

The rest of the night went no better. I was, as we say, "slammed" — running hard, unable to get two minutes to sit down, hardly able to keep the patients straight.

"It's full moon Friday the thirteenth," a nurse explained.

I was about to say that, actually, the studies show no connection. But my pager went off before I could get the words out of my mouth. I had a new trauma coming in.

The Pain Perplex

Every pain has a story, and the story of Rowland Scott Quinlan's goes back to an accident that happened years ago, when he was fifty-six. A Boston architect and avid sailor with a shock of white hair and a predilection for bow ties and Dutch cigarillos, Quinlan headed a thriving Beacon Street firm in his name and had designed such buildings as the University of Massachusetts Medical School. Then, in March of 1988, he fell off a plank at the construction site of one of his commissions—a pavilion at the Franklin Park Zoo. His back was fine, but he dislocated and fractured his left shoulder, and it required several operations. In the fall, he returned to his drafting table, and there he was hit by a spasm of pain like a writhing snake in his back. The attacks recurred, and although at first he tried to ignore them, they soon became unbearable. More than once, while he was standing with a client the back pain suddenly burst forth and it was all he could do to keep from crying out while the client caught him and helped him to a seat or to the floor. Sitting in a restaurant with a colleague, he was overcome by pain so severe that he vomited right there at the table. Soon he wasn't able to work more than two or three hours a day, and he had to give up the firm to his partners.

Quinlan's orthopedist had taken numerous X rays. They revealed little — perhaps a bit of arthritis, but nothing out of the ordinary. So Quinlan was sent to a pain specialist, who injected a long-needle syringe full of steroids and local anesthetic into his spine. The first few of these epidural injections worked for days, sometimes weeks, but subsequent shots provided steadily diminishing relief, until they didn't work at all.

I had seen his CT scans along with a sheaf of other tests and medical images. Nothing in them would have led me to expect the severity of his back pain: there was no fracture, no tumor, no infection, not even a sign of arthritic inflammation. The vertebrae were aligned perfectly, like checkers in a stack. None of the soft gel-like disks that sit like cushions between the vertebrae had ruptured. In the lower back, the lumbar spine, two disks bulged a bit, but that is common in men of his age, and the bulges didn't seem to be pressing against any nerves. Even an intern could see that there was no cause for operating on this back.

When doctors encounter a patient who has chronic pain without physical findings to account for it — and such patients are exceedingly common — we tend to be dismissive. We believe the world to be decipherable and logical, to come with problems we can see or feel or at least measure with some machine. So a pain like Quinlan's, we're apt to conclude, is all in the head: not a physical pain but a different, somehow less real, "mental" pain. In fact, Quinlan's orthopedist recommended that he see a psychiatrist as well as a physical therapist.

When I visited Quinlan at his home, in a seaside town outside Boston, I found him at what turned out to be his usual perch: a worktable in the kitchen facing a wall-length window with a view of a small garden. Blueprints of unfinished projects were curled up in rolls on the table. A telephone headset lay to one side. A dozen different kinds of drawing pens, along with small rulers and a protractor, sat in a holder. He grimaced as he rose to greet me. I thought

about his thorough medical workup and those clean images of his spine: Was he faking it?

When I asked him, he smiled wanly, and told me he sometimes wondered that himself. "I've got it pretty cushy here," he said. Quinlan has handicap license plates, financial security, and none of the pressures of running a business, and if he doesn't want to do something he merely has to say his back is killing him. But, despite a patch on his arm that infuses high doses of the narcotic fentanyl through his skin twenty-four hours a day, he can't do even the simplest thing — stand in a line, walk up stairs, or even sleep more than four hours at a stretch — without the acute sensation that, as he puts it, "someone is wringing out a muscle in my back."

I asked his wife, a tall woman several years younger than him with fine features and sad eyes, if she ever thought he fakes the pain. She told me that day in and day out for a decade now she has seen the pain and lived with the increasing limits it places on his life and hers. She has seen the pain defeat him in ways that she knows he is too proud to fake. He'll try to carry the groceries, and then, shamefaced, have to hand them back a few moments later. Though he loves movies, they have not been to the cinema in years. There have been times when the pain of movement has been so severe that he has soiled his pants rather than make his way to the bathroom.

