The most widely used tranquilizer in America is more addictive than Valium—and is often less effective than nondrug treatments for anxiety.

The woman we'll call Rachel G.—now age 31—had experienced attacks of anxiety since she was a child. But those occasional inci­dents did not prevent her from mar­rying and taking a responsible job at East Coast biotechnology com­pany. Then, in late 1990 and early 1991, her life took a stressful turn. She was out of control at the lab where she worked, her mother fell serious­ly ill, her grandmother committed suicide, and her marriage deteri­orated. In early April of 1991, after a confrontation with her boss, she had full-blown panic attack.

"I broke into a cold sweat," she calls. My heart was palpitating. I wore I was having a heart attack. It was scared that I was dying. . . . I couldn't walk. I couldn't even move." The attacks went on for two days.

Rachel G. went to a psychologist for help, and simultaneously asked her regular internist for a pill to ease her suffering. Her physician pre­scribed Xanax (alprazolam). That was no surprise. In 1990, Xanax had come the only drug ever approved by the U.S. Food and Drug Administra­tion for the treatment of panic disorder—repeated, intense bouts of anxiety that can make life almost unbearable.

problem. After about three months on Xanax, she tried to cut het-dose in half. Within 48 hours, she recalls, "I couldn't sleep. My heart was rac­ing, and I was getting dizzy spells. Only going back up to an intermedi­ate dose would suppress the with­drawal symptoms.

In February 1992, Rachel G. began having frightening th 1ts of killing herself. She visited a psychiatrist who prescribed Tofranil (imipra­mine), an antidepressant that also works against panic. Today, she is doing well, still taking imipramine—and also Xanax. Though she feels the Xanax is no longer helping her, she can't bring herself to try that. "I know I'm going to have to experience the withdrawal symptoms," she says, "and those are the exact symp­toms that I went on it to esOpe from in the first place.

Rachel G.'s problem is far from unusual. Xanax is not only the most common treatment for panic attacks, but also the drug most often pre­scribed for run-of-the-mill anxie­ty—the kind that anyone might experience during a rough period in life. It is now the nation's largest-selling psychiatric drug; more than that, it is the fifth most frequently prescribed drug in the U.S.

Even if you've never taken Xanax for an extended period—even as lit­tle as a few weeks—risks developing a stubborn dependency.

Xanax is just the latest in a long line of tranquilizers that have promised to deliver psychia­try's holy grail: relief from anxiety with no significant side effects. And like the pills that came before it, Xanax has fallen short. As psychia­trists and their patients are discovering, Xanax does have some serious drawbacks—more than the drugs it was supposed to improve on.

like the sleeping pill Halcion (triazolam), its closest chemical relative, Xanax demonstrates that no pill can deliver peace of mind without a price. Even if you've never taken Xanax for an extended period—even as lit­tle as a few weeks—risks developing a stubborn dependency.

Anxious and blue? This ad suggests Xanax is espe­cially useful for anxious people who are also depressed. While the FDA has never approved this claim, many clini­cians take issue with it.

The selling of Xantu has been fueled by a vigorous promotional campaign. The drug's manufacturer, the Upjohn Co., has made Xantu highly visible in the medical commu­nity by promoting it as a uniquely effective drug for panic disorder. But Xantu does not represent a remark­able treatment advance so much as a marketing coup. In fact, it is little different from other related tran­
The more things change... 1967 CU report on Xanax's predecessor, Valium, pointed out that it didn't work much better than an inactive placebo in soothing the symptoms of anxiety.

The first drug in this category, Librium (chlordiazepoxide), came on the market in 1960: Valium (diazepam) came along three years later.

In 1979, a survey showed that 11 percent of Americans were taking antianxiety drugs, mostly benzodiazepines. The figure has dropped only slightly since then.

That was also the year the hazards of these drugs gained national attention through hearings held by Senator Edward Kennedy. As the hearings made clear, Valium and similar drugs caused problems: Physical dependency and sedation. People on benzodiazepines often found that they couldn't stop taking the drugs, and that they couldn't function unless while they were on them. The drugs accumulated in the body; over time, they made the user more and more sluggish, drowsy, and forgetful.

