

manufacturing depression

THE SECRET HISTORY OF A MODERN DISEASE



GARY GREENBERG



The Noble Lie
The Self on the Shelf

MANUFACTURING DEPRESSION

The Secret History of a Modern Disease



Gary Greenberg

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Ring the bells that can still ring
Forget your perfect offering
There is a crack, a crack in everything
That's how the light gets in
—*Leonard Cohen, "Anthem"*

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MANUFACTURING

DEPRESSION

CHAPTER 1

MOLLUSKS

When Betty Twarog opens the door to her cavernous rooms at the University of Maine's Darling Marine Laboratory, you're smacked in the face with mist and the smell of brine, and the sound of water everywhere. Pumped out of Boothbay Harbor, it hisses and sprays and gurgles through pipes overhead and sluiceways underfoot, flowing through huge dark tanks full of sea urchins and starfish and other gnarly marine creatures before pouring back into the harbor. With a finger raised to her lips and a sharp shake of her head, she shushes the questions I shout over the din. At first I think she's afraid I will disturb her spat, the baby clams and scallops gestating in the bucket she's leaning over. But, she later explains, her job—to measure out precise portions of the three algae concoctions that are bubbling in tall plastic tuns in an adjacent room and feed them to her tiny charges—requires her total focus. So for a half hour, she attends to her task with silent concentration. A slightly built woman with ramrod-straight posture and long dark hair drawn back tightly from a dramatic widow's peak, she moves with the fluid grace of someone who has been doing chores like these for just over a half century. You wouldn't know it to look at her, but Betty Twarog is seventy-seven years old.

Something else you wouldn't know as she tends her mollusks is that Betty Twarog made one of the most important scientific discoveries of the twentieth century, one that changed the course of neuroscience and medicine and set off a revolution in the way we think of ourselves. In 1952, when she was a twenty-five-year-old woman in a man's world, armed with nothing but a fresh Ph.D. and a hunch about an old scientific mystery, Twarog discovered serotonin in the brain and laid the cornerstone of the antidepressant revolution.

That's not what she had in mind. All she really wanted to do was to answer [a question first posed in 1884](#) by Ivan Pavlov—yes, *that* Ivan Pavlov—when he took a brief excursion into the world of invertebrates. Pavlov, on a postgraduate fellowship in Leipzig, was trying to figure out the secrets of digestion. In large part, moving food along the alimentary tract is a matter of smooth muscle functioning, and Pavlov decided to investigate the byssus retractor, the smooth muscle that *Mytilus edulis*, the common mussel, uses to close its shell. He was particularly interested in how it was possible for the creature to hold its shell shut against the outside world without expending far more energy than it could possibly take in.

His interest in this question didn't last long, and in the single paper he published on the subject before resuming the inquiries that led to his Nobel Prize (and to his eventual fascination with the salivation reflex in dogs) he offered only the merest hint of an answer. Seventy years later, Betty Twarog, for reasons she can't quite explain, found the remaining mystery irresistible. And she thought she had the answer, but it was too fantastic, too off the charts to be credible—until Abbott Pharmaceuticals just happened to mail her the means to check out her hunch.

Abbott had offered samples of a compound it had just synthesized to leading scientists around the country, including John Welsh, Twarog's mentor at Harvard. The molecule didn't have a name yet, or, more accurately, it had a number of them. Chemists called it 5-hydroxytryptamine after its molecular structure. Some biologists were calling it enteramine because they had found it in the guts of squid and octopi, while the biologists who had found it in blood called it serotonin. Abbott wanted the scientists to use their free samples to figure out what exactly the stuff was, what it did, and how it could be used. The company was hoping to find a way to make a drug, or a target for drugs, out of the new compound. They had no idea what they had stumbled upon.

But Twarog did, or so she believed. Pavlov, she thought, had gone much farther toward a solution than he knew. “It’s perfectly beautiful,” Twarog told me, “because to this day his paper summarized the control of these muscles. He insisted that they contract under nervous stimulation and that they hold that contraction until they are signaled by relaxing nerves that turn it off.” The mussel, that is, didn’t clamp down its byssus retractor and then squeeze it tight like you or I would clench our fingers around a quarter; instead, Twarog hypothesized, it closed the shell and threw a lock, which remained latched until a signal opened it like a key.

Twarog, unlike Pavlov, had the benefit of a discovery made in 1921 by a German scientist, Otto Loewi. Loewi wondered exactly how nerves signaled muscles—in particular, whether the process was purely electrical or somehow mediated by chemicals. He claimed that an answer came in a dream on [Easter night](#). He sprang out of bed and rushed to his lab, where he cut the hearts out of two frogs and bathed them separately in salt water. Dissected hearts in saline will continue to beat, and Loewi had left intact the nerves that control the pulse rate—the vagus nerve, which slows it, and the accelerator nerve, which does what you think it does. He sent an electric charge from a battery into the vagus nerve; the heart slowed, just as he expected. But then he took the salt water from that bath and dripped it into the other heart’s solution. When that heart slowed without any electrical stimulation, Loewi concluded that a chemical released from the vagus nerve and into the saline, and not electricity, had slowed down the heart. He repeated the experiment on the accelerator nerve, with the same result, and by 5:00 a.m. on Easter Monday had proved the principle of chemical neurotransmission.

