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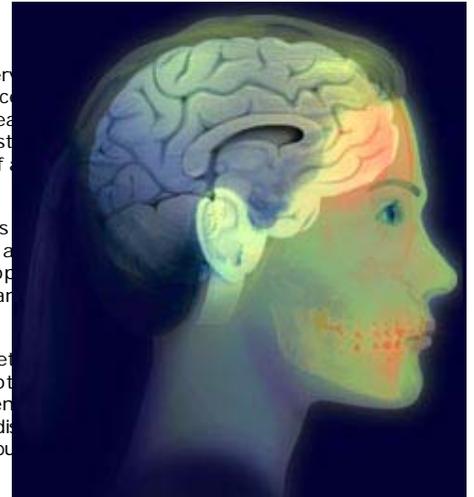
Anxiety Disorders

Treatment

Unfortunately, the presence of anxiety symptoms alone often does not seem sufficient incentive for a person with an anxiety disorder to seek help. A recent study revealed that even people with severe anxiety symptoms wait up to 12 years from onset of symptoms before they seek treatment (Jenike, 1996). Another study found the time span from onset of symptoms, at age 14.5 years, to the start of treatment, at age 31.5 years, at 17 years (Hollander et al., 1996a).

The treatment of anxiety disorders has been indistinct, and was not always based on sound scientific data; it is only now that new and effective treatments are available. A structured treatment algorithm for the different anxiety disorders is developed. Frequently used treatments such as the benzodiazepines have limitations and side effects that affect patient compliance and outcome negatively.

There is no one medication or intervention available that will 'cure' an anxiety disorder. However, anxiety disorders can usually be treated successfully with psychotherapy and pharmacotherapy. Without treatment, anxiety symptoms can persist, often for years. Lives may become disrupted because of them. Some people with anxiety disorders become housebound and suffer from concurrent depression, substance abuse, and other mental disorders.



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Pharmacotherapy

Pharmacological agents for treating anxiety disorders are initially prescribed at the lowest dose and increased until the person feels effective relief of their symptoms.

An overview of the traditional pharmacological agents for the treatment of anxiety disorders is given in Table 5. These drugs have proven efficacy in the treatment of anxiety disorders but often have many adverse effects, especially orthostatic hypotension, weight gain, physical dependence and the development of tolerance (Gorman et al, 1997; DeVane, 1997).

Table 5: Pharmacological Agents for the Treatment of Anxiety Disorders	
Benzodiazepines (BZDs) eg alprazolam, lorazepam, diazepam, oxazepam	Activate a specific benzodiazepine receptor that facilitates inhibitory GABAergic transmission
Tricyclic antidepressants (TCAs) eg imipramine, amitriptyline, clomipramine	Enhance the functional activity of noradrenaline and serotonin by blocking the reuptake of both neurotransmitters
Selective serotonin reuptake inhibitors (SSRIs) eg fluoxetine, citalopram, paroxetine	Block the reuptake of serotonin to enhance its functional activity
Monoamine oxidase inhibitors (MAOIs) eg phenelzine	Enhance the functional activity of noradrenaline and serotonin by inhibiting the degradation of both neurotransmitters by monoamine oxidase
Beta-blockers eg oxprenolol, propranolol	Block beta-adrenergic receptors to prevent the functional activity of adrenaline and noradrenaline
Antihistamines eg hydroxyzine	Block histamine receptors to prevent its functional activity
Azaspirones eg buspiron	Enhances some noradrenaline and dopamine neurotransmission while reducing serotonin and acetylcholine neurotransmission in the brain

Benzodiazepines

Benzodiazepines (BZDs) offer relief from the debilitation caused by the acute symptoms of anxiety disorders and the BZD alprazolam may be particularly effective in people with anxiety disorders.

People who have strong desire for control over their anxiety symptoms often prefer to take BZDs only when they feel unusually stressed. However, because of the addictive nature of this class of drugs and the high risk of physical dependency associated with their prolonged use, BZDs are not usually recommended for long term use and should be given to people who are at high risk of substance abuse with great care (Gorman et al, 1997).

Adverse effects associated with BZDs include daytime sedation and cognitive impairment (Keller and Hanks, 1995). In addition, evidence suggests that some BZDs, such as clonazepam, may cause depression (Lydiard et al, 1988).

Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) act by inhibiting the uptake of both noradrenaline and serotonin from the synaptic cleft; they are a well-established treatment of depression and anxiety disorders, in particular [panic disorder](#). TCAs are more effective than BZDs for the treatment of some of the anxiety disorders to remission (Tiller et al., 1997, Hoehn-Saric et al., 1988); for example, TCAs are more effective than BZDs in the treatment of generalised anxiety disorder (GAD) (Rickels et al., 1993). Hoehn-Saric et al. (1988) compared imipramine (TCA) with alprazolam (BZD) in people who were diagnosed with GAD according to DSM-III-R criteria (DSM-III-R). Because of its immediate effect in reducing hypervigilance and somatic symptoms, alprazolam was more effective during the first 2 weeks of treatment. From the third week onwards, however, imipramine became more effective in reducing the psychic symptoms.

TCAs with strong antihistaminergic properties, such as doxepin and amitriptyline, have sedating properties that are useful when treating people with anxiety disorders who have insomnia. It was hypothesised that the sedative effect of some TCAs would be an advantage in the early treatment of anxiety, but this has not been demonstrated in controlled trials (Kasper, 1994).

The disadvantages of the TCAs, which lead to poor compliance, include daytime sedation, anticholinergic side effects, cardiotoxicity, toxic psychosis and initial worsening of the condition. Other side effects, such as impairment of cognitive skills and psychomotor abilities, may have profound implications on day-to-day activities, including driving and operating machinery. TCAs may interact with several other pharmacological agents, including MAOIs, alcohol, oral contraceptives and anticholinergic drugs, which further limits their use (Bakish et al, 1998). More troublesome, however, is the risk of lethal overdose with these drugs.

For the reasons listed above, TCAs are not considered as a first-line treatment option in anxiety therapy (Bakish et al., 1998).

Selective Serotonin Reuptake Inhibitors

Selective serotonin reuptake inhibitors (SSRIs) work indirectly to decrease the activity of inhibitory serotonin 5-HT_{1A} receptors. On account of their indirect action via receptor modulation, they usually take 1–4 weeks to exert any real clinical benefit.

SSRIs are at least as effective as BZDs in the treatment of anxiety disorders. In the short term there may be equal efficacy but in the medium and long term the SSRIs have proved superior to BZDs in the treatment of GAD, social anxiety disorder and panic disorders (Davidson et al., 1994). SSRIs have fewer side effects than TCAs (Boyer, 1992; Feighner and Boyer, 1992; Anderson and Tomenson, 1995; Montgomery and Kasper, 1995; Nutt, 1995a), which enhances patient compliance and improves the treatment outcome.

Although some patients and patient groups prefer TCAs to SSRIs because of their lower cost per dose, recent studies have shown that when all service costs for depressed patients are calculated, SSRIs are no more costly to the health care system than are TCAs (Jönson and Bebbington, 1993).

Monoamine Oxidase Inhibitors

Some clinicians believe that Monoamine oxidase inhibitors (MAOIs) are the most potent agent for the treatment of anxiety, and the most prescribed drug for many anxiety disorders is phenelzine (Bakish et al, 1998). MAOIs are effective in the treatment of anxiety disorders, although their use may be limited due to their considerable side effects and harsh dietary restrictions (Jefferson, 1997).

The classical MAOIs are not considered first-line treatments for depression with anxiety. Although, moclobemide, a newer, reversible, selective monoamine oxidase-A inhibitor (RIMA) is effective in a wide range of depressive and anxiety disorders, such as panic disorder and PTSD. Moclobemide binds to MAO-A and leaves MAO-B free to metabolise tyramine, eliminating the need for dietary restrictions (Tiller et al, 1997; Priest et al, 1995). However, in recent studies, the efficacy of this drug has been disputed (Schneier et al, 1996). A study of the treatment of SAD found that moclobemide was not superior to placebo as a treatment option, even at doses as high as 900 mg/day (Noyes et al, 1997).

Bupirone

The treatment of GAD with buspirone, a partial serotonin 5-HT_{1A} receptor agonist, is successful, does not have any severe side effects and has a good response in patients with moderate to severe anxiety symptoms. Buspirone is equal to or superior to BZDs in the treatment of the psychic symptoms of generalised anxiety (Rickels et al, 1982). Buspirone is often used in combination with SSRIs in the treatment of anxiety associated with depression (Thase and Rush, 1997).

Buspirone has a specific effect on the serotonergic system. It is chemically and structurally unrelated to the BZDs and decreases symptoms associated with the muscular and autonomic systems (Goa and Ward, 1986); it also lacks sedating effects, interactions with CNS depressants and does not have an abuse potential (Sussman, 1993). The side effects of buspirone are mild and are primarily nausea, dizziness and headaches, which are often transient but may prove intolerable for some patients (Bakish et al, 1998).

