



Harvard Mental Health Letter

VOLUME 27 • NUMBER 12 | JUNE 2011

Generalized anxiety disorder

People who worry about everything—and nothing in particular—have several treatment options.

When people turn on the television, chances are they will experience a barrage of anxiety-provoking news—a sagging economy, international political conflicts, natural disasters. At the same time, they may be dealing with their own personal stress—such as worries about job security or health. Anxiety is often a healthy response to uncertainty and danger, but constant worry and nervousness may be a sign of generalized anxiety disorder.

This common disorder affects about 5% to 6% of Americans at some point in their lives. Women are twice as likely as men to develop generalized anxiety disorder. Some research suggests that prevalence of this disorder increases with age. Generalized anxiety disorder usually first appears from young adulthood through the mid-50s—a later onset than seen with other psychiatric disorders.

While other types of anxiety disorders—such as specific phobias or social anxiety disorder—arise from particular situations, generalized anxiety disorder is characterized chiefly by debilitating worry and agitation about nothing in particular or anything at all. The constant and continually changing worries of people with generalized anxiety disorder are mostly about everyday matters. They can't shake the feeling that something bad will happen and they will not be prepared. They may worry to excess about missing an appointment, losing a job, or having an accident. Some people even worry about worrying too much.

Physical symptoms—racing heart, dry mouth, upset stomach, muscle tension, sweating, trembling, and irritability—are an integral part of generalized anxiety disorder. Over time, these physical manifestations of anxiety may adversely affect health. One example:

people with generalized anxiety disorder are at greater risk than other people for heart attack and other cardiovascular problems.

Generalized anxiety disorder often occurs in conjunction with other psychiatric disorders. About two-thirds of people with generalized anxiety disorder also have major depression. About one-quarter have panic disorder. Many have substance use disorders or alcohol dependence.

Generalized anxiety disorder can also affect cognition—although in a different way than depression does. People with generalized anxiety disorder tend to ruminate about potential misfortune, while people with major depression are more likely to have difficulty making a mental effort.

Brain basis of anxiety

Generalized anxiety disorder, like other types of anxiety, probably arises from an excessive activation of the brain mechanism underlying fear and the fight-or-flight response.

When someone confronts a dangerous situation, two brain circuits become active and relay sensory information about the danger—such as the sight and smell of fire—to different parts of the brain. One circuit extends to the cerebral cortex, the outermost part of the brain, which is used for thinking and decision making. The other circuit involves a deeper structure called the amygdala that is central to emotional processing. The amygdala monitors the body's reactions to the environment, evaluates an event's emotional significance, and organizes responses that a person may or may not be conscious of.

Although several brain circuits are activated simultaneously, the amygdala initiates a fast response to danger. It communicates with the hypothalamus at the base of the

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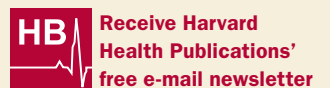
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Subscriptions \$72 per year (U.S.)

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Published by Harvard Health Publications,
a division of Harvard Medical School

Editor in Chief Anthony L. Komaroff, MD
Publishing Director Edward Coburn

© 2011 Harvard University (ISSN 0884-3783)
Proceeds support the research efforts of Harvard Medical School.

Harvard Health Publications
10 Shattuck St., 2nd Floor, Boston, MA 02115

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Generalized anxiety disorder *continued*

brain, prompting quick release of hormones that raise heart rate and blood pressure, tense the muscles, and generally ready the body to fight or to flee. This system is activated before the cerebral cortex can process what is happening. This has survival value. For example, a person crossing the street may lunge out of the way of a speeding car before being consciously aware of the danger.

The amygdala also works with other brain structures to store emotional memories, including memories of frightening events. In people with anxiety disorders, however, this can become a problem. The amygdala may be so sensitive that it overreacts to situations that aren't really threatening, inadvertently triggering the brain circuits that provoke an emergency stress response. Over time, anxiety becomes attached to situations, thoughts, and memories unrelated to genuine sources of danger. In this sense, the brain may inadvertently create its own fears.

Certain genetic variations may predispose people to develop anxiety disorders. A leading gene candidate is 5-HTT, a gene that regulates the neurotransmitter serotonin. Other neurotransmitters associated with anxiety are gamma-aminobutyric acid (GABA) and norepinephrine. GABA directs nerve cells to stop signaling and await further instructions.

Serotonin and norepinephrine, acting over time, regulate the responsiveness of brain circuits governing mood, stress responses, and conditioned fears. Anti-anxiety drugs alter the action of one or more of these neurotransmitters. Benzodiazepines act at receptors for GABA; antidepressants act at receptors for norepinephrine, serotonin, or both. (These drugs are described in detail at right.)

Life experiences also contribute to anxiety disorders. Severe or constant stress can produce a hyperactive anxiety reaction. People with some personality traits, such as shyness, may also be more vulnerable to developing anxiety disorders. Psychotherapies help people to recognize and address the psychological contributors to anxiety.

Medication options

The medications most often used to treat generalized anxiety disorder are antidepressants such as selective serotonin reuptake inhibitors (SSRIs) or dual serotonin and norepinephrine reuptake inhibitors (SNRIs). These drugs take longer to work than the traditional anti-anxiety drugs, benzodiazepines, but also may provide greater symptom relief over time.

