with generalized anxiety disorder	Sedation, dry mouth, confusion, and urine retention
Anticonvulsant	Pregabalin, 300–600 mg/d	Well tolerated; effects were significant as early as week 1	Sedation, rash

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such as the selective serotonin reuptake inhibitors, are preferred as first-line drug therapy because they are as effective as benzodiazepines but lack the risk for dependency and cognitive impairment (31-39). In patients older than 60 years, a randomized, controlled trial suggested that sertraline may be superior to CBT for treating anxiety (40). Patient preference and potential side effects should guide decisions on drug therapy. Short-term treatment with alprazolam or diazepam can rapidly control anxiety symptoms during the period before the anxiolytic properties of an antidepressant take effect (41). Clinicians can consider prescribing a benzodiazepine for 4 weeks, followed by a 2- to 4-week taper. Diazepam may also enhance the effect of psychological treatment in patients who are initially unresponsive to this treatment alone (31). However, clinicians must balance the benefits of benzodiazepines with the risk for dependence and cognitive impairment or delirium.

Azapirones, such as buspirone, are alternatives to benzodiazepines. Two systematic reviews have shown that azapirones are superior to placebo and equivalent to benzodiazepines in the treatment of GAD (31, 42). However, sedation and dizziness are common side effects of these drugs and can occur more frequently than in patients given benzodiazepines. Azapirones can also take weeks to achieve their effect. If antidepressants, azapirones, or benzodiazepines are ineffective or poorly tolerated, alternative medication options include antipsychotics (43, 44), hydroxyzine (31), and pregabalin (31, 45, 46). All have proven effectiveness in GAD but have significant side effects. Clinicians should consider consulting with a mental health specialist before prescribing these infrequently used drugs.

How should clinicians monitor patients?

Patients with GAD should be monitored in person or by phone every 2 to 4 weeks until stable and then every 3 to 4 months during maintenance therapy. Structured instruments may help clinicians monitor symptom severity in patients with GAD. However, there is little evidence to recommend one instrument over another and several are available. The PRIME-MD (22) and GAD-7 (Table 4) (21) can be used to guide diagnosis and monitor symptoms. Each response in the GAD-7 is assigned a value of 0, 1, 2, or 3; summary scores of 5, 10, and 15 are cut-off points for mild, moderate, and severe anxiety. There are no formal recommendations for treatment discontinuation or augmentation based on GAD-7 scores. Downloadable forms of this instrument are available in over 50 languages (www.phqscreeners.com/) (47). The new DSM-V includes a variety of additional monitoring instruments, including one that monitors symptom severity in adults with

Generalized Anxiety Disorder 7-Item Scale

Over the last 2 weeks, how often have you been bothered by the following problems?	*Not at all*	*Several days*	*Over 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's 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

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GAD (www.psychiatry.org/practice/dsm/dsm5/online-assessment-measures#Disorder) (48). However, these additional instruments have not been evaluated as rigorously as the GAD-7 and may be more cumbersome to use in a busy primary care practice. Along with symptom assessment, clinicians should consistently ask about medication adherence, treatment side effects, and suicide risk.

Pharmacotherapy should be continued for 6–12 months after symptom response is achieved (48). After discontinuation of medications, 20%–40% of patients relapse within 6–12 months (49, 50). Some patients with severe chronic anxiety for many years may require long-term medication (>1 year) (49).

A trial of continuation of treatment among 429 GAD patients who had responded previously to duloxetine found that only 13.7% of patients who continued treatment relapsed over the 26-week continuation phase compared with 41.8% of patients receiving placebo during the same period (50).

When should patients be hospitalized?

Although most patients with GAD can be treated as outpatients, patients with GAD who are actively suicidal should be hospitalized. Suicidal ideation is not uncommon in patients with GAD with or without co-occurring depression. Clinicians should assess risk for suicide in all patients with GAD at each follow-up encounter (51). Many of the screening and monitoring instruments do not include a question about suicidality, so clinicians might consider using the following item from PRIME-MD: "Over the last 2 weeks, how often have you been bothered by thoughts that you would be better off dead or of hurting yourself in some way?" (www.phqscreeners.com/).

