THE NEW MIDDLE AGES

Self-Nonmedication

By BRUCE STUTZ
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Seven years ago, not long after my father died, with my editing job lost, my finances frail, my 26-year marriage failing, a child in college and a mortgage to pay, my brain seemed to lose its way. Sometimes it could barely think at all. Sometimes it tortured a single thought for hours. And sometimes, in desperation and without aim, it released a barrage of anger upon itself.

Horacio Salinas for The New York Times

I could come up with a hundred descriptions of how I felt — as if the train I'd been riding had gone off track, as if the ground beneath me had given way and swallowed me up, as if I were in a black hole being compressed to nothingness — none of them very original, I suppose, because this was not, for a man just past 50, a very extraordinary midlife situation. But it was mine, and I saw no way out of it. Immobilized by indecision or agitated to the point of exhaustion, I could enumerate every stressful circumstance, but I was simply unable or unwilling to resolve any of them. Instead, I dithered miserably while I staved off creditors, struggled to write, sparred with marriage counselors and rued the emotional havoc I was wreaking on myself and everyone around me. Frustrated, I felt angered and at times utterly hopeless. I needed help.

At our first meeting, I told the psychiatrist that what I thought I needed was something to enable me to focus my thinking, something like the amphetamines I used to take in college to study. He demurred but said that an antidepressant might prove worthwhile and accomplish the same thing. He prescribed Prozac, but after only a few days on it, I began having nightmares that verged on the hallucinatory. So he suggested a switch to Effexor, and without much thought as to what this was or how it worked, I took the prescription and the handful of blister-packed capsules he offered (I had, when I was younger, tried many things given me by far lesser authorities) and agreed that we should meet regularly. The medication, he said, would begin working after a few weeks of gradually increasing dosage. I had no adverse reaction to it.

We met weekly and, like engineers examining a weakening structure, began to analyze each point of stress and how I might deal with it. This was not easy since, in the course of living, working and rearing children, I had developed many ways of specifically not dealing with many things — especially those that involved determining who I was and what I thought without reference to my being son, father, husband, lover or friend. I was not breaking new psychoanalytic ground here, but if one of the characteristics of depression —as it has been said of insanity — is thinking the same thing over and over and expecting to get different results, then I was depressed. I found little pleasure in anything; I couldn't sleep. Each day seemed to drag on forever, and yet I never seemed to have enough time to accomplish even the simplest tasks.

After several weeks of sessions, my brain began to clear. Whether this was because of the drug or from just taking the time to consider my circumstances, I don't know. Still, it took nearly three years of therapy before I began to lose my fear of thinking about things differently and accepting the fact that change held possibility along with uncertainty. But change was still hard — on everyone. My marriage did not make it through. I was living alone in a 17-by-6-foot below-ground studio in Brooklyn that my kids called "the Batcave," still challenged by money and work. But the siege had lifted, the panic had vanished and I felt older, wiser and abler.

My last session with my psychiatrist lacked drama. I thanked him. We shook hands. He wished me luck. There was no mention of going off my antidepressant, and satisfied with the way things were going, I continued to take my 150 milligrams once a day. I still struggled with work and money, but I stayed focused. Over the next several months, I wrote a proposal for a book that would, in examining the nature of spring, consider the nature of change. In March of the following year I began my travels, heading north across the country for four months, following the increasing hours of daylight, seeking to reach spring's climax and complete my spiritual renewal when I reached the Arctic at the summer solstice. But there, I also came to another realization: exhilarated by the 24 hours of Arctic daylight, hoping for a transformative escape from time, I had removed my watch. I was watching the timeless sight of caribou herds crossing the vast Arctic plain — and found myself worrying that I had no way of knowing when I should take my next dose of antidepressant.

In the past I experienced what happened if I didn't take it on time. When I missed my morning dose, by 2 p.m. I would begin to space out. A prickliness in my neck would give way to a restless agitation that left me edging toward panic. All I would be able to think of was how far away I was from home, my pill, relief. Within 20 minutes of taking the pill, I would feel better. I would feel better just knowing I'd taken it.