Buspirone does not provide immediate relief of symptoms and must be taken for more than a week before its therapeutic effects occur (Hoehn-Saric 1998). It is indicated in patients who have persistent psychic anxiety and hence need long-term treatment. However, the overall effectiveness of buspirone has been somewhat disappointing (Porsolt, 1993). Although controlled studies exist, clinical experience suggests that antidepressants are more effective anxiolytics than buspirone in the treatment of many anxiety disorders.

Beta-Blockers

Beta-blockers, (beta-adrenergic antagonists), such as propranolol, atenolol and pindolol, often rapidly reduce anxiety in panic disorder, GAD and social and specific phobias. Beta-blockers may be useful in the treatment of anxiety in patients with pronounced cardiac symptoms or tremor, as the attenuation of physical symptoms has a calming effect in some patients. Beta-blockers have a rapid onset of clinical effect and can be taken either as a single dose or on a regular basis (Liebowitz et al, 1992).

Beta-adrenergic antagonists block the effects of adrenaline and noradrenaline at beta-receptors and the anxiolytic effects of beta-blockers are mediated via peripheral receptors rather than acting centrally (Hoehn-Saric, 1998). Thus, they have no direct effect on anxiety, but diminish patients' preoccupation with their physical state by reducing tremor and the cardiac response to anxiety (Tyrer, 1976). This heightens patients' self-confidence about coping with stressful situations. However, beta-blockers may increase peristalsis in the gastrointestinal tract, thereby exaggerating rather than diminishing the effects of anxiety on this system. Beta-blockers are used particularly to counteract situational anxiety (eg 'stage fright') in musicians and singers, since they reduce tremor.

At high dosages, beta-blockers that can cross the blood-brain barrier (eg propranolol) may cause tiredness, vivid dreams, depression and, rarely, delirium. Therefore, it is preferable to use beta-blockers that do not penetrate the blood-brain barrier such as atenolol. Caution is required when combining beta-blockers with medications that lower blood pressure, and beta-blockers should be avoided in patients with bradycardia, heart block, cardiac failure, asthma or any form of bronchospasm. Rebound hypertension may occur in hypertensive patients in whom beta-blockers are suddenly withdrawn. Neither tolerance nor dependence on beta-blockers occurs.

In patients with marked cardiac symptoms, the combination of a beta-blocker with a BZD can reduce the required dosage of the BZD (Hallstrom et al, 1981).

In the elderly, beta-blockers are effective in the treatment of agitation and violent behaviour, and they may also reduce violent behaviour in young people. Pindolol is currently the beta-blocker of choice in the elderly since it produces less hypotension and bradycardia than propranolol (Jenike, 1996).

Antihistamines

Antihistamines are often sedating and so are sometimes used for the treatment of anxiety disorders; the sedation has a quick onset, and rapid relief from anxiety symptoms is observed. However, antihistamines have not been evaluated effectively for the treatment of anxiety disorders in controlled clinical trials.

Histamine is a neurotransmitter that plays an important role in arousal. The arousing effect is mediated through the histamine H₁ receptor and is attenuated by antihistamines. Antihistamines induce drowsiness, sedation and, in high dosages, impair psychomotor performance of complex tasks (Schwartz et al, 1991). Mild tolerance to the sedative effects may occur with long term use. The effects of antihistamines on the autonomic nervous system are mixed. They have anticholinergic properties, causing dry mouth, increased heart rate and decreased gastro intestinal activity. They have no direct effect on the muscular system (Hoehn-Saric, 1998). Antihistamines appear predominantly to affect hyperarousal. They decrease vigilance and hyper-alertness, but have little effect on psychic anxiety.

Antihistamines have many potential side effects, including disturbed co-ordination, weakness, inability to concentrate, urinary frequency, palpitations and hypotension. In addition, their anticholinergic properties make them poor choices for patients taking other anticholinergic agents, such as TCAs, neuroleptics and anti-arrhythmic agents.

Antihistamines have weaker anxiolytic effects than the BZDs, and effective dosages of antihistamines may produce marked adverse effects. However, they remain popular

because they have no abuse potential. They have an immediate effect in relieving acute anxiety symptoms, and can be administered in single doses or as a longer term prescription.

These traditional pharmacological agents have been used for many years now, despite their side effects and occasional lack of effect. However, they are all still considered useful and have distinct advantages for particular patients. Since neither antidepressants nor buspirone attenuate sympathetic functions (important in the treatment of anxiety disorders) a combination of these drugs with a BZD or a beta-blocker may be useful in patients who experience situational exacerbation of somatic symptoms of their anxiety (Hoehn-Saric, 1998), and who may also require a lower dose of the BZD (Hallstrom et al, 1983). However, this practice is not recommended.

