for having a disease, as though it were a sign of some moral lapse or spiritual unworthiness.

The truth lies somewhere between these extremes. By sorting through the scientific data, my aim is to clarify the contradictions and replace the nonsense with a clearer understanding of the degree to which our emotions—and emotional intelligence—play a part in health and disease.

THE BODY'S MIND: HOW EMOTIONS MATTER FOR HEALTH

In 1974 a finding in a laboratory at the School of Medicine and Dentistry, University of Rochester, rewrote biology's map of the body: Robert Ader, a psychologist, discovered that the immune system, like the brain, could learn. His result was a shock; the prevailing wisdom in medicine had been that only the brain and central nervous system could respond to experience by changing how they behaved. Ader's finding led to the investigation of what are turning out to be myriad ways the central nervous system and the immune system communicate—biological pathways that make the mind, the emotions, and the body not separate, but intimately entwined.

In his experiment white rats had been given a medication that artificially suppressed the quantity of disease-fighting T cells circulating in their blood. Each time they received the medication, they ate it along with saccharin-laced water. But Ader discovered that giving the rats the saccharin-flavored water alone, without the suppressive medication, still resulted in a lowering of the T-cell count —to the point that some of the rats were getting sick and dying. Their immune system had learned to suppress T cells in response to the flavored water. That just should not have happened, according to the best scientific understanding at the time.

The immune system is the "body's brain," as neuroscientist Francisco Varela, at Paris's Ecole Polytechnique, puts it, defining the body's own sense of self—of what belongs within it and what does not.[1] Immune cells travel in the bloodstream throughout the entire body, contacting virtually every other cell. Those cells they recognize, they leave alone; those they fail to recognize, they attack. The attack either defends us against viruses, bacteria, and cancer or, if the immune cells misidentify some of the body's own cells, creates an autoimmune disease such as allergy or lupus. Until the day Ader made

his serendipitous discovery, every anatomist, every physician, and every biologist believed that the brain (along with its extensions throughout the body via the central nervous system) and the immune system were separate entities, neither able to influence the operation of the other. There was no pathway that could connect the brain centers monitoring what the rat tasted with the areas of bone marrow that manufacture T cells. Or so it had been thought for a century.

Over the years since then, Ader's modest discovery has forced a new look at the links between the immune system and the central nervous system. The field that studies this, psychoneuroimmunology, or PNI, is now a leading-edge medical science. Its very name acknowledges the links: *psycho*, or "mind"; *neuro*, for the neuroendocrine system (which subsumes the nervous system and hormone systems); and *immunology*, for the immune system.

A network of researchers is finding that the chemical messengers that operate most extensively in both brain and immune system are those that are most dense in neural areas that regulate emotion.[2] Some of the strongest evidence for a direct physical pathway allowing emotions to impact the immune system has come from David Felten, a colleague of Ader's. Felten began by noting that emotions have a powerful effect on the autonomic nervous system, which regulates everything from how much insulin is secreted to blood-pressure levels. Felten, working with his wife, Suzanne, and other colleagues, then detected a meeting point where the autonomic nervous system directly talks to lymphocytes and macrophages, cells of the immune system.[3]

In electron-microscope studies, they found synapselike contacts where the nerve terminals of the autonomic system have endings that directly abut these immune cells. This physical contact point allows the nerve cells to release neurotransmitters to regulate the immune cells; indeed, they signal back and forth. The finding is revolutionary. No one had suspected that immune cells could be targets of messages from the nerves.

To test how important these nerve endings were in the workings of the immune system, Felten went a step further. In experiments with animals he removed some nerves from lymph nodes and spleen—where immune cells are stored or made—and then used viruses to challenge the immune system. The result: a huge drop in immune response to the virus. His conclusion is that without those nerve endings the immune system simply does not respond as it should to

the challenge of an invading virus or bacterium. In short, the nervous system not only connects to the immune system, but is essential for proper immune function.