Ironically, while the Kennedy hearings offered frightening testimony on Valium, they also set the stage for its successor, Xanax. Introduced in 1981, Xanax was hailed as the first of a new chemical class edge. The patent on Valium expired in 1984, just as sales of Xanax were beginning to build. As generic competitors undercut Valium's sales, the drug's manufacturer promoted it less actively, and sales of Valium dropped further. Upjohn took advantage of the opportunity. By 1986, Xanax had overtaken Valium as the most widely prescribed benzodiazepine. By 1987, it reached fourth place on the national sales list of all prescription drugs. And in 1991, Xanax accounted for almost one-fifth of Upjohn's worldwide sales.

The trouble is, Xanax has now turned out to be more addictive than Valium itself.

Sluckonla-
All benzodiazepines produce physical dependency if you take them long enough. Over time, it seems, the brain "learns to expect a certain level of the drug. If the drug is removed, the brain reacts with agitation, sleeplessness, and anxiety-the symptoms that led people to take the drug in the first place. Frequently, these symptoms are worse than the original ones, a phenomenon known late the doses they take over.

But they do have a true physical dependency, and their withdrawal symptoms make the benzodiazepines extremely difficult to kick.

A number of clinical studies have found that Xanax and other benzodiazepines that are eliminated relatively slowly from the body produce a quicker and more severe rebound effect than drugs like Valium that are eliminated more slowly. Some people who take Xanax three times a day, a standard schedule for panic disorder, find that when they even have symptoms a day after taking the drug wears off between one dose and the next.

In one major study, Dr. Rickels and his colleagues at the University of Pennsylvania tracked anxious patients who had been on benzodiazepines for a year or more and tried to take them off their medication. Fully 57 percent of the patients on Xanax and similar simJy could not stop taking the drug, but only 27 percent of the people on drugs like Valium were that physically dependent.

Other studies have produced similar results. A Yale study of pa...
only 30 percent had been able to stop the drug entirely. Similarly, a study of long-term Xanax users reported by Toronto's Addiction Research Foundation found that two-thirds had tried to stop using the drug and failed.

The experience of a few doctors underscores the problem. In 1988, researchers at Johns Hopkins School of Medicine interviewed American physicians who specialize in helping people withdraw from the benzodiazepines. Asked which drugs were especially helpful for patients to stop, up 84 percent of the doctors ifically mentioned Xanax, while 29 percent cited Valium. Even the best of circumstances, clinicians find that, to get people off Xanax, they must reduce the dose tiny steps—a process that often takes months.

‘eraser’ for the mind?

One fact that so many people try so hard to quit Xanax—as difficult as it is to do—shows that it is not an overly pleasant drug to take. One man we spoke with, a 41-year-old medical writer in San Francisco, spent taking Xanax to deal with the anxiety that made her feel like she was going headlong toward a frightening and dangerous nown. After taking Xanax for 14 months, she decided to stop because, as she put it, "I made me too sick, I just couldn't function properly. People would say things, and I'd be in a sort of fog and be able to respond appropriately." (She ultimately succeeded in quitting, but had to go through a very difficult withdrawal process even though she was taking a low dose, one her psychiatrist told her would not cause dependency.)

1990 report by the American Chiatric Association backs up this man's experience. It found that benzodiazepines tend to impair memory; a person on one of these drugs may have difficulty retaining information.

Clinicians report the same problems. One patient of mine, a physi-
an extended period of time to deal with their chronic panic attacks. Since these panic attacks, it's not at all clear how much they were really helped.

A panic attack is intense anxiety in a concentrated dose. Victims with a severe case may suffer several full-scale attacks a day, during which their hearts race and they hyperventilate, sweat, tremble, and feel a profound sense of terror. According to the largest, most thorough survey of psychiatric problems, conducted in the 1980s by the National Institute of Mental Health (NIMH), between 4 and 7 percent of Americans have panic attacks that are frequent enough to be considered a panic disorder. The majority of people with panic disorder also have the condition, agoraphobia—a term now used to describe a fear of ordinary activities, such as driving a car or shopping at the supermarket, that can leave the sufferer housebound.

By the early 1980s, researchers had begun to recognize that at least some types of benzodiazepines, in addition to easing ordinary anxiety, could also stop panic attacks. Upjohn proceeded to spend lavishly on studies to see whether Xanax could be used to treat panic disorder, and enlisted highly respected consultants in the effort. 'The most senior psychiatrists in the world were flooded with offers of consultancies,' recalls Dr. Isaac Marks, a professor of experimental psychopharmacology at the University of London's Institute of Psychiatry.