Psychotherapy

Psychotherapy is used in the treatment of anxiety disorders to help people acquire better coping mechanisms, re-organise maladaptive attitudes, acquire new skills and change their lifestyle. Behavioural therapy and cognitive behavioural therapy (CBT) are the forms that have shown the clearest experimental evidence of efficacy in the treatment of anxiety disorders, and they are often used in combination (Michels, 1997).

Self-monitoring is required to make these therapies effective, and people with anxiety disorder are encouraged to recognise situations that make them anxious, to learn to detect the initial onset of symptoms and to identify overt behaviour, thoughts, images, emotions and physiological reactions (Boulenger et al, 1997).

Cognitive Behavioural Therapy

Since excessive worrying is the main symptom of anxiety, cognitive approaches have been found to be particularly useful in the treatment of GAD (Kaplan et al., 1994).

► [Read more about the aims and techniques of cognitive behavioural therapy.](#)

CBT can result in a 50% reduction in the somatic complaints of people with anxiety, and the positive effects of CBT seem to persist even after the therapy has been terminated. CBT can reduce muscular tension, lower autonomic functions and diminish feelings of distress. CBT should be practised daily and used whenever anxiety is experienced (Borkovec and Costello, 1993).

The efficacy of CBT has lent further support to the suggestion that non-pharmacological management of patients with anxiety can result in an enhanced response to treatment (Michels, 1997). Studies reporting comparisons of CBT with pharmacological treatments indicate that in the short term the pharmacological treatments have a superior effect; this effect may diminish in the long term, and in some anxiety disorders CBT may have a better long term treatment outcome when compared with pharmacotherapy alone. Ideally, a patient should receive both CBT and pharmacotherapy (Borkovec and Costello, 1993).

However, Westra and Stewart (1998) reported that the treatment of anxiety with CBT and pharmacotherapy may be non-complementary, and even incompatible in some cases. They describe cognitive factors, such as catastrophic beliefs, self-efficacy, selective attention and memory, which may have a detrimental effect on treatment responsiveness. Although studies of people with anxiety symptoms suggest that a combination of psychotherapy and pharmacotherapy enhances the outcome of treatment (Luborsky et al., 1975).

Psychoeducation

► [Read more about the aims and techniques of psychoeducation.](#)

The psychotherapeutic treatment of people with anxiety disorder must be considered individually, and will depend on:

- the type, severity and chronicity of symptoms
- the triggers that elicit or aggravate the symptoms
- life stressors
- coping ability
- learning potential
- specific personality traits
- motivation to change.

The approach necessary for people who have predominantly psychic symptoms will differ to the approach needed for people with anxiety disorder, who also exhibit strong somatic symptoms.

The non-pharmacological treatment of anxiety disorders is extremely important as it has the potential to alleviate symptoms successfully.

Treating Specific Anxiety Disorders

Specific anxiety disorders are usually treated as follows:

- **Panic disorder** is treatable and most people respond well to pharmacological treatment. Learning to recognise the onset of a panic attack is an important part in treatment, and psychotherapy should form an important part of the treatment plan. CBT is best known and supported by research. Compliance with sessions

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and follow-up exercises are essential. If medication is required, BZDs, SSRIs or TCAs are usually prescribed as a secondary measure.

- **OCD.** Exposure and response prevention therapy, a type of CBT should be an important part of the treatment plan. Pharmacological treatments prescribed for OCD often require a higher dose of SSRI than the doses used to treat depression. Virtually no treatment is curative, but most will reduce symptoms by 50–80%.
- **Social phobia.** Pharmacological treatment is similar to that for panic disorder and may include SSRIs, MAOIs (eg moclobemide) and beta-blockers (for specific performance anxieties). Cognitive behavioural treatments should be tried before medication is prescribed, and exposure therapy is usually effective.
- **Specific phobia.** The treatment for specific phobias is essentially psychotherapy. Drug therapy is useful in cases where the phobia is related to a specific situation, such as flying. Either short-acting BZDs or beta-blockers are useful in this situation.
- **GAD.** Psychotherapy should focus on behavioural therapy and be oriented towards reducing low level, constant feelings of anxiety. Relaxation techniques should be taught and the importance of compliance with these techniques emphasised. Help in identifying and subsequently learning to cope with individual stressors should be given. If the symptoms of anxiety are serious, BZDs, TCAs or buspirone should be prescribed. Self-help can also benefit some people with GAD, as support groups allow individuals to share their common experiences and feelings of anxiety.

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