Another key pathway linking emotions and the immune system is via the influence of the hormones released under stress. The catecholamines (epinephrine and norepinephrine—otherwise known as adrenaline and noradrenaline), cortisol and prolactin, and the natural opiates beta-endorphin and enkephalin are all released during stress arousal. Each has a strong impact on immune cells. While the relationships are complex, the main influence is that while these hormones surge through the body, the immune cells are hampered in their function: stress suppresses immune resistance, at least temporarily, presumably in a conservation of energy that puts a priority on the more immediate emergency, which is more pressing for survival. But if stress is constant and intense, that suppression may become long-lasting.[4]

Microbiologists and other scientists are finding more and more such connections between the brain and the cardiovascular and immune systems—having first had to accept the once-radical notion that they exist at all.[5]

TOXIC EMOTIONS: THE CLINICAL DATA

Despite such evidence, many or most physicians are still skeptical that emotions matter clinically. One reason is that while many studies have found stress and negative emotions to weaken the effectiveness of various immune cells, it is not always clear that the range of these changes is great enough to make a *medical* difference.

Even so, an increasing number of physicians acknowledge the place of emotions in medicine. For instance, Dr. Camran Nezhat, an eminent gynecological laparoscopic surgeon at Stanford University, says, “If someone scheduled for surgery tells me she’s panicked that day and does not want to go through with it, I cancel the surgery.” Nezhat explains, “Every surgeon knows that people who are extremely scared do terribly in surgery. They bleed too much, they have more infections and complications. They have a harder time recovering. It’s much better if they are calm.”

The reason is straightforward: panic and anxiety hike blood pressure, and veins distended by pressure bleed more profusely when

cut by the surgeon's knife. Excess bleeding is one of the most troublesome surgical complications, one that can sometimes lead to death.

Beyond such medical anecdotes, evidence for the *clinical* importance of emotions has been mounting steadily. Perhaps the most compelling data on the medical significance of emotion come from a mass analysis combining results from 101 smaller studies into a single larger one of several thousand men and women. The study confirms that perturbing emotions are bad for health—to a degree.[6] People who experienced chronic anxiety, long periods of sadness and pessimism, unremitting tension or incessant hostility, relentless cynicism or suspiciousness, were found to have *double* the risk of disease—including asthma, arthritis, headaches, peptic ulcers, and heart disease (each representative of major, broad categories of disease). This order of magnitude makes distressing emotions as toxic a risk factor as, say, smoking or high cholesterol are for heart disease—in other words, a major threat to health.

To be sure, this is a broad statistical link, and by no means indicates that everyone who has such chronic feelings will thus more easily fall prey to a disease. But the evidence for a potent role for emotion in disease is far more extensive than this one study of studies indicates. Taking a more detailed look at the data for specific emotions, especially the big three—anger, anxiety, and depression—makes clearer some specific ways that feelings have medical significance, even if the biological mechanisms by which such emotions have their effect are yet to be fully understood.[7]

When Anger Is Suicidal

> A while back, the man said, a bump on the side of his car led to a fruitless and frustrating journey. After endless insurance company red tape and auto body shops that did more damage, he still owed $800. And it wasn't even his fault. He was so fed up that whenever he got into the car he was overcome with disgust. He finally sold the car in frustration. Years later the memories still made the man livid with outrage.

This bitter memory was brought to mind purposely, as part of a study of anger in heart patients at Stanford University Medical School. All the patients in the study had, like this embittered man, suffered a first heart attack, and the question was whether anger might have a significant impact of some kind on their heart function. The effect was

striking: while the patients recounted incidents that made them mad, the pumping efficiency of their hearts dropped by five percentage points.[8] Some of the patients showed a drop in pumping efficiency of 7 percent or greater—a range that cardiologists regard as a sign of a myocardial ischemia, a dangerous drop in blood flow to the heart itself.