In fact, the research could just as well have been done with another benzodiazepine—one called lorazepam (Ativan) —that is also cleared from the body quickly, and has also been shown to stop panic attacks. But this drug has not been under patent protection for years—and since it has not had the profit potential that Xanax has, it has not been aggressively tested and promoted. Today, a bottle of 100 one-milligram Xanax tablets costs $72.55, according to the Red Book, a standard drug price guide. The same amount of generic lorazepam in a therapeutically equivalent dose costs as little as $3.75.

With panic disorder, because they are prescribed high doses of the drug for an extended period of time to deal with their chronic panic attacks. Since these
Upjohn's major study on panic was a two-phase project called the Cross-National Panic Study. Phase One, conducted in the U.S., Canada, and Australia, involved more than 500 participants.
Though Xanax is the best-selling psychiatric drug in the U.S., it's not the most notorious. Vying for that distinction are Prozac, a drug for depression, and Halcion, a benzodiazepine, pine sold as a sleeping pill.

Both Halcion and Prozac have been reported to induce irrational behavior, including outbursts of murderous violence and suicide attempts. (Halcion was even blamed by some observers for President Bush's illness on his trip to Japan.) Lawsuits have been reported to induce irrational behavior, including an antianxiety drug.

Meanwhile, Prozac remains the nation's best-selling antidepressant.

Halcion (triazolam)

Though marketed as a sleeping pill, not an antianxiety drug, Halcion is actually Xanxilux's close chemical cousin. Like Xanax, Halcion is a benzodiazepine that's eliminated from the body very rapidly, miring you can take it to get to sleep at night without being drowsy the next day. But in marketing Halcion in 1991, the drug and the largest-selling sleeping pill in the U.S.

The disadvantages of Halcion eventually made themselves known. People who used it for any length of time found that, when they tried to stop, they experienced Mrerefoundsomnia worse than the original. There were also reports that Halcion seemed to make some people hostile or paranoid.

The FDA was notified, and analyzed the thousands of voluntary reports of adverse reactions to Halcion the agency had received from doctors. Halcion indeed was linked to more hostility reactions than any other sleeping pill relative to the numbers prescribed.

Another troublesome side effect also emerged: Some people who took even small doses experienced a bizarre reaction called anterograde amnesia. The day after they took Haldon to get to sleep they were up and about, apparently functioning normally. But later, they would have absolutely no memory of their actions. In 1991, Halcion was banned in the United Kingdom.

An FDA advisory committee decided, in May of 1992, to let Halcion stay on the U.S. market. But the panel agreed that the original recommended dose of 0.5 milligrams a day was too high, especially for elderly people; a lower dose of 0.25 milligrams was less likely to cause side effects (though it could also make the drug less effective). The committee also recommended strengthening the package insert's warnings on rebound insomnia and hostility reactions.

While the controversy over Prozac didn't seem to affect its upward sales trajectory, Halcion's sales have suffered. By 1991 it had fallen to 38th place. And last November, in a widely publicized case, a Dallas jury decided Halcion had been partly responsible for driving a man to murder—a decision that may damage the drug's reputation even more.

No panacea for panic

Since receiving FDA approval for its market Xanax for panic disorder, Upjohn has been using data from Phase One of the Cross-National Study in ads for the drug—included ads in journals for general-practice physicians. These doctors are less likely to be unfamiliar with the actual results of the study, and to the Upjohn's word for what it showed.

But despite the ads' claims, the study produced highly ambiguous results.

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WAXES AND WANS OVER TIME, AND THAT DRUGS MAY HAVE LITTLE EFFECT AFTER THEIR INITIAL BENEFIT

Recommendations

If anxiety is an inevitable part of the human condition, then the wish for a magic potion to banish anxiety is probably a timeless human desire. In our own time, drug companies have marketed one tranquilizer after another, each one supposedly safer and more effective than the one before. But tranquilizers-in particular, the benzodiazepines-are still powerful, potentially dangerous drugs, subject to abuse and misuse.

Given the hazards and their widespread use, we still know surprisingly little about the risks and benefits of long-term benzodiazepine use—and too little in particular about Xan(JJ): now the leader of the pack.

No one knows how many people are physically dependent on Xan(JJ) and how they may be affected by it. But there are some warning signs. A recent FDA analysis of reports of adverse reactions to drugs, which physicians send to the agency voluntarily, showed a number of cases in which the drug seemed to cause bouts of rage and hostility. Those side effects were rare, and were much less common with Xan(JJ): than with Halcion. But they were six times more common with Ativan relative to each drug’s sales. And Xan(JJ):’s suspected side effects have been included in a pending British class-action lawsuit against its manufacturer.