A meta-analysis of suicide risk among participants in recent clinical trials of new antianxiety medications found that among 4333 patients in GAD treatment trial, the crude death rate due to suicide was 0.05%. Information on suicide attempts was not available (51).

Hospitalization might also be required for intractable symptoms, for grave disability, or to address co-occurring illness. GAD can complicate treatment of co-occurring disorders and adversely affects prognosis.

In a cohort of U.S. veterans, co-occurring depression and GAD was associated with increased cardiovascular mortality (hazard ratio, 2.68 [CI, 1.22–5.88]) (52).

When should clinicians consider consulting a psychologist, psychiatrist, or other specialist?

Consultation with a psychologist, psychiatrist, or other specialist should be considered if patients have not improved after 12–16 weeks of CBT or if they do not respond after 6 weeks of first- or second-line medication therapy. Consultation is also warranted if patients are unable to tolerate drug therapy; express suicidal thoughts; or have comorbid substance, mood, or anxiety disorders or if the clinician is considering prescribing third-line medications.

TREATMENT... Primary care physicians play an important role in managing anxiety disorders. CBT is the treatment of choice for GAD in most adults. If CBT is not available, is ineffective, or if the patient is not interested in nondrug therapy, then second-generation antidepressants are the first-line medication options. Clinicians should assess risk for suicide in all GAD patients and refer more complex GAD patients to mental health specialists.

CLINICAL BOTTOM LINE

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Practice Improvement

Are there measures that stakeholders use to evaluate the quality of care for patients with generalized anxiety disorder?

Currently, there are no recommended measures to evaluate the quality of GAD care. However a study from the University of California, San Diego, used the following 3 metrics as quality indicators in the treatment of primary care patients with anxiety disorders in university-affiliated outpatient clinics: mental health referral, anxiety counseling, and use of appropriate antianxiety medications during the previous 3 months. In this population, less than 1 in 3 patients had received anxiety treatment that met a single quality-of-care indicator (53). These metrics could be implemented for quality improvement programs; however, their impact on patient outcomes are not yet known.

What do professional organizations recommend regarding the care of patients with generalized anxiety disorder?

There are currently no formal practice guidelines from U.S. professional societies for the management of GAD. The United Kingdom's National Institute for Health and Clinical Excellence (NICE) published clinical guidelines for GAD and panic disorder in 2011 (www.nice.org.uk/cg113). These guidelines describe a stepped-care model for GAD management (54). Step 1 involves patient education and active monitoring as first-line treatment. Step 2 involves low-intensity psychological interventions for patients who do not improve with step 1. Step 3 involves CBT or drug treatment for patients who do not respond to step 2 or who have marked functional impairment. The final step, step 4, involves mental health specialists, complex drug and/or psychological treatment regimens, and hospitalization for treatment-refractory patients or individuals at risk for self-harm or self-neglect.

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In the Clinic

Tool Kit

Generalized Anxiety Disorder

ACP Smart Medicine Module

http://smartmedicine.acponline.org/content.aspx?gbosId=58

ACP Smart Medicine on generalized anxiety disorder from the American College of Physicians.

Patient Information

www.nlm.nih.gov/medlineplus/anxiety.html

www.nlm.nih.gov/medlineplus/ency/article/000917.htm

www.nlm.nih.gov/medlineplus/spanish/ency/article/000917.htm

Resources related to anxiety from MedlinePLUS of the National Institutes of Health (NIH), including patient handouts in English and Spanish.

http://nihseniorhealth.gov/anxietydisorders/aboutanxietydisorders/01.html

http://nihseniorhealth.gov/videolist.html#anxietydisorders

http://nihseniorhealth.gov/anxietydisorders/quizzes.html

Information on anxiety from the NIH Senior Health, including videos and tutorials.

www.nimh.nih.gov/health/publications/generalized-anxiety-disorder-gad/generalized-anxiety-disorder-gad-when-worry-gets-out-of-control.shtml

www.nimh.nih.gov/health/publications/espanol/trastorno-de-ansiedad-generalizada-cuando-no-se-pueden-controlar-las-preocupaciones/index.shtml

Patient handouts on generalized anxiety disorders from the National Institute of Mental Health, in English and Spanish.

