

Wonder Drugs

Of all the “wonder drugs” that have appeared in recent years, none has excited more interest or created more controversy than Prozac and the new antidepressants that have bubbled up in its wake.

That shouldn't be surprising. If a drug is effective enough to attract major notice when it's released, it's probably powerful enough to generate a backlash.

That's certainly been the case here.

The fact is that Prozac is a powerful drug that operates at a deep level of the brain to correct a biochemical imbalance that not only seems to underlie depression, but a variety of other body/mind problems as well.

Does it work? It seems to, for most people who take it as directed. Still, everyone who uses it or a drug like it should be aware of potential side effects and notify their physician of problems immediately—particularly if the depression worsens or they begin to feel suicidal.

The fact is that the new SSRI's *have* produced amazing results for many users. But that shouldn't obscure the fact that others have had problems with them.

That's worth keeping in mind as we consider Prozac's risks and benefits and weigh its pros and cons.

Because even though Prozac *is* a wonder drug in many ways, it's also a wonder how easily we forget that it—and drugs like it—can cause problems as easily as they take them away. ■



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PROZAC PAXIL ZOLOFT

and other antidepressants



Pros & Cons

X Y & Z

It happens so often, you'd think we'd have gotten used to it by now...

■ **Item:** Company X announces Product Y, a treatment for Condition Z, a problem that's baffled the best minds in science for years.

The media jumps on Product Y's bandwagon, accentuating positives, eliminating negatives, and generally rhapsodizing about how great it's going to be without Z around, messing up all our lives. Sales skyrocket, caution is thrown to the wind, and everyone basically hopes for the best.

Sound familiar? If so, the rest of the story should, too.



Bluesbuster #1. Prozac has helped millions beat the blues while racking up billions in worldwide sales.

Times passes. A report is published, linking Y to Side Effects A, B, and C. The media weighs in again, now clucking that the early euphoria was premature, and declaring that a closer, careful look at Y is clearly in order.

Public-interest groups leap into the fray. They petition the U.S. Food and Drug Administration for [take your pick] new controls/warning labels/an outright ban. They charge that X rushed Y into release without sufficient concern for possible problems.

The first lawsuits are filed. Attorneys for Ms. Q or Mr. E file multi-million-dollar liability suits, alleging that X knew all along that Y was dangerous, but ignored warnings in its haste to foist a bad product on a gullible market.

More time passes. The public is confused. Is Y still a cure for Z or a deadly rip-off that causes A, B, and C?

If the above scenario sounds absurd, it is. But in some ways, it's more fact than fiction. And it covers most of the public perceptions about Prozac® and a wave of similar antidepressant drugs that rolled in on its wake over the past 15 years.

Prozac drew raves early on, due to its effectiveness in undoing depression and other problems.

Prozac sparked a media frenzy when it was introduced, igniting a heated debate on the ethics of using drugs to change our feelings the way we once could only change our laundry detergents.



little truth in them.

And that's what makes sorting things out such a challenge, and so necessary.

■ What is Prozac?

Prozac is one in a new class of drugs used to treat depression and other emotional problems. Its chemical name is *fluoxetine*.

Released in 1987, Prozac turned heads from the start, both literally and figuratively. In the process, it became the most popular antidepressant in the United States (more than 14 million Americans have used it so far) and one of the most talked-about drugs in the world.

In fact, for a time, Prozac seemed more than just a *drug*. It was a cultural phenomenon, the subject of a media fascination that played itself out on magazine covers and TV talk shows and best-seller lists for years, and an equally intense debate into the ethics of using drugs to change our feelings the way we once could only change our laundry detergents.

The interest proved so intense—and sales so profitable—that it inspired a flurry of activity among pharmaceutical makers to concoct chemicals like it. The result?

A sudden swarm of act-alike drugs (including Paxil®, Zoloft®, and others), known collectively as *selective serotonin reuptake inhibitors*—SSRI's, for short.

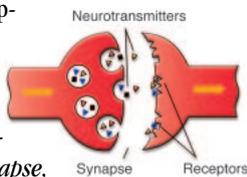
Similar to traditional antidepressants—including tricyclic antidepressants (TCA's) and monoamine oxidase inhibitors (MAOI's)—in some ways, SSRI's differ in the way they actually work in the body.

■ How do they work?

By altering the action of a specific set of *neurotransmitters*, chemicals involved in the transfer of signals from cell to cell in the central nervous system.

Specifically, SSRI's increase the supply of *serotonin*, a neurotransmitter that figures into mood, pain, sleep, and a variety other body/brain processes.

They do that by blocking removal of serotonin from its receptors in the brain. By stopping these receptors from "turning off" serotonin, Prozac and drugs like it permit more of the transmitter to be available at the *synapse*, the gap between nerve cells.



For reasons no one fully understands, this simple biochemical change often results in improved mood.

■ How are SSRI's different from other antidepressants?

Other drugs affect more body systems—and cause more potential problems in the process.

TCA's, for example, interact with other neurotransmitter systems. Like Prozac, they boost serotonin, but also affect another neurotransmitter, *norepinephrine*.

MAOI's work differently. They block *monoamine oxidase*, an enzyme that breaks down other neurotransmitters in addition to serotonin.