Consumers believe that more information is necessary in order to determine the frequency of side effects from Xan(JJ)—not only its effects on mood, but its potential for impairing memory and causing other cognitive problems. Careful surveillance of the drug’s clinical use could do much to resolve these questions.

In the meantime, if you or a loved one has a serious problem with anxiety, you need to understand your options clearly.

If you’re not normally an anxious person...
person, but are going through a particularly difficult time—a divorce or the death of a parent, for instance—
-term users are people who use benzodiazepines for a year or more, and 70 percent of these are women. The medication, used extremely carefully when driving, since these drugs impair coordination. Do not exceed the prescribed dose, and don't drink alcohol while on the drug. (The interaction can be disastrous.) The least, it can worsen the shaking, speech, poor coordination, dizziness, and mental slowness that stem from use of benzodiazepines. Inform your doctor immediately of any unexpected side effects, such as feelings of rage or agitation. You should seriously consider trying some form of psychotherapy to gain insight into your problem.

**SHORT-TERM PSYCHOTHERAPY**

**RELIEF WITHOUT DRUGS**

People with serious anxiety— including those with panic attacks— don’t need to choose between a life on tranquilizers and a life under severe stress. The past decade has seen the development of a new type of nondrug treatment called cognitive-behavioral therapy. While it doesn’t give the immediate relief of a drug like Xanax, does produce results quickly—and may be the most helpful approach over the long term.

Cognitive-behavioral therapists believe that many people, perhaps even most, have panic symptoms at one time or another—a stressful situation, for example, may trigger a racing heartbeat or a feeling of impending insanity or death.

"They tend to catastrophize their symptoms," explains Dr. obert Iberman, who treats panic-attack patients at the UC Irvine's psychiatry Institute. Anyone might feel dizzy, getting sudenly out of a chair. A person vulnerable to panic might exaggerate that feeling, leading to sustained feelings of panic.

Cognitive-behavioral therapy works by teaching panic victims a few basic facts about their physical symptoms. "The therapies consciously induce panic sensations—spinning patients on a chair to get dizzy, or having them run up and down stairs to get breath," Iberman says. Even when their heart is pounding, and they're short of breath and dizzy, they learn that nothing terrible happens and that these sensations naturally subside.

This technique and variations on it have been studied at anumber of centers, with consistent results: After an average of a dozen weekly sessions, patients have few or no panic symptoms. More important, they maintain their improvement for a year or more.

Dr. David Barlow and his colleagues at the Center for Stress and anxiety Disorders in Albany conducted one such study, comparing cognitive-behavioral therapy with Xanax and placebo over 15 weeks. The Xanax and behavior-therapy groups experienced roughly equivalent declines in general anxiety. But two weeks after the study ended, 57 percent of the behavior-therapy patients were completely free of panic attacks, while half of those in the Xan group were still having attacks. Even though almost all were on the drug, late in 1991, cognitive-behavioral therapy was endorsed by an expert panel convened by the National Institute of Mental Health to evaluate treatments for panic disorder.

Short-term therapy for depression, has similarly positive results in a study conducted over the past decade by the National Insti
tute of Mental Health. For people with mild to moderate depression, both cognitive therapy and a form of short-term treatment called interpersonal psychotherapy worked as well as drug treatment (this case, imipramine). For patients with severe depression, the treatment worked slightly better than either kind of therapy.

Despite the evident advantages of cognitive-behavioral therapy, it is still less accessible to most people than drug treatment. Relatively few psychologists and psychiatrists are trained in this form of therapy. Most health-insurance plans reimburse poorly for psychotherapy. And without the kind of expensive publicity that the drug companies can put behind their products, nondrug approaches have received less attention than they deserve.

Not everyone is a good candidate for cognitive-behavioral therapy. "You have to have someone who is highly motivated," says Dr. John Pecknold, a Mc
t University psychiatrist who participated in Upjohn's Xanax study.

Nevertheless, CU's medical consultants believe psychiatrists and patients should more frequently consider this kind of short-term therapy as a treatment for anxiety and other psychological problems. These focused, effective methods entail less risk and offer better long-term results than drug therapy generally does. They may also have the potential to be highly cost-effective.

One recent study, for example, found even a single therapy session helped many people with panic attacks to overcome their prob