Clinical Guidelines

www.guidelines.gov/content.aspx?id=34280

Practice guideline on the management of generalized anxiety disorder and panic disorder in adults from the United Kingdom's National Institute for Health and Clinical Excellence, released in 2011.

http://summaries.cochrane.org/CD001848/psychological-therapies-for-people-with-generalised-anxiety-disorder

*http://summaries.cochrane.org/CD008120/second-generation-antipsychotic-drugs-for-anxiety-disorders_*

Cochrane review on psychological therapies for people with generalized anxiety disorder, published in 2010, and on second-generation antipsychotic drugs for anxiety disorders, published in 2011.

Diagnostic Tests and Criteria

http://smartmedicine.acponline.org/content.aspx?gbosId=58

Screening tools (GAD-2 Screening Instrument; Selected CIS-R Questions for Anxiety; Kessler 6 Scale; SIGH-A Scale) for assessing generalized anxiety disorder from ACP Smart Medicine.

http://smartmedicine.acponline.org/content.aspx?gbosId=58

List of laboratory and other tests for generalized anxiety disorder from ACP Smart Medicine.

in the clinic

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THINGS YOU SHOULD KNOW ABOUT ANXIETY

In the Clinic
Annals of Internal Medicine

What is anxiety?

- Everyone feels worried or fearful sometimes.
- But in some people, these feelings become overwhelming, persistent, or interfere with daily life.
- Anxiety disorders include panic disorder, phobias, obsessive-compulsive disorder, and posttraumatic stress disorder.

What are the signs and symptoms?

- Extreme nervousness or worry.
- Feeling intensely panicked.
- Feeling a sense of doom or powerlessness.
- Rapid breathing (hyperventilating) and an increased heart rate.
- Sweating.
- Trembling or feeling weak or tired.
- Irresistible urges to perform purposeless acts or rituals.
- Reexperiencing the feelings of traumatic events.

How is it diagnosed?

- Your doctor will ask questions about your symptoms and conduct a careful examination.
- Laboratory tests or other tests may help identify whether your anxiety has a medical cause.

- Underlying causes for anxiety include heart disease, diabetes, thyroid problems, asthma, and drug abuse or alcohol withdrawal.

How is it treated?

- Psychotherapy (also known as cognitive behavioral therapy or psychological counseling).
- Lifestyle changes, such as avoiding alcohol and coffee and quitting smoking.
- Relaxation techniques, such as meditation or regular exercise.
- Medication, such as an antidepressant or antianxiety medication.

For More Information

www.adaa.org/
Education, support, and other resources on anxiety disorders from the Anxiety and Depression Association of America.

www.apa.org/helpcenter/anxiety-treatment.aspx
www.apa.org/centrodeapoyo/tratamiento.aspx
Answers to frequently asked questions about anxiety disorders from the American Psychological Association, in English and Spanish.

www.nimh.nih.gov/health/publications/mental-health-medications/complete-index.shtml
Information on mental health medications and on psychotherapy options, from the National Institute of Mental Health.

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Patient Information

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CME Questions

MKSAP
MEDICAL KNOWLEDGE Self-Assessment Program

1. A 38-year-old woman is evaluated for a 2-year history of irritability and frequent headaches, accompanied by nausea and sweating. She is a housecleaner and has had increasing difficulty concentrating at work over the past year, and it takes her much longer to clean houses lately. She has a difficult time getting to sleep and frequently arises after 2 to 3 hours of fitful sleep in bed. Her mood is good. She worries frequently about her ability to pay her bills and what she will do for retirement. She has cut back on activities with friends and does not like to go out in social situations anymore. She has asthma, and her only current medication is albuterol as needed.