Yet there are aspects of the pain that puzzle her and make her wonder whether it is in some respects in his head. She notices that when he is anxious or irritable, the pain is worse, and that when he is in a good mood or is simply distracted, the pain can disappear. He has bouts of depression which seem to bring on terrible spasms almost regardless of what he is doing physically. Like his physicians, she wonders how a pain can be so incapacitating yet arise from no identifiable physical abnormality. And what about the circumstances that tend to bring on an attack — a mood, a thought, sometimes nothing at all? These traits strike her as unusual, as needing explanation. But

the disturbing truth is that Roland Scott Quinlan isn't unusual. Among chronic pain sufferers, his case is altogether typical.

Dr. Edgar Ross, an anesthesiologist in his forties, is the director of the chronic-pain treatment center at Brigham and Women's Hospital in Boston, where Quinlan is seen. Patients come to Dr. Ross with every imaginable kind of pain: back pain, neck pain, arthritic pain, total-body pain, neuropathic pain, AIDS-related pain, pelvic pain, chronic headaches, cancer pain, phantom-limb pain. Often, they have already seen numerous doctors and tried multiple therapies, including surgery, to no avail.

The center's waiting room looks like any other doctor's office. It has the flat blue carpet, the dated magazines, the row of expressionless patients sitting silently against the wall. A glass case displays thank-you letters. But when I visited Dr. Ross recently I noticed that the letters were not quite the typical testimonials that doctors like to put up. These patients did not thank the doctors for a cure. They thanked the doctors merely for taking their pain seriously—for believing in it. The truth is that doctors like me are grateful to the pain specialists, too. Though we want to be neutral in our feelings toward patients, we'll admit among ourselves that chronic-pain patients are a source of frustration and annoyance: presenting a malady we can neither explain nor alleviate, they shake our claims to competence and authority. We're all too happy to have someone like Dr. Ross to take these patients off our hands.

Ross led me into his office. Soft-spoken and unhurried, he has a soothing demeanor that fits perfectly with his line of work. Quinlan's kind of problem, he told me, is the one he sees most frequently. Chronic back pain is now second only to the common cold as a cause of lost work time, and it accounts for some 40 percent of workers' compensation payments. In fact, there is a virtual epidemic of back pain in this country today, and nobody can explain why. By convention, we think of it as a mechanical problem, the result of

misplaced stress on the spine. We therefore have had some sixty years of workplace programs, and now there are even "back schools," which teach the "correct way to lift," among other things. Despite the fact that the number of people who engage in manual labor has steadily declined, however, more people have chronic back pain than have ever had it before.

The mechanical explanation is almost certainly wrong, Ross noted. It's true that lifting something the wrong way can cause a muscle pull or a slipped disk. But that sort of strain occurs in almost everyone at some time, and in most people it never becomes a persistent problem. Scores of studies have looked for physical factors that can predict which acute back injuries will evolve into chronic back pain, but they haven't found any. For instance, doctors used to assume that damaged disks were associated with pain, but recent findings have not borne this out. Spinal MRI scans show that most people without back pain have disk bulges. Conversely, a large percentage of patients with chronic back pain, like Quinlan, are found to have no structural lesion. And even among those with abnormalities there is no relation between the severity of the pain and the severity of the abnormalities.

If the condition of your back doesn't predict whether you'll get chronic back pain, what does? Well, it's the mundane stuff that neither doctors nor patients much like to consider. Studies point to such "inorganic" factors as loneliness, involvement in litigation, receipt of workers' compensation, and job dissatisfaction. Consider, for example, the epidemic of back pain in the medical profession itself. Disability insurers once saw doctors as ideal customers. Nothing stopped doctors from working—not years of stooping over operating tables, not arthritis, not even old age. Insurers used to try to outbid one another with cheap rates and generous benefits to attract their business. In the last few years, however, the number of doctors with disabling back or neck pain has risen dramatically. Needless to say, doctors aren't suddenly being required to carry heavy packages around. But

one known risk factor has been identified: with the growing role of managed care, job satisfaction in the medical profession has plunged.