The drop in pumping efficiency was not seen with other distressing feelings, such as anxiety, nor during physical exertion; anger seems to be the one emotion that does most harm to the heart. While recalling the upsetting incident, the patients said they were only about half as mad as they had been while it was happening, suggesting that their hearts would have been even more greatly hampered during an actual angry encounter.

This finding is part of a larger network of evidence emerging from dozens of studies pointing to the power of anger to damage the heart.[9] The old idea has not held up that a hurried, high-pressure Type-A personality is at great risk from heart disease, but from that failed theory has emerged a new finding: it is hostility that puts people at risk.

Much of the data on hostility has come from research by Dr. Redford Williams at Duke University.[10] For example, Williams found that those physicians who had had the highest scores on a test of hostility while still in medical school were seven times as likely to have died by the age of fifty as were those with low hostility scores—being prone to anger was a stronger predictor of dying young than were other risk factors such as smoking, high blood pressure, and high cholesterol. And findings by a colleague, Dr. John Barefoot at the University of North Carolina, show that in heart patients undergoing angiography, in which a tube is inserted into the coronary artery to measure lesions, scores on a test of hostility correlate with the extent and severity of coronary artery disease.

Of course, no one is saying that anger alone causes coronary artery disease; it is one of several interacting factors. As Peter Kaufman, acting chief of the Behavioral Medicine Branch of the National Heart, Lung, and Blood Institute, explained to me, “We can’t yet sort out whether anger and hostility play a causal role in the early development of coronary artery disease, or whether it intensifies the problem once heart disease has begun, or both. But take a twenty-year-old who repeatedly gets angry. Each episode of anger adds an additional stress to the heart by increasing his heart rate and blood

pressure. When that is repeated over and over again, it can do damage," especially because the turbulence of blood flowing through the coronary artery with each heartbeat "can cause microtears in the vessel, where plaque develops. If your heart rate is faster and blood pressure is higher because you're habitually angry, then over thirty years that may lead to a faster buildup of plaque, and so lead to coronary artery disease."[11]

Once heart disease develops, the mechanisms triggered by anger affect the very efficiency of the heart as a pump, as was shown in the study of angry memories in heart patients. The net effect is to make anger particularly lethal in those who already have heart disease. For instance, a Stanford University Medical School study of 1,012 men and women who suffered from a first heart attack and then were followed for up to eight years showed that those men who were most aggressive and hostile at the outset suffered the highest rate of second heart attacks.[12] There were similar results in a Yale School of Medicine study of 929 men who had survived heart attacks and were tracked for up to ten years.[13] Those who had been rated as easily roused to anger were three times more likely to die of cardiac arrest than those who were more even-tempered. If they also had high cholesterol levels, the added risk from anger was five times higher.

The Yale researchers point out that it may not be anger alone that heightens the risk of death from heart disease, but rather intense negative emotionality of any kind that regularly sends surges of stress hormones through the body. But overall, the strongest scientific links between emotions and heart disease are to anger: a Harvard Medical School study asked more than fifteen hundred men and women who had suffered heart attacks to describe their emotional state in the hours before the attack. Being angry more than doubled the risk of cardiac arrest in people who already had heart disease; the heightened risk lasted for about two hours after the anger was aroused.[14]

These findings do not mean that people should try to suppress anger when it is appropriate. Indeed, there is evidence that trying to completely suppress such feelings in the heat of the moment actually results in magnifying the body's agitation and may raise blood pressure.[15] On the other hand, as we saw in Chapter 5, the net effect of ventilating anger every time it is felt is simply to feed it, making it a more likely response to any annoying situation. Williams resolves this paradox by concluding that whether anger is expressed or not is less important than whether it is chronic. An occasional display of

hostility is not dangerous to health; the problem arises when hostility becomes so constant as to define an antagonistic personal style—one marked by repeated feelings of mistrust and cynicism and the propensity to snide comments and put-downs, as well as more obvious bouts of temper and rage.[16]