But what I was experiencing 4,000 miles away from New York felt absurd. Why, more than two years after leaving therapy, feeling fine, able to work, write and face setbacks and frustrations without panic or depression, was I still taking an antidepressant? I decided that being in the middle of writing the book was no time to stop, and stayed on for another two years. But once the book was published, I began to wonder again whether I needed to keep taking this pill.

Since the time I had stopped seeing my psychiatrist, other doctors had, with no questions asked, written prescriptions. My G.P. was the prescriber of the moment.

"I was thinking of getting off Effexor," I told him.

"Do you feel O.K. on it?" he asked.

I said I did.

"Then why go off it?"

Well, for one thing, this fear of forgetting my pills. And for another, I was beginning to suffer some undesirable sexual side effects.

"There are other drugs with fewer sexual side effects," he offered. "And there's always Viagra."

Didn't it seem strange to have to counteract the effects of one drug with another drug? Why not just get off the antidepressant?

"In my experience," he said, "most people who go off eventually go back on."

Somehow I couldn't believe I had to take this pill for the rest of my life. I was feeling fine. At least I thought I was feeling fine. The image that came to mind was of Dumbo the elephant believing that what allowed him to fly was the feather the crows had given him. Only when he drops the feather does he realize that he truly has the gift of flight. Could I let go?

Friends had plenty of stories of trying to go off antidepressants. One said her medication made her lose interest in sex, so that soon after she began taking it she quit but felt guilty telling her therapist, who went on thinking she was on it. Another said she kept trying to get off because she couldn't deal with the amount of weight she'd gained. But she kept returning to it. One said that within two weeks of quitting, she and her husband both found her unbearable, and she went back on.

All of them questioned my decision to go off. Didn't I understand that depression was caused by a chemical imbalance? It was a disease, they insisted, like diabetes, and antidepressants were like insulin. But a diabetic knows what will happen if he goes off his insulin. I was in a psychopharmacological Catch-22: the only way to know whether my depression would return if I went off of my antidepressant was to go off my antidepressant and risk depression.

My friends and I are children of the modern drug age; we never knew a time before antibiotics or antipsychotics, so our working assumption is that every disease has its cure. Sooner or later, as in the movies, an Erlich, a Pasteur or a Salk, working late in the lab, has a eureka moment, and the magic bullet is found.

When it came to depression, serotonin was deemed that magic bullet. One of life's most venerable chemicals — plants were making use of it long before humans evolved — serotonin is one of several chemicals, including norepinephrine and dopamine, called neurotransmitters, which nerve cells release into the tiny gaps among themselves and their neighbors to allow signals to pass among them. Once a message has been sent and received, the sending cell absorbs ("reuptakes" is the scientific term) the leftover neurotransmitter.

During the 1960s and 1970s, researchers recognized that some drugs that improved patients' moods had the ability to inhibit the sending cell's reuptake process, thereby leaving more neurotransmitter lingering in the synapses. Inductive reasoning led them to conclude that what must have caused these patients' mood disorders in the first place was an insufficiency of these same chemical neurotransmitters. Restore the brain's "chemical balance," the thinking went, and depression could be alleviated. The antidepressant age was born.

Early antidepressants worked on a number of neurotransmitters. In 1987, Prozac became the first selective serotonin reuptake inhibitor (S.S.R.I.) introduced in America, followed by Paxil and Zoloft. Effexor (generically, venlafaxine hydrochloride), the drug I was taking, focused on both serotonin and norepinephrine (and so is referred to as an S.N.R.I), inhibiting their reuptake, increasing the amounts in my synapses and thereby presumably enabling my brain to keep depression at bay.

It has long been known that the body's chemistry responds to stress. Recent studies suggest that when stress becomes chronic, the persistence of the chemicals that respond to it may damage or reduce the number of serotonin receptors, inhibit the production of proteins that mobilize serotonin receptors and even shrink neurons in the hippocampus, the part of the brain involved most with memory. How the chemistry of chronic stress results in depression is uncertain. It's also uncertain whether a deficiency of serotonin might lead to chronic stress. But the presumption is that antidepressants, by increasing serotonin, reduce the effects of chronic stress and thereby arrest depression.