The explanation of pain that has dominated much of medical history originated with René Descartes, more than three centuries ago. Descartes proposed that pain is a purely physical phenomenon—that tissue injury stimulates specific nerves that transmit an impulse to the brain, causing the mind to perceive pain. The phenomenon, he said, is like pulling on a rope to ring a bell in the brain. It is hard to overstate how ingrained this account has become. Twentieth-century research on pain has been devoted largely to the search for and discovery of pain-specific nerve fibers (now named A-delta and C fibers) and pathways. In everyday medicine, doctors see pain in Cartesian terms—as a physical process, a sign of tissue injury. We look for a ruptured disk, a fracture, an infection, or a tumor, and we try to fix what's wrong.

The limitations of this mechanistic explanation, however, have been apparent for some time. During the Second World War, for example, Lieutenant Colonel Henry K. Beecher conducted a classic study of men with serious battlefield injuries. In the Cartesian view, the degree of injury ought to determine the degree of pain, rather like a dial controlling volume. Yet 58 percent of the men—men with compound fractures, gunshot wounds, torn limbs—reported only slight pain or no pain at all. Just 27 percent of the men felt enough pain to request pain medication, although such wounds routinely require narcotics in civilians. Clearly, something that was going on in their minds—Beecher thought they were overjoyed to have escaped alive from the battlefield—counteracted the signals sent by their injuries. Pain was becoming recognized as far more complex than a one-way transmission from injury to “ouch.”

In 1965, the Canadian psychologist Ronald Melzack and the British physiologist Patrick Wall proposed that the Cartesian model be replaced with what they called the Gate-Control Theory of Pain.

Melzack and Wall argued that before pain signals reach the brain they must first go through a gating mechanism in the spinal cord, which could ratchet them up or down. In some cases, this hypothetical gate could simply stop pain impulses from getting to the brain. In fact, researchers soon identified a gate for pain in a portion of the spinal cord called the dorsal horn. The theory explained such ordinary puzzles as why rubbing a painful foot makes it feel better. (The rubbing sends signals to the dorsal horn that close the gate to nearby pain impulses.)

Melzack and Wall's most startling suggestion was that what controlled the gate was not just signals from sensory nerves but also emotions and other “output” from the brain. They were saying that pulling on the rope need not make the bell ring. The bell itself—the mind—could stop it. Their theory prompted a great deal of research into how factors such as mood, gender, and beliefs influence the experience of pain. In one study, for example, researchers measured pain threshold and tolerance levels in fifty-two dancers from a British ballet company and fifty-three university students using a standard method called the cold-pressor test. The test is ingeniously simple. (I tried it at home myself.) After immersing your hand in body-temperature water for two minutes to establish a baseline condition, you dunk your hand in a bowl of ice water and start a clock running. You mark the time when it begins to hurt: that is your pain threshold. Then you mark the time when it hurts too much to keep your hand in the water: that is your pain tolerance. The test is always stopped at a hundred and twenty seconds, to prevent injury.

The results were striking. On average, female students reported pain at sixteen seconds and pulled their hands out of the ice water at thirty-seven seconds. Female dancers went almost three times as long on both counts. Men in both groups had a higher threshold and tolerance for pain—as expected, since studies show women to be more sensitive than men to pain, except during the last few weeks of pregnancy—but the difference between male dancers and male nondancers was nearly as large. What explains the difference?

Probably it has something to do with the psychology of ballet dancers—a group distinguished by self-discipline, physical fitness, and competitiveness, as well as by a high rate of chronic injury. Their driven personalities and competitive culture evidently inure them to pain: that's why they are able to perform through sprains and stress fractures, and why half of all dancers develop long-term injuries. (Similar to other nondancing males, I started to feel pain at around twenty-five seconds; but I had no trouble keeping my hand in for the whole hundred and twenty seconds. I will let others speculate on what this says about the submissiveness inculcated in surgical residents.)

Other studies along these lines have shown that extroverts have greater pain tolerance than introverts, that drug abusers have low pain tolerance and thresholds, and that, with training, one can diminish one's sensitivity to pain. There is also striking evidence that very simple kinds of mental suggestion can have powerful effects on pain. In one study of five hundred patients undergoing dental procedures, those who were given a placebo injection and reassured that it would relieve their pain had the least discomfort—not only less than the patients who got a placebo and were told nothing but also less than the patients who got a real anesthetic without any reassuring comment that it would work. Today, it is abundantly evident that the brain is actively involved in the experience of pain, and is no mere bell on a string. Today, every medical textbook teaches the Gate-Control Theory as fact. There's a problem with it, though. It doesn't explain people like Roland Scott Quinlan.