   On physical examination, she is afebrile, blood pressure is 130/72 mm Hg, pulse rate is 98/min, and respiration rate is 14/min. BMI is 22. Serum thyroid-stimulating hormone level, complete blood count, and urinalysis are normal.

   Which of the following is the most likely diagnosis?

   A. Attention deficit–hyperactivity disorder
   B. Bipolar disorder
   C. Generalized anxiety disorder
   D. Major depressive disorder

2. A 60-year-old woman is evaluated for increased irritability and anxiety. She was in an automobile accident 3 months ago in which she was rear-ended by a car at a stop light. Since that time she has nightmares about the incident and states she has not returned to driving for fear of being in another accident. Her sleep is poor, and her husband states she is becoming more socially isolated since she has stopped driving. She has continued to perform her usual hobbies at home. She has no suicidal thoughts. On physical examination, all vital signs are normal.

   Which of the following is the most likely diagnosis?

   A. Generalized anxiety disorder
   B. Major depressive disorder
   C. Obsessive-compulsive disorder
   D. Posttraumatic stress disorder

3. An 81-year-old man is evaluated for a 3-week history of shortness of breath, chest pain, palpitations, difficulty sleeping, early morning awakening, and lack of interest in getting out of bed in the morning. The patient's wife died of cancer 9 months ago. He says that he has been seeing her face at night when he closes his eyes and frequently awakes at night thinking that she is next to him in bed. Medical history is significant for hypertension and hyperlipidemia. Medications are hydrochlorothiazide, atorvastatin, and diphenhydramine at bedtime as needed for sleep. Results of the physical examination are normal.

   Chemistry panel and complete blood count are normal. Electrocardiogram reveals normal sinus rhythm with left ventricular hypertrophy without ischemic changes. Chest radiograph is normal. Exercise treadmill test is negative for cardiac ischemia.

   Which of the following is the most likely diagnosis?

   A. Anticholinergic drug side effect
   B. Complicated grief
   C. Generalized anxiety disorder
   D. Major depression with psychotic features

4. A 62-year-old man is evaluated in the emergency department for recent onset of fever and severe abdominal pain. He also reports a history of anxiety, frequent palpitations, difficulty concentrating, dyspnea, diarrhea, nausea, vomiting, and weight loss (total, 9.1 kg [20 lb]) over the past few months. He has had no neck discomfort. An abdominal CT scan with iodine contrast obtained several weeks ago when he first experienced abdominal pain was normal. The patient also has a 6-month history of Graves disease treated with methimazole. He takes no other medication.

   Physical examination shows an anxious and agitated man. Temperature is 38.9 °C (102.0 °F), blood pressure is 160/90 mm Hg, pulse rate is 130/min and regular, and respiration rate is 22/min. Cardiac examination shows a grade 2/6 holosystolic murmur, and crackles are heard on lung examination. Eye examination shows no acute inflammatory findings. Findings from an examination of the pharynx are normal. The thyroid gland is firm and enlarged bilaterally with no specific nodules palpated. A thyroid bruit is heard. No cervical lymphadenopathy is noted. The skin is warm and moist. Abdominal examination reveals a palpable liver 2 cm below the right costal margin. Examination of the extremities shows 2+ peripheral leg edema. Neurologic examination reveals that the patient is oriented to place but not time, giving an incorrect answer when asked for the year.

   Results of laboratory serum studies show a thyroid-stimulating hormone level of less than 0.01 µU/mL (0.01 mU/L), a free thyroxine (T4) level of 8.2 ng/dL (106 pmol/L), and a triiodothyronine (T3) level of 650 ng/dL (10 nmol/L).

   Which of the following is the most likely diagnosis?

   A. Euthyroid sick syndrome
   B. Myxedema coma
   C. Subacute thyroiditis
   D. Thyroid storm

Questions are largely from the ACP's Medical Knowledge Self-Assessment Program (MKSAP, accessed at http://www.acponline.org/products_services/mksap/15/?pr31). Go to www.annals.org/intheclinic/ to complete the quiz and earn up to 1.5 CME credits, or to purchase the complete MKSAP program.

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