By the time Twarog became intrigued by her mussels, Loewi’s principle had been firmly established, but most scientists had settled into the belief that Loewi’s chemicals—acetylcholine and epinephrine—were the only two neurotransmitters in the body. Twarog, however, was sure that there had to be another—the one that the mussel used to lock and unlock its shell—and she had a hunch that it was the chemical Abbott had sent.

In May 1952, Twarog and Welsh laid out the mussels on a lab bench. As soon as Abbott’s serotonin hit them, the byssus retractors retracted. Twarog was right. Serotonin was the missing neurotransmitter.

As disturbing as the news of a new neurotransmitter might have been to scientific orthodoxy, Twarog’s next idea was downright heretical. She said that serotonin would be found in the mammalian brain, which meant, of course, the human brain. At the time most biologists believed that humans were different from the rest of the animal kingdom, and the brain different from the rest of the body. In particular, they thought that electrical signals leapt around the brain like sparks, a throwback perhaps to René Descartes’ idea that the pineal gland sent out ethereal messengers bearing the soul’s instructions to the body.

Twarog thought this kind of reasoning was “sheer intellectual idiocy.” It didn’t make scientific sense—“what was the difference really between the brain and the rest of the body?” she says, still incredulous after all these years. “This is how nerves worked, no matter where they are.” And, maybe more important, it didn’t make philosophical sense either. “You know Tennyson’s poem ‘Flower in the Crannied Wall’?” She quoted from memory: “‘Little flower—but if I could understand / What you are, root and all / and all in all, I should know what God and man is.’ This is how it had to be.”

Two years later, Twarog moved to Ohio to follow her husband to a university job. Restless, she applied for a position with Irvine Page, a Cleveland Clinic doctor who was trying to understand the role of serotonin in regulating blood pressure. On the day of her interview, it was pouring rain and, she recalls, “I looked like something the cat had dragged in.” Still dripping on Page’s floor, Twarog described her ideal job: a lab, an assistant, and the time to study the distribution of serotonin in the brain. He grilled her—after all, her hypothesis went against everything he’d been taught about the nervous system—but finally agreed to give her the bench space and a technician. Within a year, she

had found serotonin in the brains of rats, dogs, and monkeys.

[Twarog's first paper](#)—the one about her experiment at Harvard—didn't get published until 1954. She didn't even hear back from the editor of the *Journal of Cell Physiology*—Detlev Bronk, the president of Johns Hopkins University—until John Welsh, the Harvard professor, called to inquire about the status of the article. Bronk told him that he wasn't about to ask his peers to review a speculative article by an unknown girl on such an important topic. While the paper was moldering on Bronk's desk, other scientists, much more prominent than Twarog, were arriving at a similar conclusion about serotonin. Once they had published their findings, it was safe for Bronk to let the girl have her say. [Her paper with Irvine Page](#) on cerebral serotonin also had to wait until the big boys said it first. But today no one disputes that she was the first with both discoveries.

Betty Twarog soon returned to marine biology, her first love. But many of the others went on to figure out the biology of neurotransmission, establishing within a decade that electricity really didn't fly from neuron to neuron like angels, that the brain really ran on chemicals like the rest of the body. And more than a half century later, new neurotransmitters are still turning up under the microscope as the subtleties of their metabolism still emerging.

None of these discoveries would be of much interest outside the lab were it not for some chance observations made in the early 1950s—that, for instance, an antitubercular drug that had induced an unexpected (although not unwelcome) euphoria inhibited an enzyme that breaks down serotonin, that lysergic acid diethylamide (LSD), already famous for its profound effects on consciousness, has a chemical structure similar to serotonin. Out of these and other findings, scientists began to cobble together a theory: that mental illness in general and depression in particular are caused by imbalances in neurotransmitters, and especially in serotonin. This theory was of obvious interest to pharmaceutical companies, and by 1958 drugs had come to market designed to cure depression by fixing these supposed imbalances. In 1988, Prozac was introduced, and by 2005, the last year for which reliable figures are available, 27 [million Americans](#)—10 percent of the adult population—were taking antidepressants, most of which act on serotonin, at an annual cost of more than ten billion dollars. It was a success far beyond anything Abbott could have dreamed of when they sent the serotonin to John Welsh's lab.

This is how the best science stories start—with a chance discovery that leads to a vast change in our everyday lives. Take the brilliant insight, the dogged determination, and the sheer good fortune behind an achievement like Betty Twarog's, throw in the poignant contrast between her anonymity and the significance of the knowledge she uncovered, add to it some gee-whiz-interesting science, and the next thing you know you have not only a great tale, but also an excellent example of the way that scientists take us up toward Parnassus—in this case the heights of happiness and health. A good science story can make you feel even better about progress and the prospects for humankind.

That's not the kind of story I'm going to tell in this book.

The invention of antidepressants is not the kind of achievement that contributes unambiguously to the betterment of our species. You probably already suspect that. Unless you've been living off the grid for the last half century, and especially the past two decades, you already know that serotonin has become a household word and Prozac and its chemical cousins—known collectively as selective serotonin reuptake inhibitors, or SSRIs—have become staples of the American medicine chest. And you know about the controversies that have ensued. You've had conversations about them with friends or family—or with yourself, when you wondered if your unhappiness or worry were signs of the disease we call depression, or when your doctor wrote a prescription for you and you hesitated to fill it.

it, or when you took the pills, felt better, and wondered what that meant about you. And you've probably found that these discussions leave you just as confused as you were before. One thing antidepressants don't do is end confusion about antidepressants. You'd need a different drug to do that.