Like Prozac, MAOI's and TCA's all reduce depression. And also like Prozac, no one really knows why they work—only that they usually *do* work, probably by increasing the available supply of serotonin.

■ Which is better?

That depends on who you ask. According to the Public Citizen Health Research Group, a Washington-based consumer health advocacy group, Prozac works well but is "somewhat less effective" than a common tricyclic, imipramine.

Others give Prozac and the SSRI's higher marks, claiming that the drugs can trigger transformations of self so total that some users say they "feel like [themselves] for the first time" in their lives—which raises profound questions about who we are and how we know for sure.

Still, even the biggest boosters of SSRI's acknowledge they only work about 60-70 percent of the time—the same as other antidepressants.

But even if the new drugs don't always work *better*, they are usually *safer* than older antidepressants.

In fact, earlier drugs caused so many side effects that many users were unable to stay on them long enough to derive any real benefit.

SSRI's have side effects, too, but they're usually milder and more manageable.

■ What sort of side effects?

That depends on the drug, but common initial problems often include nervousness and insomnia, or drowsiness and fatigue. Skin rash, nausea, and diarrhea also occur.

An effect common to many SSRI's is some degree of sexual dysfunction—ranging from an inability to achieve orgasm all the way to a complete loss of interest in sex. Some researchers guess the rate of SSRI-related sexual impairment at up to 50 percent.

The risk of other problems is low, but real. In fact, Prozac's manufacturer admits that 15 percent of all patients receiving Prozac in pre-release trials stopped taking it due to adverse reactions.

Still, most therapists (and most of their patients) think SSRI's stack up pretty well against the competition, since both TCA's and MAOI's can cause weight gain, changes in blood pressure and heart beat, constipation, and blurred vision.

And SSRI's look better still when you add in some of their "good" side effects.

■ What 'good' side effects?

One of the SSRI's "best" side effects—or, at least, most users' favorite—is appetite reduction and weight loss. In fact, that was a big reason that Prozac found fame so fast. In one study, 65 percent of Prozac users lost at least a pound during a six-week testing period.

And two tests involving subjects who were overweight



Claims that the drugs can trigger transformations so total that some users "feel like themselves for the first time" raise profound questions about who we are and how we know for sure.



but not depressed made Prozac (and presumably the subjects) look even better, with an average loss of 10 pounds over 8 weeks.

On the other hand, Prozac doesn't fight fat for everyone. In fact, underweight people tend to *gain* weight while on the drug. And although researchers aren't sure

why, they suspect it's linked to Prozac's effects on serotonin and its role in appetite control.

■ Do SSRI's help with other problems?

As a matter of fact, they do. They've been tried with varying degrees of success against a variety of other problems, including obsessive-compulsive disorder, panic, eating disorders, Tourette's syndrome, borderline personality disorder, and schizophrenia. More research is needed, but results thus far have advanced the view that there may well be a single biochemical basis for these and other mental health problems—and reinforced researchers' determination to prove it.

And for the present, evidence strongly suggests that the common link is serotonin.



Balancing Act. Prozac's effects are linked to changes it triggers in brain levels of serotonin.

▶ Violence & Prozac: Is There a Connection?

Although the initial response to Prozac was mostly euphoric, rumors have swirled around it since the early years, alleging a fearful, dark side to the drug, including incidents of murder and suicide by users. At times, the rumors have even seemed a roar as ex-users came forward with charges that Prozac caused violent or suicidal impulses—a process helped along by critics in the Church of Scientology, which has coordinated an anti-Prozac information campaign as a part of its larger goal of discrediting psychiatry in general and psychiatric drugs in particular.

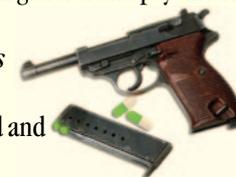
And while the furor may have died down, for many people the question still remains: *Does* Prozac ever cause violence or suicide?

The question is complex, but the best answer seems to be no, according to the U.S. Food and Drug Administration.

The FDA points out that all antidepressants can cause a level of arousal that can be disorienting, at first. And these feelings usually *do* emerge before the full antidepressant effects of the drug kick in, and could conceivably push a depressed user past the line that separates self-preservation from self-destruction.

Regardless, Prozac advocates claim, the documented risk of suicide is greater with tricyclics—and even with placebos—than it is with Prozac. And the highest known suicide risk factor of all is untreated depression.

The best solution, according to experts, is educating patients about possible side effects and maintaining close communication with the prescribing physician to reduce the risk of side effects ever getting out of hand. ■



Brave New Drugs: A Downside Guide

Trade/Generic Name	Dose/day	Possible Side Effects
Effexor®/venlafaxine	75-375 mg	high blood pressure, sexual dysfunction
Paxil®/paroxetine	20-50 mg	fatigue, sexual dysfunction
Prozac®/fluoxetine	20-80 mg	anxiety, insomnia, sexual dysfunction
Serzone®/nefazodone	300-600 mg	drowsiness
Wellbutrin®/bupropion	300-450 mg	weight loss, slight (.4%) risk of seizures
Zoloft®/sertraline	50-200 mg	drowsiness, insomnia, sexual dysfunction

Source: American Health