Antidepressants. These drugs act on neurotransmitters involved in many regions of the brain, affecting anxiety, mood, and arousal. SSRIs prescribed for anxiety include fluoxetine (Prozac), sertraline (Zoloft), and citalopram (Celexa). The SNRIs venlafaxine (Effexor) and duloxetine (Cymbalta) may also be effective. Side effects of antidepressants include sexual problems, weight gain, and insomnia. There may be a mild (and usually preventable) reaction when antidepressants are discontinued, but they present no risk of abuse.

Benzodiazepines. These drugs offer rapid relief of anxiety disorders and cause few side effects. The main risks are drowsiness, loss of coordination, and physical dependence (especially in people dependent on alcohol or other drugs). Options include alprazolam (Xanax), diazepam (Valium), and lorazepam (Ativan).

If people decide to stop taking benzodiazepines, they should do so gradually, lowering the dose over weeks or months. This approach reduces the risk of having a withdrawal reaction with symptoms that include anxiety, agitation, and, rarely, seizures.

Other options. Buspirone (BuSpar), a drug with a different mechanism of action, is less likely to cause physical dependence than a benzodiazepine but may not be as effective. Buspirone also takes longer to take effect than a benzodiazepine. Often it doesn't work because a person is taking too low a dose. At therapeutic doses, however, buspirone has more physical side effects.

Clinicians may also prescribe both a benzodiazepine and an antidepressant. The person starts by taking the two drugs

together, and then the benzodiazepine dose can gradually be reduced as the antidepressant begins to take effect.

Tricyclic antidepressants are a further option. These drugs have side effects that may be more uncomfortable than SSRIs or SNRIs (for example, dizziness, constipation, blurred vision, and trouble urinating). Still, some people with anxiety actually feel better on tricyclics and find the side effects manageable or even preferable to other drugs, underscoring the importance of individualizing treatment.

Psychotherapy

People with generalized anxiety disorder can also benefit from psychotherapy. Cognitive behavioral therapy (CBT) is probably the most studied approach, but other options show promise as well.

CBT. This therapy helps people with generalized anxiety disorder to recognize and correct misperceptions that contribute to anxiety. A cognitive behavioral therapist helps people with generalized anxiety disorder to recognize when they are misinterpreting events, magnifying difficulties, and making pessimistic assumptions on little evidence. People with generalized anxiety disorder tend to pay attention to anything that seems threatening and incorporate a vague sense of danger into all their thinking. They worry constantly in an attempt to define and describe their problems, reducing anxiety temporarily but in the end maintaining the feeling that they lack control. Anticipation of disaster and the physical symptoms of anxiety are mutually reinforcing.

During CBT, patients may keep a diary for recording and examining their thoughts and feelings, with special attention to those that cause or relieve anxiety. The therapist helps the patient to become aware of automatic thoughts and assumptions so that he or she can make vague worries more specific, evaluate them, and determine whether they are unrealistic.

Symptoms of generalized anxiety disorder

Generalized anxiety disorder is excessive anxiety and worry that is difficult to control and causes serious distress or interferes with daily activities. These symptoms occur more days than not for at least six months, along with at least three of the following:

- restlessness or feeling on edge
- irritability
- tiring easily
- muscle tension
- difficulty concentrating
- sleep problems.

The symptoms are not the result of a medical condition, a medication, or a nonmedical drug, and they don't occur only during a mood disorder, a psychotic disorder, or post-traumatic stress disorder. The symptoms do not necessarily include fear of specific objects (simple phobias), fear of having a panic attack (panic disorder), fear of being embarrassed in public (social phobia or performance anxiety), fear of being contaminated (obsessive-compulsive disorder), fear of gaining weight (anorexia), or fear of having a serious illness (hypochondriasis).

Adapted from the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*.

The behavioral side of CBT involves learning new ways to solve problems and respond to anxiety-provoking situations. Patients may receive problem-solving skills training and learn how to set goals and establish priorities. The methods include role-playing, rehearsal, and modeling (learning by imitation).

Applied relaxation. This modified form of CBT helps patients learn relaxation techniques to tamp down the nervous system arousal that occurs during stress. Often that starts with controlling rapid breathing. They learn to apply these relaxation techniques as anxiety-provoking thoughts or situations occur.

Psychodynamic therapy. This type of therapy recognizes that early relationships and life history continue to affect people as adults, that behavior reflects both unconscious and conscious motivations, and that gaining insight into these factors in the context of a helping relationship can provide relief. A preliminary study found that short-term psychodynamic therapy was as effective as CBT for treating generalized anxiety disorder.

Questions for the future

There is still much to learn about how best to treat generalized anxiety disorder. People with anxiety would benefit from more detailed comparisons of treatments, including the various types of psychotherapy and the currently available medications. Specifically, we need more information about what combinations of psychotherapy and medication are most effective, and how to tailor treatment to individuals.

And new treatments for generalized anxiety disorder will also be welcome. The condition tends to be chronic, with symptoms that wax and wane throughout life. Identifying new treatment options will provide hope to those individuals who continue to struggle with debilitating anxiety after trying multiple medications and psychotherapy. ♥

Alwahhabi F. "Anxiety Symptoms and Generalized Anxiety Disorder in the Elderly: A Review," *Harvard Review of Psychiatry* (July-Aug. 2003): Vol. 11, No. 4, pp. 180-93. *

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