You'll also need a different book to do that. I'm not going to end this confusion for you. In part that's because my subject is not the drugs so much as the condition they purport to treat, the disease of depression. But it's also because ongoing uncertainty is a hazard of reading a book by an old-fashioned psychotherapist like me, who believes that when it comes to important and complex questions, the best approach is to leave yourself in doubt for as long as possible, to live with inner conflict rather than to end it, to withstand yourself rather than to become someone different, to understand how you arrived at an important juncture rather than strike out down a road simply for the sake of getting on with life.

In this case, the crossroads that we've all arrived at is as crucial as it gets, and what I will do in this book is to show you how we arrived here, how we got to a point in our history where it is common, not mandatory, to think of our unhappiness as a disease. And I'm going to do something else here: I'll try to convince you that what is at stake with antidepressants and the disease they treat isn't only the question of whether or not to take drugs for our unhappiness, or even whether or not it's really a good idea to call our unhappiness clinical depression. What's at stake is who we are, what kind of people we want to be, what we think it means to be human.

If that seems like a stretch, then you should listen to Peter Kramer.

One of the strangest things about the antidepressant revolution, and one indication that more is going on here than biochemistry, is that the drugs that started it—the SSRIs, which first appeared in the United States in 1988—are [no more effective at treating depression](#) than the generation of drugs invented in the immediate aftermath of Betty Twarog's discovery. And that's not very effective. Nearly half the time, [the drugs fail to outperform placebos](#) in clinical trials. In real life (which generally lasts longer than a clinical trial and allows for modifications in dosage and brand), they seem to make a positive difference in perhaps 60 percent of the people who take them. You would think that if depression were really biochemical in nature and the drugs were really targeted at the culprit, they'd work better than that. Of course, the first part of that statement remains speculative despite their best efforts—and notwithstanding what doctors tell their patients when they prescribe them antidepressants—scientists have yet to find a single brain anomaly that is correlated with a case of depression, let alone one that causes it.

There are many reasons that antidepressants took hold despite these inconvenient truths, but one of the most important factors in their ascent was Kramer's *Listening to Prozac*, which began to fly off bookstore shelves in the mid-1990s, about the same time that Prozac prescriptions began to fly off doctors' pads. Kramer managed to articulate something that all of us—patients, their families and friends, doctors, and drug companies—needed: a credible justification for taking drugs whose principal effect was to make us feel better about ourselves. *Listening to Prozac* helped make the world safe for antidepressants.

In his book, Kramer starts out like many of us do about this subject—tentative, searching, and ambivalent. As he gathers momentum, however, his case for using the drugs—not only to treat depression, but to [“remake the self,”](#) as his subtitle put it—grows stronger, until it turns into a restrained but unmistakable endorsement. And while you have to wonder about that title—Eli Lilly himself couldn't have asked for better product placement—the fact that permission came not from a

ad man but from a neutral expert, a sensitive and honest and articulate eyewitness to the revolution only strengthened the case for the drugs.

Listening to Prozac ends with a prophecy. Having spent the better part of three hundred pages worrying over the complexities of using drugs to solve our problems, Kramer speculates that questions like these may already be pointless.

[By now, asking about the virtue](#) of Prozac...may seem like asking whether it was a good thing for Freud to have discovered the unconscious. Once we are aware of the unconscious, once we have witnessed the effect of Prozac, it is impossible to imagine the modern world without them. Like psychoanalysis, Prozac exerts influence not only in its interaction with individual patients but through its effect on contemporary thought. In time, I suspect we will come to discover that modern psychopharmacology has become, like Freud in his day, a whole climate of opinion under which we conduct our different lives.

Antidepressants' most important side effect, Kramer seems to be saying, is the way they change our understanding of ourselves—altering not only our neurochemistry but our sense of its importance. And once that has happened, there's no more point in inquiring into their virtues than there is in wondering if winter ought to be so cold and snowy. It's an ironic end to a book that asks about little besides Prozac's virtue—and which did so much to usher in the climate of opinion under which we think of our unhappiness as a disease.

Kramer borrowed the phrase *climate of opinion* from [W. H. Auden's elegy](#) "In Memory of Sigmund Freud." Freud, Auden wrote, was no longer just a person:

*he quietly surrounds all our habits of growth
and extends, till the tired in even
the remotest miserable duchy
have felt the change in their bones and are cheered*

There was a time, and it wasn't very long ago, when people didn't feel in their bones that they "had depression," when the Centers for Disease Control weren't calling depression "[the common cause of mental illness](#)," when the World Health Organization wasn't claiming that depression was "[the leading cause of disability](#)...and the 4th leading contributor to the global burden of disease." It's possible that doctors have gotten better at recognizing depression. It's possible that contemporary life imposes demands that exceed the neurochemistry bequeathed to us by natural selection. It's even possible that global warming, widespread warfare, the worldwide economic collapse—that the seemingly irremediable conditions are making us sick with worry. Indeed, all of these explanations for the apparent depression epidemic could be true at the same time, but there is another possible explanation: every new climate of opinion about who we are has its distinctive form of lousy weather. Clinical depression—unhappiness rendered as disease—is ours.