Since I was no longer feeling depressed, the experiment I was about to embark upon would test whether without the drug to keep my serotonin up, my depression would return. A risky proposition, considering all I'd gone through to get well, but if I really was well, perhaps my serotonin levels might adjust on their own. Or perhaps I was well enough to live with a chemical imbalance, if that's what I had.

Drug-company brochures and Web sites reported that the symptoms of going off antidepressants were usually mild and short-lived — a week or two. They all recommended tapering off, preferably by half-steps, in consultation with a doctor. I thought about calling my psychiatrist, but it had been four years, and I didn't want to return to the place, physically or mentally, where I had gone through so much pain. I also knew my psychiatrist well enough to know that he didn't take his job lightly and would have most likely asked me to come in. But I couldn't afford more sessions.

While I was still undecided whether or when to begin, serendipity came into play. Instead of prescribing a month's worth of 150-milligram capsules to be taken once a day, my doctor mistakenly prescribed 75-milligram capsules to be taken twice a day. I took it as an omen. This would make it easy for me to halve my dose. So I began.

I expected that for the first couple of days I would feel the muscle-twitching anxiety that came when I missed a dose, but it was not so bad, and I had hopes that I might taper off quickly. On the third day, however, I began to find it difficult to focus and was unable to sit at my desk for more than a half-hour at a time. I was agitated, restless and hyperaware of sounds. When I read, sentences seemed to run into one another on the page, and I realized that this was not just because of difficulty focusing my mind but also my eyes. By early evening on that day, I felt so jittery and anxious that I decided I needed more medication. Somewhere, I recalled, a couple of years earlier I stashed a blister pack of 37.5-milligram capsules, a sample my doctor had passed on to me. But where? Although I could have split open a 75-milligram capsule, in my anxious state I became bent on finding those 37.5's. An hour or more later, after manically scavenging through everything in the apartment, I found them — six remaining in the blister pack. I took one and felt as if I could now go on. I felt relieved to have them. I would stay with my reduced dosage as long as I could, but they would be my backup if I found that I absolutely needed them.

Over the next several days they came in handy, especially at night, when I would wake up feeling dizzy, almost seasick, disoriented and in a heavy sweat, the pillow soaked. One night, awake and not eager to go back to lying restlessly in bed, I went online, typed in "Effexor withdrawal" and found bulletin boards full of pained, plaintive and sometimes angry posters who had quit taking their medication and were suffering a broad but surprisingly consistent range of symptoms: dry mouth, muscle twitching, sleeplessness, fatigue, dizziness, stomach cramps, nightmares, blurred vision, tinnitus, anxiety and, weirdest of all, what were referred to as "brain zaps" or "brain shivers." While there were those who went off with few or no symptoms at all, others reported taking months to feel physically readjusted. In the face of those symptoms, many despaired, gave up and returned to the drugs.

By the end of the second week, I felt confident that I could continue on 75 milligrams a day. But then my symptoms became more physical: the chills at night and the cold sweats continued. I felt tingling in my shoulders and hands, spasms in my legs. These came and went, seemingly with no reason. And then one night as I lay back to go to sleep, I felt a quick spasm in my head as if an electrical current had suddenly been sent through a circuit somewhere inside my brain. Two more followed in quick succession. With each came a wave of nausea. I sat up. They seemed to disappear. They returned. I realized these were the brain zaps, and over the next few weeks they would come, with no distinguishable pattern, several times a day.

Coping with the ever-changing and seemingly capricious symptoms was beginning to exhaust me. I couldn't stick to any sleep schedule. I couldn't think clearly. I was becoming unfocused, agitated and unable to sit long enough to read or work. The stress of anxiety and sleeplessness that I'd almost forgotten seemed to be returning. And that scared me.

Was my depression returning, or could getting off this drug actually cause so many and various symptoms? I spoke with neuroscientists, research psychiatrists and practicing therapists. All of them knew of the difficulties some people had in getting off not only Effexor but other antidepressants as well. They also all agreed that most of these symptoms were caused by a deficiency of serotonin.