The hopeful news is that chronic anger need not be a death sentence: hostility is a habit that can change. One group of heart-attack patients at Stanford University Medical School was enrolled in a program designed to help them soften the attitudes that gave them a short temper. This anger-control training resulted in a second-heart-attack rate 44 percent lower than for those who had not tried to change their hostility.[17] A program designed by Williams has had similar beneficial results.[18] Like the Stanford program, it teaches basic elements of emotional intelligence, particularly mindfulness of anger as it begins to stir, the ability to regulate it once it has begun, and empathy. Patients are asked to jot down cynical or hostile thoughts as they notice them. If the thoughts persist, they try to short-circuit them by saying (or thinking), "Stop!" And they are encouraged to purposely substitute reasonable thoughts for cynical, mistrustful ones during trying situations—for instance, if an elevator is delayed, to search for a benign reason rather than harbor anger against some imagined thoughtless person who may be responsible for the delay. For frustrating encounters, they learn the ability to see things from the other person's perspective—empathy is a balm for anger.

As Williams told me, "The antidote to hostility is to develop a more trusting heart. All it takes is the right motivation. When people see that their hostility can lead to an early grave, they are ready to try."

Stress: Anxiety Out of Proportion and Out of Place

> I just feel anxious and tense all the time. It all started in high school. I was a straight-A student, and I worried constantly about my grades, whether the other kids and the teachers liked me, being prompt for classes—things like that. There was a lot of pressure from my parents to do well in school and to be a good role model.… I guess I just caved in to all that pressure, because my stomach problems began in my sophomore year of high school. Since that time, I've had to be really careful about drinking caffeine and eating spicy meals. I notice that when I'm feeling worried or tense my stomach will flare up, and since I'm usually worried about something, I'm always nauseous.[19]

Anxiety—the distress evoked by life's pressures—is perhaps the emotion with the greatest weight of scientific evidence connecting it to the onset of sickness and course of recovery. When anxiety helps us prepare to deal with some danger (a presumed utility in evolution), then it has served us well. But in modern life anxiety is more often out of proportion and out of place—distress comes in the face of situations that we must live with or that are conjured by the mind, not real dangers we need to confront. Repeated bouts of anxiety signal high levels of stress. The woman whose constant worrying primes her gastrointestinal trouble is a textbook example of how anxiety and stress exacerbate medical problems.

In a 1993 review in the *Archives of Internal Medicine* of extensive research on the stress-disease link, Yale psychologist Bruce McEwen noted a broad spectrum of effects: compromising immune function to the point that it can speed the metastasis of cancer; increasing vulnerability to viral infections; exacerbating plaque formation leading to atherosclerosis and blood clotting leading to myocardial infarction; accelerating the onset of Type I diabetes and the course of Type II diabetes; and worsening or triggering an asthma attack.[20] Stress can also lead to ulceration of the gastrointestinal tract, triggering symptoms in ulcerative colitis and in inflammatory bowel disease. The brain itself is susceptible to the long-term effects of sustained stress, including damage to the hippocampus, and so to memory. In general, says McEwen, "evidence is mounting that the nervous system is subject to 'wear and tear' as a result of stressful experiences."[21]

Particularly compelling evidence for the medical impact from distress has come from studies with infectious diseases such as colds, the flu, and herpes. We are continually exposed to such viruses, but ordinarily our immune system fights them off—except that under emotional stress those defenses more often fail. In experiments in which the robustness of the immune system has been assayed directly, stress and anxiety have been found to weaken it, but in most such results it is unclear whether the range of immune weakening is of clinical significance—that is, great enough to open the way to disease.[22] For that reason stronger scientific links of stress and anxiety to medical vulnerability come from prospective studies: those that start with healthy people and monitor first a heightening of distress followed by a weakening of the immune system and the onset of illness.