Climates of opinion don't descend fully formed from the heavens any more than occupying

governments do. If they did, if Betty Twarog's discovery had simply led to a sudden and cataclysmic change in the way we think of our unhappiness and what to do about it, then the skirmish that broke out in 1995 between David Wong and Arvid Carlsson in the pages of the journal *Life Sciences* would never have happened. Wong, the Eli Lilly scientist who first formulated Prozac, claimed in passing that [his drug was the first SSRI](#)—an assertion to which Carlsson, who won the Nobel Prize for his pioneering work in the neurochemistry of Parkinson's disease, took exception. Carlsson knew better because he had invented the first SSRI, zimelidine, which the Swedish pharmaceutical company Astra brought to market as an antidepressant named Zelmid in 1982, five years before Prozac. *Life Sciences* was forced to print a retraction and apology.

The reason that the editors of *Life Sciences* didn't catch Wong's overreaching—and that you have most likely never heard of Zelmid either—is that Astra never took its drug very seriously, at least not as a big moneymaker. Or so you must conclude from the fact that on the eve of its introduction into the United States, when it began to seem that patients taking Zelmid were prone to contracting the rare neurological disorder Guillain-Barré syndrome, Astra decided not to do the studies necessary to investigate the connection. Instead, it simply pulled the drug from its shelves. The company executives just didn't think there was enough of a market for an antidepressant to make it worth the shareholders' while. Or to put it another way, they didn't think there were enough depressed people out there.

To judge from the industry's willingness to spend huge amounts of money to minimize their drug's association with violence and suicide and other, less dramatic side effects, that's not a problem anymore.

The climate changes slowly and imperceptibly, and once it's settled in, it's as invisible to us as the sea is to a fish. But if you start to look for it, it's awfully hard to miss.

For instance, let's say you haven't been able to shake off a setback or a loss, and you find yourself preoccupied and worried, prone to tears, avoiding sex and other pleasures, overeating and undersleeping and just plain not enjoying life as much as you once did. And let's say you resist the idea that you have an illness, but on the other hand, you're mighty tired of feeling this way, and one sleepless night cruising the Internet, you end up at [depressionisreal.org](#), a coalition of “[several preeminent medical, advocacy, and civic groups](#) who have joined forces to educate the public about the true nature of depression and how people can live and thrive with this biological disease.” There you can tune into a podcast of the *Down & Up Show*, which promises to “separate fact from fiction” about depression. You can find out about depression rates in the United States. You can read about depression and women or depression and the Latino community. You can download a mood tracking calendar. You can even take a test that tells you whether or not you have depression. And if it turns out that you do, you can read about resources that you can contact tomorrow, or you can click over and get some comfort right now from Paul Greengard, a doctor who, as it happens, shared the Nobel Prize with Arvid Carlsson. Dressed in his white lab coat, Greengard gazes reassuringly from beside the message:

[Some say depression is all in your head](#). Well, that's right. And wrong. It's right because depression is in the head, or more precisely, the brain. In fact, we've seen how it destroys the connections between brain cells.

But saying depression is all in your head is also wrong. There's nothing imaginary about

depression. It's a serious medical condition that affects every aspect of a person's health.

Greengard is hardly the only doctor—or even the only Nobel laureate—to deliver this message. It has saturated American popular culture to the point that it is nearly inescapable. And it has done some good. The idea that depression is a treatable medical condition has given people permission to talk to their doctors about suffering for which they might otherwise never seek relief. It has saved lives by preventing suicide, kept families together, helped people to stay productive. And it has had enormous benefits for basic neuroscience: industry interest in finding drugs to treat depression has opened up the coffers to researchers trying to figure out how the brain works.

Nonetheless, there is indeed something, if not quite imaginary, then certainly invented, about depression. Greengard gives us only two choices: that it is *real*, which in the current fashion means that it is the result of neurochemical events, or that it is *fake*, a product of our fickle imaginations and our weak wills. He overlooks a third possibility: that it is made up not *by* us, but *for* us, that depression—or at least the version of depression that Greengard is describing—is manufactured.

Depression is surely an affliction, one that at least in some cases may well have a specific, although still undiscovered, brain pathology—a disease in the usual sense of that word. This is a powerful and compelling idea: if you are unhappy in a certain way, then you are suffering from a brain illness, not different in principle from any other illness. That idea has become part of the way we think about ourselves, part of the incessant chatter of our own minds (or is it our brains?), of the constant self-evaluation by which we mark our lives.

Am I happy enough? has been a staple of American self-reflection since Thomas Jefferson declared ours the first country on earth dedicated to the pursuit of happiness. *Am I not happy enough because I am sick?* on the other hand is a question that has just arisen in the last twenty years. This is the sentiment in which depression has been manufactured—not as an illness, but as an idea about our suffering, its source, and its relief, about who we are that we suffer this way and who we will be when we are cured. Without this idea, the antidepressant market is too small to bother about. With it, the antidepressant market is virtually unlimited.