What was happening was this: When I started taking Effexor, the drug began inhibiting my brain cells' process of reabsorbing "excess" serotonin — that is, the serotonin that had gone unused in sending signals across the synapses from one neuron to another. This was the purpose of taking the drug — to increase the amount of serotonin my cells had to work with and therefore, in theory, enable me to cope with my stress and depression. I say "in theory" because even 20 years since the introduction of drugs like these, every researcher with whom I spoke was cautious about presuming a direct relationship between increased serotonin levels in neural synapses and a decrease in depression. First, no one has ever measured the amount of serotonin in the synapses between anyone's brain cells. No one knows what constitutes a low, high or even standard level. Second, for reasons unknown, only a little better than half the people treated with antidepressants respond to them. Third, studies have shown that placebos have only a slightly lesser rate of effectiveness than the drugs. Fourth, serotonin levels are affected by many things — exercise, light, sleep, diet and even time of day. And finally, serotonin has so much influence on chemistry and functions in so many places in the body and brain relating to mood, sleep, sexual desire, appetite and body temperature that to say that it acts in any one particular way is impossible.

Research suggests that as the effects of the drug set in, my cells became more receptive to serotonin and the brain compensated to ensure that there wasn't a serotonin overflow. This function is important, because an excess of serotonin can not only cause severe psychological effects but can also, in rare cases, be fatal. During the first weeks of taking an antidepressant, then, until the drug's ability to inhibit reuptake of serotonin matches the brain's ability to withhold it, the

brain apparently has less serotonin to work with than it had before. During this period patients can suffer a range of uncomfortable side effects, from sleeplessness to anxiety, that make many patients quit taking the drug before they ever reach an effective dose. It's also the period during which some patients suffer such severe agitation that the chances that they will attempt suicide increase significantly enough that the F.D.A. requires what is known as a "black box" warning on the labels of S.S.R.I.'s for pediatric patients and is considering extending this warning to adults.

What I was doing now by decreasing my dose of Effexor was essentially reversing the process that I went through when I began taking it. As the amount of the drug in my system declined, my neurons once again began to take up the excess serotonin. But while the reuptake mechanism may respond quickly, the serotonin system can take weeks or months to readjust. In the meantime I was going to be short on serotonin and would have to suffer the effects. And because serotonin is so ubiquitous in the nervous system, the effects might be almost anything. They might even feel like depression. Or worse, they might even be depression.

None of these symptoms would come as news to most researchers. In 1996, nearly a decade after the introduction of Prozac, its manufacturer, Eli Lilly, sponsored a research symposium to address the increasing number of reports of patients who had difficult symptoms after going off their antidepressants. By then it had become clear that drug-company estimates that at most a few percent of those who took antidepressants would have a hard time getting off were far too low. Jerrold Rosenbaum and Maurizio Fava, researchers at Massachusetts General Hospital, found that among people getting off antidepressants, anywhere from 20 percent to 80 percent (depending on the drug) suffered what was being called antidepressant withdrawal (but which, after the symposium, was renamed "discontinuation syndrome").

They also found that the withdrawal effects depend on a given antidepressant's half-life — that is, the amount of time it takes for half the medication to be washed out of the body. Since this is a measure of the length of time the drug is effective, you will more quickly feel the effects of missing a dose of an antidepressant with a short half-life than of one with a long half-life. If you're taking your full medication daily, this isn't relevant. But when, say, you reduce the dosage of a short-half-life drug by half, that half is, by the nature of the drug, quickly halved again. In their studies, Rosenbaum and Fava found that Paxil and Zoloft, with half-lives of one day, proved more difficult to get off than Prozac, with a half-life of four to six days. Effexor, the drug I was on, has the shortest half-life of all: five or six hours. That explained why, if I forgot to take my medication in the morning, by afternoon I was facing a panic attack. It was also why, Rosenbaum and Fava told me, when a patient is having trouble getting off Effexor they might recommend switching to Prozac to ease the transition.