Gate-Control Theory accepts Descartes's view that what you feel as pain is a signal from tissue injury transmitted by nerves to the brain, and it adds the notion that the brain controls a gateway for such an injury signal. But in the case of Quinlan's chronic back pain, where is the injury? Or take something like phantom-limb pain. After amputation of a limb, most people suffer a period of constant, intractable burning or cramping that feels exactly as if the limb were still there. Without a limb, however, there are no nerve impulses for

the gate to control. So where does the pain come from? The rope and clapper are gone, but the bell can still ring.

One spring day in 1994, Dr. Frederick Lenz, a neurosurgeon at the Johns Hopkins Hospital, brought to his operating table a patient suffering from severe hand tremors. The patient, whom I'll call Mark Taylor, was only thirty-six, but over the years his hands had come to shake so violently that the simplest of tasks—writing, buttoning his shirt, drinking from a glass, or typing on his keyboard at his job as a purchasing agent—grew absurdly difficult. Medications failed, and he lost jobs more than once because of his difficulties. Desperate for a return to a normal life, he agreed to a delicate procedure: brain surgery that would destroy cells in a small structure called the thalamus, which was already known to contribute to such excessive stimulation of the hands.

Taylor had another big problem, though: for seventeen years, he had struggled with a severe panic disorder. At least once a week, while he was working at his computer terminal or was at home in the kitchen feeding a child, he would suddenly be overcome by severe chest pains, as if he were having a heart attack. His heart would pound, his ears would ring; he would grow short of breath and would have an overwhelming urge to escape. Nevertheless, a psychologist Lenz consulted assured him that the disorder was unlikely to hinder the operation.

Initially, Lenz says, everything went as he had expected. He injected a local anesthetic—the operation is done with the patient awake—and burred a small opening in the top of Taylor's skull. Then he cautiously inserted a long, thin electrical probe deep inside, right down into the thalamus. Lenz talked to Taylor the whole time, asking him to stick out his tongue, to move a hand, to do any of a dozen other tasks that showed he was all right. The danger in this type of surgery is that it might destroy the wrong cells: the thalamic cells involved in tremor lie just fractions of a millimeter away from cells that are essential for sensation and motor activity. So

before cauterizing with a second, larger probe, the surgeon had to find the right cells by stimulating them with a gentle electric pulse. The probe was in a portion of Taylor's thalamus that Lenz labeled Site 19, and he zapped it with low voltage. He had been here a thousand times before, and typically, he told me, zapping the site makes people feel a prickle in the forearm. Sure enough, this is what Taylor felt. Lenz then zapped an adjacent area he labeled Site 23, where stimulation generally produces a mild and very ordinary tingling in the chest. This time, however, Taylor felt an unexpectedly far more harsh pain—in fact, the exact chest pain of his panic attacks, along with the suffocation and instant sense of doom that always accompanied them. It made him cry out and nearly leap off the table. When Lenz stopped the stimulation, however, the sensation disappeared, and Taylor became instantly calm again. Puzzled, Lenz zapped Site 23 once more, and found that doing so produced the same effect again. He stopped, apologized to Taylor for the discomfort, and went on to locate the cells controlling his tremor and to cauterize them. The operation was a success.

Yet even as Lenz completed the procedure, his mind was racing. Only once before had he seen anything like this kind of effect. It was in a sixty-nine-year-old woman with a long history of difficult-to-manage angular pain that came on not only with strenuous activity but even with mild physical exertion that wouldn't be expected to stress her heart. Performing a similar operation on her, Lenz found that stimulating the microscopic section of her brain that usually triggered mild chest tingling had instead, as with Taylor, brought on her more severe and familiar chest pain—a sensation she described as "deep, frightful, squeezing." The implications might have easily been lost, but Lenz had spent many years researching pain and realized that he had witnessed an important and telling effect. As he later noted in a report published in the journal *Nature Medicine*, the response in these two patients was wildly out of proportion to the stimulus. What in most people produces no more than a tingle was torture to them. Areas of the brain governing ordinary sensations

appeared to have become abnormally sensitized—set to fire in response to perfectly harmless stimuli. In the woman's case, her chest pain had begun as a signal of her heart disease but now appeared in circumstances that did not reflect anything like an impending heart attack. Even more oddly, in Taylor's case, the pain had not begun with any such bodily damage, but with his panic disorder, which is understood to be a psychological condition. Lenz's findings suggest that, in fact, all pain is "in the head"—and further that sometimes, as with Mark Taylor or perhaps Roland Scott Quinlan, no physical injury of any kind is needed to make the pain system go haywire.