In one of the most scientifically compelling studies, Sheldon Cohen, a psychologist at Carnegie-Mellon University, working with scientists at a specialized colds research unit in Sheffield, England, carefully assessed how much stress people were feeling in their lives, and then systematically exposed them to a cold virus. Not everyone so exposed actually comes down with a cold; a robust immune system can—and constantly does—resist the cold virus. Cohen found that the more stress in their lives, the more likely people were to catch cold. Among those with little stress, 27 percent came down with a cold after being exposed to the virus; among those with the most stressful lives, 47 percent got the cold—direct evidence that stress itself weakens the immune system.[23] (While this may be one of those scientific results that confirms what everyone has observed or suspected all along, it is considered a landmark finding because of its scientific rigor.)

Likewise, married couples who for three months kept daily checklists of hassles and upsetting events such as marital fights showed a strong pattern: three or four days after an especially intense batch of upsets, they came down with a cold or upper-respiratory infection. That lag period is precisely the incubation time for many common cold viruses, suggesting that being exposed while they were most worried and upset made them especially vulnerable.[24]

The same stress-infection pattern holds for the herpes virus—both the type that causes cold sores on the lip and the type that causes genital lesions. Once people have been exposed to the herpes virus, it stays latent in the body, flaring up from time to time. The activity of the herpes virus can be tracked by levels of antibodies to it in the blood. Using this measure, reactivation of the herpes virus has been found in medical students undergoing year-end exams, in recently separated women, and among people under constant pressure from caring for a family member with Alzheimer's disease.[25]

The toll of anxiety is not just that it lowers the immune response; other research is showing adverse effects on the cardiovascular system. While chronic hostility and repeated episodes of anger seem to put men at greatest risk for heart disease, the more deadly emotion in women may be anxiety and fear. In research at Stanford University School of Medicine with more than a thousand men and women who had suffered a first heart attack, those women who went on to suffer a second heart attack were marked by high levels of fearfulness and anxiety. In many cases the fearfulness took the form of crippling phobias: after their first heart attack the patients stopped driving, quit

their jobs, or avoided going out.[26]

The insidious physical effects of mental stress and anxiety—the kind produced by high-pressure jobs, or high-pressure lives such as that of a single mother juggling day care and a job—are being pinpointed at an anatomically fine-grained level. For example, Stephen Manuck, a University of Pittsburgh psychologist, put thirty volunteers through a rigorous, anxiety-riddled ordeal in a laboratory while he monitored the men's blood, assaying a substance secreted by blood platelets called adenosine triphosphate, or ATP, which can trigger blood-vessel changes that may lead to heart attacks and strokes. While the volunteers were under the intense stress, their ATP levels rose sharply, as did their heart rate and blood pressure.

Understandably, health risks seem greatest for those whose jobs are high in "strain": having high-pressure performance demands while having little or no control over how to get the job done (a predicament that gives bus drivers, for instance, a high rate of hypertension). For example, in a study of 569 patients with colorectal cancer and a matched comparison group, those who said that in the previous ten years they had experienced severe on-the-job aggravation were five and a half times more likely to have developed the cancer compared to those with no such stress in their lives.[27]

Because the medical toll of distress is so broad, relaxation techniques—which directly counter the physiological arousal of stress—are being used clinically to ease the symptoms of a wide variety of chronic illnesses. These include cardiovascular disease, some types of diabetes, arthritis, asthma, gastrointestinal disorders, and chronic pain, to name a few. To the degree any symptoms are worsened by stress and emotional distress, helping patients become more relaxed and able to handle their turbulent feelings can often offer some reprieve.[28]

The Medical Costs of Depression

She had been diagnosed with metastatic breast cancer, a return and spread of the malignancy several years after what she had thought was successful surgery for the disease. Her doctor could no longer talk of a cure, and the chemotherapy, at best, might offer just a few more months of life. Understandably, she was depressed—so much so that whenever she went to her oncologist, she found herself at some point bursting out into tears. Her oncologist's response each time: asking her to leave the