Still, the symptoms of discontinuation syndrome could be fierce. Fava, in a 2006 paper, cited "agitation, anxiety, akathesia, panic attacks, irritability, aggressiveness, worsening of mood, dysphoria, crying spells or mood lability, overactivity or hyperactivity, depersonalization, decreased concentration, slowed thinking, confusion and memory/concentration difficulties." So I decided to stick with 75 milligrams a day for a while to give my serotonin system time to catch up. But in my third week, I still felt constantly uncomfortable and often irritable. The brain zaps were sometimes blinding. No one seemed to know what caused them. I even went to an ear, nose and throat specialist to see if I was suffering from some sinus problem, but he found nothing. One day, trying to repair a cabinet drawer, I ruined the glide and, suddenly and blindly angered, began pounding my head with my fist. Worse was that my failure at something so trivial triggered more general, undefinable feelings of failure similar to those I suffered when I was depressed.

Ron Duman, a researcher at the Yale University School of Medicine in the psychiatry department, told me recently that there was no specific mechanism that would explain my symptoms, but that my system was trying to readapt. "Your neurons," he said, "are literally sensing the lack of serotonin." That was the bad news. The good news: "That the brain is able to adapt to stress, to environmental impact or pharmacological stimuli and change over time is really a key concept of how the brain works."

My choice then, as I saw it, was either to go back to taking the medication or find another way to try and raise my serotonin levels, or at least help the process along. Duman, an athletic-looking guy himself, told me that studies have shown that exercise can improve the serotonin system as much as antidepressants can. So I began a serotonin-boosting regimen — getting out and taking daily walks around Prospect Park, near my home in Brooklyn. No jogger, I completed the three-mile loop in 45 minutes to an hour. After a few days, I noticed that these walks relieved my restlessness. I began to sleep better.

Sleep, Efrain C. Azmitia of the biology department and the Center for Neural Science of New York University, told me, increases serotonin levels, too. Azmitia, who has conducted research on the serotonin system for four decades, said that light and good nutrition can also increase serotonin. Anything, in fact, that relieves severe stress, which, he has found, is disruptive to the serotonin system. It's why therapy might work just as well as medication, why placebos may work. The stress is relieved, and the system recovers.

I was feeling so much better by the end of the fourth week that I decided to cut back on my dosage again. At the bottom of my computer bag I'd found more blister packs of 37.5-milligram capsules, part of my hidden caches of medication. The first day went fine. But that night I screamed so loudly in my sleep that it seemed to echo in the room long after I sat up awake. It was 4 a.m. I was having brain zaps. I decided to take another 37.5 milligrams but then to try to make it last me through the next day. It did.

Around this time, I began to feel sensations, smells and sounds more intensely. Had the drug, in keeping me focused, also lowered my response to life's pleasures? When I asked Rosenbaum, the researcher at Mass General, about this, he insisted that there was no evidence that antidepressants have what he called "a dulling effect." But others disagree. Joseph Glenmullen, a clinical instructor in psychiatry at Harvard Medical School, says he has had many patients describe it. I know that I felt it.

One evening, sitting in the movie theater and watching "Little Miss Sunshine," I suddenly found myself welling up with tears. I put my head back and closed my eyes, but the tears came. I wondered for a moment whether it was a sign of depression but realized that I never cried when I was depressed. I didn't have the focus for it. Over the next weeks, when out walking or listening to music (Count Basie's "Li'l Darlin'," in particular), I found myself weeping for no reason at all.

What I was gradually beginning to feel was the difference between clicking on a book on Amazon.com and wandering through library shelves, allowing my gaze to wander from spine to spine. I imagined that when I allowed myself such pleasures, I was disarming stress and that my serotonin responded accordingly.

I was now down to 37.5 milligrams a day. It had been two full months since I began getting off Effexor. I decided to see if I could go without. I felt a bit panicked that morning but by noon was still fine. Perhaps, I thought, this was it. But the brain zaps increased throughout the day. Feeling disoriented that night, I took another 37.5 milligrams. I put off taking another dose for 24 hours and then decided to try to make it through the night. By morning I'd gone 36 hours. Should I try to keep going? But the blister pack held another capsule. Maybe just half of it, I thought. I opened the capsule, poured out the tiny white granules, took half into my palm and swallowed it with a glass of water. When I looked down at the counter with the open capsule, the remaining grains of medicine, and the trail of white power where I'd scraped the rest into my hand, I realized that it was time to move on.