This is the newest theory of pain. Its leading proponent is, once again, Melzack, who abandoned Gate-Control Theory in the late 1980s and began telling incredulous audiences to revise their understanding of pain once again. Given the evidence, he now says, we should stop thinking that pain or any other sensation is a signal passively "felt" in the brain. Yes, injury produces nerve signals that travel through a spinal-cord gate, but it is the brain that generates the pain experience, and it can do so even in the absence of external stimuli. If a mad scientist reduced you to nothing but a brain in a jar, Melzack says, you could still feel pain—indeed, you could have the full range of sensory experience.

According to the new theory, pain and other sensations are conceived as "neuromodules" in the brain—something akin to individual computer programs on a hard drive, or to tracks on a compact disc. When you feel pain, it's your brain running a neuromodule that produces the pain experience, as if someone pressed the PLAY button on a CD player. And a great many things can press the button (besides a neurosurgeon zapping the right neuron with low DC voltage). The way Melzack explains it, a pain neuromodule is not a discrete anatomical entity but a network, linking components from virtually every region of the brain. Input is gathered from sensory nerves, memory, mood, and other centers, like members of some committee in charge of whether the music will play. If the signals

reach a certain threshold, they trigger the neuromodule. And then what plays is no one-note melody. Pain is a symphony—a complex response that includes not just a distinct sensation but also motor activity, a change in emotion, a focusing of attention, a brand-new memory.

Suddenly, a simple toe-stubbing no longer seems so simple. In this view, the signal from the toe still has to make it through the spinal-cord gate, but thereafter it joins a lot of other signals in the brain—from memories, anticipation, mood, distractions. Altogether, they may combine to activate a toe-pain neuromodule. In some people, however, the physical stimulus may be canceled out and the stubbed toe hardly noticed. There's nothing surprising here so far. But now we can imagine—and this is the most radical implication of Melzack's ideas—that the same neuromodule can go off, generating genuine toe pain, without a toe's having been stubbed at all. The neuromodule could—like Site 23 in Mark Taylor's brain—become primed like a hair trigger. Then virtually anything could set it off: a touch, a stab of fear, a sudden frustration, a mere memory.

The new theory about the psychology of pain has, almost perversely, helped give direction to the pharmacology of pain. For pharmacologists, the Holy Grail of chronic-pain treatment is a pill that would be more effective than morphine but lack its side effects, such as dependence, sedation, and motor impairment. If an overactive neuronal system is the problem, then what one needs is a drug that will damp it down. That's why, in what a decade ago might have seemed a strange development, pain specialists increasingly prescribe anti-epileptic drugs, like carbamazepine and gabapentin, for their most difficult-to-treat patients. After all, that's what these drugs do: they tune brain cells to modulate their excitability. So far, these kinds of drugs work only for some people—Quinlan has been on gabapentin for more than six months without much effect—but drug companies are hard at work on a new generation of similar “neuro-stabilizing” compounds.

Neurex, for example, a small Silicon Valley biotechnology company (now called Elan Pharmaceuticals), not long ago designed a pain drug from the venom of the Conus sea snail following such thinking. Venoms are, needless to say, biologically potent, and, unlike most of the proteins from nature that scientists have tried to use as drugs, they evade the body's mechanisms for breaking proteins down. The trick is to tame the venom, to modify it so it is medically useful. The Conus venom was known to kill by blocking specific pathways in the brain that are necessary in order for neurons to fire. With a few alterations, however, Neurex scientists created Ziconotide, a drug that only slightly inhibits those pathways. Instead of shutting brain cells down, it seems to merely mute their excitability. In initial clinical trials, Ziconotide effectively controlled chronic pain from cancer and from AIDS. Another new generation analgesic in development is Abbott Laboratories' ABT-594, a compound related to a poison secreted by an Ecuadorian frog, *Epiplatysdobates tricolor*. In animal experiments that were published in the journal *Science*, ABT-594 proved to be as much as fifty times as potent as morphine in relieving pain. Companies have other pain drugs in the pipeline, too, including a class of drugs known as NMDA antagonists, which also work by reducing neuronal excitability. One of these could turn out to be the painkiller that Quinlan and patients like him are looking for.