My first bout of depression began in 1987, at the same time my first marriage ended. It's not that she didn't want the divorce. In fact, it was my idea, an idea I had expressed in a time-honored if ignominious way: by falling in love with another woman. I now think of this transgression as a merciful sort of wickedness, my adultery putting us out of a misery that neither my first wife nor I had the wisdom or courage to end. We were like two comets that had crashed into each other deep in interstellar space. The collision nearly consumed us and left behind nothing but cold and darkness, and, at least for me, a smoldering pile of self-reproach.

I was thirty years old, a psychotherapist by day, a psychology doctoral student by night, and you would think that at some point—I would nominate the time I found myself on the floor watching dust specks float through sunbeams for hours (because they happened to be in my line of sight, because looking at anything else or closing my eyes and staring at my own black insides would just take too much effort), racked by some unspecifiable pain, like my whole being was a phantom limb, and thinking about that lady in the LifeFone pendant ad, the one who has fallen and can't get up—you would think that at a point like this it would have occurred to me that I was depressed. Come to think of it, that probably did occur to me. But in 1987, *depressed* didn't mean what it has come to mean in the years since. Then it was a convenient description, something to say to a friend or to myself, a shorthand that left the details to the imagination. Now it's an illness.

To be fair, depression was already an illness in 1987. It just wasn't quite so famous as it is now. In fact, it had been an official disease in more or less its current form since [the 1980 release of the third edition](#) of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*. The DSM, as it is known in the industry, is a compendium of psychological troubles, sorted into groups (affective disorders, substance use disorders, psychotic disorders) and from there into individual diagnoses (*major depressive disorder, alcohol dependence, schizophrenia*). And it is indispensable to the business of therapy. Not only does it provide a taxonomy of mental disorders which in turn gives us therapists a private language in which to talk to one another and a way to feel like we're part of a guild; it also assigns to each species of anguish a five-digit code. Written on a bit of that magic number unlocks the insurance treasuries, guaranteeing that because we therapists are treating a disease rather than, say, just sitting around and talking to people about what matters to them, we will get paid for our trouble. This is why the most recent edition of the DSM (we're now on the fourth, with the fifth due in 2012) sits on the shelf of virtually every therapist in the country, including me.

The DSM is an unparalleled literary achievement. It renders the varieties of our psychospiritual suffering without any comment on where it comes from, what it means, or what ought to be done about it. It reads as if its authors were standing on Mars observing our discontents through a telescope.

As we will see a bit later, that was exactly the intent of the authors of the third edition, which was a radical departure from the two previous DSMs and the model for subsequent versions. They meant to incite a revolution in psychiatry, a discipline that previously had not hesitated to comment on theoretical (some would say metaphysical) matters such as the origin, nature, and causes of mental anguish. It took a decade or so, and the introduction of a few new drugs, before the revolution was complete, at least with respect to depression. Had my troubles occurred later in that decade, I'd have been much more likely to reach for the LifeFone, to get my diagnosis and the meds to go with it, and to become part of the CDC and WHO statistics.

I wouldn't have avoided this path on principle; in fact, as I'll describe later, drugs (although not the drugs you might expect) did help me finally bring my black dog to heel. But it simply never occurred to me to think of myself as sick. I just figured I'd had a disaster in my life and my unhappiness was the consequence of it, as surely as whacking my thumb with a hammer would have left me injured and in pain and really mad at myself. I worried that I might never get over this, that I would be alone forever, that my finances would never recover, that my divorce was also my initiation into the reality of how hard life really was. I talked about this in therapy, of course, about this and many other subjects. I learned all sorts of things about myself that I didn't want to know. I marveled at the ability of mercifully long-forgotten chapters of my private history to insinuate themselves into waking life, the bad faith I could engage in and the pain it could cause myself and others, but my therapist and never, to my recollection, talked about me as a sick person. Whatever I had seemed like a bad specimen that I had to outwait or at least get used to while I did my best to overcome it.

I did think of depression as a disease; at least I did in my professional life. But I associated *the* depression with patients like Evelyn. A young woman who was already weeping when I went to fetch her in the waiting room, she told me right off that her life was unmitigated agony. Every success was its own punishment, and her professional achievements, the love of her family, even the sun coming up on this gorgeous spring day only made her feel worse—as she put it, it was as if she were Frankenstein's monster watching through the window while the human family lived their happy lives in their warm hut. She said she had called me because she had recently accepted an invitation for a free vacation to Hawaii, and as the date approached she was beside herself with dread. “Because of the expectations to have a good time like everyone else, and the light, that relentless sunshine, which is just going to crush me,” she said. “I know this is as good as it gets, and it's not good enough for me.”

which just makes me hate myself more.” She stopped, fixed me in her gaze, and lowered her voice to a near-whisper. “I hope the fucking plane crashes.”

And then there was Ann, the biologist who ended her promising research career to marry a truck driver who beat her and then left her, taking their son with him. She was sure she deserved this and any other failure or indignity that visited her, and her day could be ruined if someone praised her. She was a connoisseur of anguish who had more words for her blue moods than Eskimos allegedly have for snow, who wrung her hands ceaselessly and cried rivers as she talked, but who always seemed surprised when I pointed these things out or expressed concern about them. And not only surprised—she told me frequently that the fact that I paid that kind of attention to her and still seemed to like her reflected poorly on me.