In the months since going off, withdrawing, discontinuing, whatever you want to call it, I've been through life's usual stresses (and some extraordinary ones), felt good, bad, sad, unhappy, glad, even hopeless and helpless. But I've yet to feel again the chronic, painful and perspectiveless despair that characterizes major depression and that first brought me to seek help.

Will I become depressed again? Rosenbaum told me that the answer to that question may depend on the severity of the earlier depression — a major depressive episode as opposed to feeling very down or stressed — and the length of time the symptoms lasted. Sometimes, he said, patients feel better but have residual symptoms. "If you have residual symptoms, you're at risk for relapse. If you've had multiple severe episodes, if you've had chronic depression, you're at risk for relapse." Studies show that people who go through one bout with severe depression have a one-in-four chance of having another. Two bouts, and your chances double of having a third. Three bouts, and it's nearly certain you'll have another.

I wondered what my future held, since studies show that those who go through long-term therapy in conjunction with antidepressants have less of a chance of their depression returning than those who only take an antidepressant. "I believe that sometimes people can grow while on antidepressants and free up depression in a way that might buffer them to take advantage of psychosocial treatments they couldn't have taken advantage of when they were depressed," Rosenbaum told me recently. "But I've also seen people who have done hard work in cognitive therapy, but they just can't sustain it when depression returns."

What got me back on my feet? Was it the medicine, the therapy or both? Was it just the passage of time? I'm certain that there was much chemistry involved, since our capacities to think, feel and imagine all come out of the chemical makeups of our brains.

But did I need the drug to alter that chemistry? If my psychiatrist had told me, "I think you can do this without taking any drugs," would I have done just as well? If I had been told how difficult it would be to get off the drug, would I have so readily started on it? Even the doctors and researchers who most believe in the effectiveness of antidepressants acknowledge that the "chemical balance" paradigm, the magic-bullet paradigm, makes things seem simpler than they actually are. For some, these drugs may be a lifesaving treatment. But for most of us troubled or even temporarily anguished by life's difficulties, does our long-term reliance on these drugs become more of a convenience than a cure, allowing us to simply keep going in the midst of very difficult circumstances? And once we start taking them, how do we find the wherewithal to stop?

Ron Duman told me about one way that scientists try to test the effectiveness of a given antidepressant in the lab. Put a laboratory rat into a beaker of water and see how long it struggles to get out. When it stops, remove it from the beaker and treat it with the drug. Repeat the test. If it struggles for a significantly longer time than before, the drug is considered to have antidepressant potential.

Is this ability to keep us going altogether good? As Rosenbaum pointed out to me, people under stress can do great harm not only to themselves but also to those around them parents to their children, couples to each other. But when does reliance on a drug keep us from seeking ways to resolve the causes of stress? General practitioners, not mental-health specialists, write most of the prescriptions for antidepressants. For most doctors and psychiatrists, drugs, not therapy, have become the first line of defense. Only some 20 percent of people prescribed an antidepressant ever have even a single follow-up appointment.

Perhaps it was the difficult time I had getting off my antidepressant, but I never think about going back on. I'm enjoying this revitalized view of my emotional and physical worlds. Having finally dropped the feather that I believed allowed me to fly, I face life's difficulties without much fear of falling back into depression. I have no illusions about having resolved every issue or that all that happened won't continue to have repercussions on those who went through it with me. I don't believe in "closure." Life, like the brain, has too much interconnected circuitry. But it is also always changing.

"The brain has evolved to deal with sadness and grief, and having to deal with them may make the brain more flexible," Azmitia told me.

Maybe dealing with life's distresses has its own chemistry. I know I hated every second of it. I don't know if the medication helped. But I do know that I'm very glad I'm off.

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