At best, however, these drugs represent only a halfway solution. The fundamental problem for research is how to stop the pain system in such patients from going haywire in the first place. The stories that people tell of their chronic pain typically start with an initial injury. So, historically, we have tried to prevent chronic pain by preventing acute strains. A whole ergonomics industry has developed around this idea. Yet the lesson from Ross's pain clinic and Lenz's operating table is that the antecedents of pain lie elsewhere than in the muscle and bone of patients. In fact, some forms of chronic pain behave astonishingly like social epidemics.

In Australia during the early 1980s, workers—particularly keyboard operators—experienced a sudden outbreak of disabling arm pain, which doctors labeled “repetition strain injury,” or RSI. This was not a mild case of writer’s cramp but a matter of severe pain, which started with minor discomfort during typing or other repetitive work and progressed to invalidism. The average time that a sufferer lost from work was seventy-four days. As with chronic back pain, no consistent physical abnormalities or effective treatment could be found, yet the arm pain spread like a contagion. It had hardly existed before 1981, but by its peak, in 1985, enormous numbers of workers were affected. In two Australian states, RSI disabled as much as 30 percent of the workforce in some industries; at the same time there were pockets of workers who were almost entirely unaffected. Clusters appeared even within a single organization. At Telecom Australia, for example, the incidence of RSI among telephone operators in a single city varied widely between departments. Nor could investigators find any connection between RSI and the physical circumstances of the workers—the actual repetitiveness of their jobs or the ergonomics of their equipment. Then, as suddenly as it had begun, the epidemic crashed. By 1987, it was essentially over. In the late 1990s, Australian researchers were complaining that they couldn’t find enough RSI patients to study.

Chronic back pain has been with us for so long that it is hard conceptually—and even politically—to step back and recognize its social etiology, let alone figure out how cultural factors make an individual’s pain system go awry. The Australian pain epidemic demonstrates the power of those factors to cause genuine, disabling pain on a national scale, and yet our knowledge of these causes and how to control them is meager. We know from a variety of studies that social support networks—a happy marriage and satisfying employment, say—protect against disabling back pain. We know, statistically speaking, that being given certain diagnostic labels and being provided disability pay (and thus a kind of official recognition and validation) can perpetuate chronic pain. In Australia, for example, many

researchers believe that two major factors that sparked the epidemic were the coining of RSI as a diagnostic label and early action by the government to insure compensation for the syndrome as a work-related disability. When the diagnosis fell out of favor with physicians, and disability coverage became harder to get, the incidence of the symptoms associated with the disorder plummeted. It also appeared that initial publicity about the possible portents of arm pain and concerted campaigns in some places to increase the reporting of arm pains or to institute ergonomic changes only contributed to the epidemic. More recently, in the United States, a debate has erupted over the origins of a similar workplace epidemic, called, variously, repetitive-stress injury, repetitive-motion disorder, and—in the currently favored nomenclature—cumulative-trauma disorder. Once again, the salient risk factors seem to be social rather than physical.

Back and arm pain are not unique in having nonphysical causes. Studies have shown that social conditions play a dominant role in many chronic-pain syndromes, including chronic pelvic pain, temporomandibular-joint disorder, and chronic tension headache, to name just a few. Again, none of this should be taken to mean that people are faking it. As Melzack’s account suggests, pain that doesn’t arise from physical injury is no less real than pain that does—in the brain it is precisely the same. And so a compassionate approach toward chronic pain means investigating its social coordinates, not just its physical ones. For the solution to chronic pain may lie more in what goes on around us than in what is going on inside us. Of all the implications of the new theory of pain, this one seems to be the oddest and the most far-reaching: it has made pain political.