Or Barbara, who phoned me one night demanding, “You have to tell me why. Give me a reason to go through all this pain.” I told her I knew that she was suffering, that I would listen to her and stand by her and get up in the middle of the night to comfort her, that I would remind her of all the other people who loved her, all the things she still wanted to do, but that beyond that I couldn’t give her what she was asking for. She was dead the next morning, lying in bed next to one of those people who loved her. She had overdosed on her antidepressants.

That’s the disease of depression as I saw it then: severe, disabling, and deadly, unrelated to any circumstance, resistant to comfort (let alone to treatment)—and, thankfully, rare. Wounded as I was by my suffering—and that of most of my patients—wasn’t even in the same ballpark as theirs, and surely not in the same diagnostic category. Which isn’t to say we weren’t unhappy—after all, why else would we be spending our time and money complaining to therapists about our lives?—just that it didn’t seem to me (or, so far as I know, to them) that we had *depression*.

Or so I thought at the time. Now, it could be that I just didn’t want to place myself in the category of the mentally ill; after all, when it comes to those diagnoses, most of us therapists are better at dishing it out than taking it. Or that because I wasn’t looking for depression, I didn’t see it except in the most dramatic cases. If that’s so, then the last twenty years, in which it has become unthinkable for clinicians and laypeople alike *not* to consider unhappiness as a symptom, constitute a period of unparalleled triumph for public health.

But it could also be that depression has expanded like Walmart, swallowing up increasing amounts of psychic terrain, and that, also like Walmart, this rapidly replicating diagnosis, no matter how much it helps us, and no matter how economical, is its own kind of plague. It could be that the depression epidemic is not so much the discovery of a long-unrecognized disease but a reconstitution of a broad swath of human experience as illness. Depression is, in this sense, a culturally transmitted disease, the contagion carried not by some microbe or gene, but by an idea transmitted by subtle and not-so-subtle means, including clever direct-to-consumer prescription drug advertising; ruthless drug company dominance of medical education, research, and practice; those dire statistics; state laws ordering insurance companies to pay for the treatment of depression as they would for diabetes or cancer therapies; a new DSM with even more subspecies of depression; and casual conversations with diagnosed and medicated friends. Borne on these vectors and others, the notion has spread that our sorrows, our discontents, our unhappiness, and our hopelessness are the signs of a pervasive disease until it (the idea, not the disease) has taken up residence in nearly all of us. Twenty years (and a few more bouts of intense unhappiness) after my spell on the floor, I would be very unlikely to feel as I did that day and not conclude that I was probably sick. I resist this thought, but I live under the same climate of opinion as you do, so I must confess that I still don’t know whether that resistance is a mistake.

I have a couch in my therapy office. People often make nervous jokes about it before seating themselves in one of my chairs. Every once in a while, someone will lie down on it, consciously parodying the Freudian stereotype. These patients might have noticed that the office would be better off without the couch. It's not only a cliché; it's also ugly and too big for the space. But it's an outstanding place to take a nap, which is really why it is there. As long as I can remember, the hand of Morpheus has reached up from the underworld and grabbed me by the neck every afternoon at around two o'clock. He is very hard to resist, so I have never scheduled midafternoon appointments, lest I embarrass myself and infuriate my patient by nodding off in the midst of their travail.

It turns out that frequent naps—more than half an hour a day, four or more days per week—are a symptom of depression. (There's no explicit exception for countries, such as Spain, that have siesta schedules, but one imagines that therapists in those places adjust the criteria accordingly.) I did not nap more after my first marriage collapsed, although I never kept track. One day during that period, I was awakened from a particularly lovely nap by a phone call from my father. I immediately forgot everything about the conversation other than the way I felt as I fought through my grogginess: anxious to the point of nausea.

"Dread," I said to my therapist, whom I happened to be seeing later that day. "Just a feeling of dread and self-loathing. Like there he was working hard, being productive, *functioning*"—he was calling me from his office, where he spent ten-hour days until he was well into his seventies—"and here I was wasting time, crashed out on the couch in the middle of the day."

"Well, what do you think this means?" she asked. I had, I knew, lobbed her a huge hanging curveball—all that Oedipal drama captured in a single scene.

"Maybe nothing. I have to say, it felt, I don't know, *biological*."

"Biological? You mean, like there are little bugs swimming in your blood or something, making you feel dread?"

She said this as if it were the most preposterous idea in the world, as if anyone who believed it was either evading the truth or just plain deluded.

It's not preposterous anymore. There are many ways to distinguish various depressive states from one another. You could, for instance, listen to the stories I'm telling here and conclude that there are three sorts of depression—the temperamental kind that seems to sum up a considered view of the world as a not-so-happy place, the kind that seems always to have been there and has no particular reason behind it, and the kind that comes on after a setback. Evelyn's depression is a good example of the first, Ann's of the second, and, if I have to place myself in a category, mine belongs in the last. And then there are formal distinctions. For example, in the old days, which is to say before the DSM-III, doctors talked about [manic-depressive illness](#), in which patients alternated between those two poles; [involuntional psychotic reaction](#), a condition of delusional guilt and self-loathing that came on in middle age; and [depressive neurosis](#), the garden-variety unhappiness that psychoanalysts treated in the Freudian heyday. Whether these distinctions were valuable or not or based on anything other than current fashion is hard to say. But what is clear is that they no longer exist. Sometime in the twenty years since my therapist made fun of me, the "bugs" have gnawed them into so much powder.

In *Against Depression*, his sequel to *Listening to Prozac*, Peter Kramer wrote "[Depression](#) neither more nor less than illness, but illness merely." Being depressed is not simply a response to a circumstance, he argued, although it can be kindled by events in our lives. Neither is it a sign of sensitivity or intelligence or insight, nor a branch of suffering with roots in the social or political world—a despairing apprehension, say, of the world we have made. Nor is it a response to the

tragedies inherent to human life—mortality, for instance, and the inevitability of loss. Indeed, I claimed, the failure to grasp the fact that depression is just another disease, just another way our bodies have of betraying us, as purposeless and meaningless as tuberculosis (which, he points out, was once seen as a mark of refinement), is itself a symptom of a widespread and longstanding, but deeply wrongheaded, view: that melancholy signals a profound grasp of the true nature of existence.

Kramer likened depression to “[an occupying government](#),” one that has apparently colonized our collective consciousness, propagandized us, as it were, into believing that it is more than illness. Under this regime, we don’t understand that when you’re lying on the floor of your study and it feels as if someone has turned up the gravity, you’re in the throes of a disease as frank and indisputable as, say, appendicitis—and that you are just as much at risk as you would be if you ignored that pain in your lower abdomen. Kramer confessed to having fallen prey to this ideology himself—not as a practicing melancholic, but a practicing psychiatrist. He learned this, he wrote, from a patient who, once the drugs had kicked in, chided him for paying too much attention to what her depression might actually mean. But he reeducated himself, and in his book urged the rest of us—doctors and patients alike—to do the same.

We are on the brink of an epochal shift, Kramer went on—to a time when “[the eradication of depression](#) [will] seem unremarkable as a...social goal.” Only one thing stands in the way of achieving that goal, Kramer wrote: ignorance. It takes many forms, but one of them is people like me and the other critics of the depression industry who are, according to *Against Depression*, unwittingly in thrall to that colonial power and who therefore insist on pointing out certain facts. Like, for instance, that the prevalence of depression magically skyrocketed just after the drug industry introduced the SSRIs, that the diagnostic criteria underlying this increase can’t distinguish between grief and depression, and that as a result the diagnosis threatens to swallow everyday sorrows. People who continue to believe these things, as the title of his book implies, must be, wittingly or not, *for* depression.

At the risk of sounding like the man who says no when asked if he’s still beating his wife, I’ll tell you that I’m really not on the side of the suffering that afflicted Evelyn and Ann and killed Barbara—the kind that drives people to their knees, or their beds, for months or years at a time. In fact, I’m not in favor of suffering at all. By criticizing the idea of depression as a disease, I’m not wishing anguish upon us. (Nor do I think that we need to safeguard pain against the depression doctors’ attempts to do away with it; something tells me that psychic suffering will never be in short supply.) Pain, psychological and otherwise, is just a brute fact, neither noble nor evil, neither redemption nor scourge. It may play some important evolutionary role—designed, perhaps, to alert us to the fact that something is wrong or to create the necessity for invention—but it’s not hard to imagine a different mechanism fulfilling these functions, one that doesn’t hurt so much.

The division of the world into forces in favor of and against depression is as false as every other Manichaean scheme. Everyone is against depression, just as everyone is against war and child abuse and global warming. The argument is really over *who* is depressed, which is to say over whose inner life gets pathologized under the new depression regime and what the depressed people are going to do about it. That’s why it’s important to figure out just what the depression doctors mean by the diagnosis and where that meaning came from: because there are burdens to being declared ill. Unless you are a drug company, in which case the only burden of a widespread illness for which you own the treatment is figuring out what to do with the profits.

I wish I could tell you that this very lucrative notion about unhappiness has been brought to us by

the marketing departments of the big drug companies. That would make convincing you to resist it a easier job. But while I will tell you plenty of stories about shrewd and sometimes questionable corporate behavior, proving that drug companies will do what they have to do in order to sell the product is no more or less illuminating than uncovering gambling in Casablanca. It's worth noting when the usual suspects behave suspiciously—when, for instance, a website like depressionisreal.org is funded by Big Pharma, but it would be a mistake to see this as evidence that the drug companies are conspiring to change the way we think about ourselves in order to make us dependent on them for our well-being.

The captains of the pharmaceutical industry are merely doing what they get paid the big bucks to do—to sail their corporate ships expertly on the winds and currents of the times. And the times, with some help from Big Pharma, have delivered them an ideal consumer for their product: someone convinced that unhappiness is a problem for their doctors to treat.

The history of the invention and production of depression is a strange and elusive kind of secret. Most of what I'm going to expose here isn't buried in corporate files. It's as obvious as a commercial for Prozac—or, for that matter, as the fifty thousand copies of *Recognizing the Depressed Person* that Merck distributed to doctors in 1963 or *Symposium in Blues*, the compilation album of blues songs that they paid RCA to press and send out three years later with prescribing information for their latest antidepressant inserted up its sleeve. It's laid out in black and white in the scientific literature, which documents, in addition to all that breathtaking neuroscience, the poor performance of antidepressants and the failure of the serotonin imbalance theory to explain depression. It's right there in the way that over the last century or so, medicine has shaped a climate in which we feel a bone-deep conviction that disease is something biochemical, that health and illness are scientific categories, and that doctors are dispensers of magic bullets aimed at molecular bad guys. It's on the front page of the newspaper where stories about America's drug war stand as daily reminders that we are very confused about taking drugs to change our moods—a confusion that is largely circumvented when we instead take drugs to treat a disease.

These are the raw materials of depression, and they've been assembled in the clear light of day, hidden, like Poe's purloined letter, in plain sight. I'm going to show you how depression has been manufactured right before your eyes—not in order to deny that depression exists or even that it can, in some cases anyway, rightly be considered a disease that can be cured by drugs, but in order to provide you with another tool to figure out what to do if recalcitrant sadness sets in and sends you to your doctor's office. Because Peter Kramer is both right and wrong about the climate of opinion—right that psychopharmacology is a sign of a major change in the climate, wrong that it is not worth your time to “ask about the virtues” of the new climate. Once you find out how unhappiness has become an illness to be treated with drugs, and once you grasp that there is a history to your depression that has nothing to do with your biochemistry, you have another choice besides “all in your head” and “all in your brain.” If the idea that depression is a disease is as much a matter of history as it is of science, if it is, in short, a story about our suffering, then you are free to look for other stories, or to tell your own. You are free to arm yourself with information that your doctor might not even know about, to seek alternatives, to resist the regime—or to choose, because it makes sense to you and not because a drug industry-fattened doctor told you so, to subscribe to that story.

I'm not going to tell you that I don't have a dog in this hunt. I'm writing this book in part because I think that the medical industry, regardless of its intentions, has acquired far too much power over our inner lives—the power to name our pain and then sell us the cure one pill at a time. But even though I am a psychotherapist, I don't think the only alternative is what I sell in my office one hour at a time—although I will point out that it is probably the only profession built on the idea that changing the story

we tell about our suffering can relieve it. And I know, through my own experience as both a therapist and, as I'll detail later, as an officially depressed person, that drugs—although not necessarily the drugs that Pharma is selling—do work. But that doesn't mean that depression—yours, mine, or anyone else's—is the disease the depression doctors say it is.

CHAPTER 2

JOB VERSUS HIS THERAPISTS

[It is customary](#) for histories of depression to start with Hippocrates, the ancient Greek physician. There are good reasons for this. In addition to originating the oath by which physicians pledge not to harm or kill or seduce their patients, Hippocrates set Western medicine on its current course by insisting that the doctor's job was to use his own senses to acquire the actual details of his patient's suffering. When he told his disciples to seek the truth by examining the phenomenon of the illness itself, Hippocrates was urging them to kick the gods out of the clinic; as Hippocrates said of epilepsy, known in his time as the *sacred disease*, "[it appears to me to be no more divine](#) nor more sacred than any other disease, but has a cause from which it originates." This idea—that illnesses exist in nature and that it is the doctor's job to find and, if possible, to heal them—is exactly the idea behind modern medicine today, including the treatment of depression.

One of the conditions that Hippocrates took note of looks something like our depression. "[Fear and sadness](#) that is prolonged means *melancholia*," he wrote, and the melancholic patient, who suffered from an excess of black bile (which is how *melancholia* translates from the Greek) has an "aversion to food, sleeplessness, irritability, and restlessness." [He is rumored to have cured](#) the king of Macedonia's melancholia by deducing that he was secretly in love with his recently deceased father's concubine and prescribing a consummation of his desire (which makes you wonder if Hippocrates had heard about Oedipus).

It's easy to understand the depression doctors' eagerness to enlist the father of medicine in support of their contention that depression is a disease. The winners get to write history, after all, so why wouldn't they claim this patrimony? But even leaving aside for the moment the fact that so much of what Hippocrates and his followers wrote is fanciful at best—for instance, that "[it is a dead symptom](#)...when the patient sleeps constantly with his mouth open" or that lying "with the hands on the neck, and legs tossed about in a disorderly manner and naked...indicates aberration of intellect"—you have to wonder why, if depression is such a common disease and Hippocrates such a voluble commentator on a vast range of human suffering, his work on melancholia is so scant. His notes on the subject are scattered throughout his works, and he doesn't tell us much about it, not even how the problem was related to the other black bile disorders, which ranged from hypersexuality to hemorrhoids (a condition that, unlike melancholia, [he devoted an entire book](#) to).

Hippocrates' lack of attention to melancholia doesn't mean that depression isn't an illness. But to cite Hippocrates as an authority for its existence is a little like citing George Washington as an authority on wooden teeth or cherry tree removal: just because he was a great man who had some interest in the matter, we shouldn't necessarily privilege his opinion about it. There is, however, an ancient account of depression that is much more robust than Hippocrates'—and much more like our current version of the malady. It's also much older. In fact, [according to one scholar](#), as soon as people started taking enough notice of themselves to put stylus to clay tablet—in around 5000 B.C., 4,500 years before Hippocrates, in the Mesopotamian society known as Sumer—they wrote down a story about a whopping case. (It would be a mistake to conclude from this ancient lineage that depression, like, say, the common cold, has been with us from the beginning. After all, we know virtually nothing of the inner lives of *Homo sapiens* for the 200,000 or so years prior to the advent of writing, so its appearance at the dawn of history could just mean that people became despondent as soon as they started paying enough attention to themselves to take notes.) The Sumerian version of this story is

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