

**T**HE REVEREND STEPHEN FULTON falls a lot. Once he toppled into a freezer case at the grocery store. He has difficulty walking, and he can't sit or stand for long periods. He can't garden anymore, and had to retire early from his regular pastoral duties—all because of the excruciating pain that grips his lower back and radiates into his left leg and foot. "It's like a vise around the base of my spine," he says. His pain started after another driver rear-ended his car, and it has persisted for 16 years despite prescription drugs, injections, physical therapy, and electric nerve stimulation. It has affected just about everything in his life, including his relationships. "If you fall and break a leg, people know to send flowers or to visit," he says. "But if you have chronic pain, people don't know what to do."

Fulton, a 61-year-old resident of Brookline, Massachusetts, has faced many obstacles in his quest for pain relief. At first, he had to forgo treatments because his insurance company wouldn't cover the expense. Later, he encountered an even bigger problem:

Nociceptive pain is very clear, says professor of anesthesiology Carol A. Warfield, chief of anesthesia, critical care, and pain medicine at Beth Israel Deaconess Medical Center in Boston. When you cut your finger, she says, you know darn well that it's your finger that hurts; in fact, you could close your eyes and easily identify the location of the cut. Usually you feel a sharp pain, then throbbing, and finally, after a short time, the pain goes away. Pain that occurs suddenly and has a real, definable source is considered acute pain. Rapid in onset and relatively short in duration, it generally follows a traumatic event such as a bone fracture or a surgical procedure, but can occur in other situations, such as when a hemophiliac suffers internal bleeding. Doctors often treat acute pain with strong drugs, knowing that it will fade as the healing process takes over.

Sometimes, however, the pain message system goes awry, says Warfield, and people perceive pain for much longer than it's useful. That's when problems with chronic pain arise, as in Fulton's case. One type of chronic pain is *neuropathic pain*, which results

# The Science of Hurt

Medical researchers and doctors work to close the "gates" on pain.

doctors who doubted the severity of his pain. In their eyes, says Fulton, "If the hole wasn't big enough, you couldn't be hurting that much." He can't explain the pain, he says, so he ends up feeling that no one believes him: "My integrity is important to me, and having professionals and others question me was almost as devastating as the pain was."

## Good Pain—and Bad

**T**HOSE WHO SUFFER the devastating effects of chronic pain may fantasize about a life that is completely pain-free. In fact, such a life is far from idyllic. People who are born with congenital insensitivity to pain, a rare genetic disorder, chew their tongues and lips to pieces, burn their flesh, and fracture their bones without realizing the harm they are doing to their bodies. Lacking a warning system to protect themselves from dangers in the environment, they tend to die young, often in their twenties.

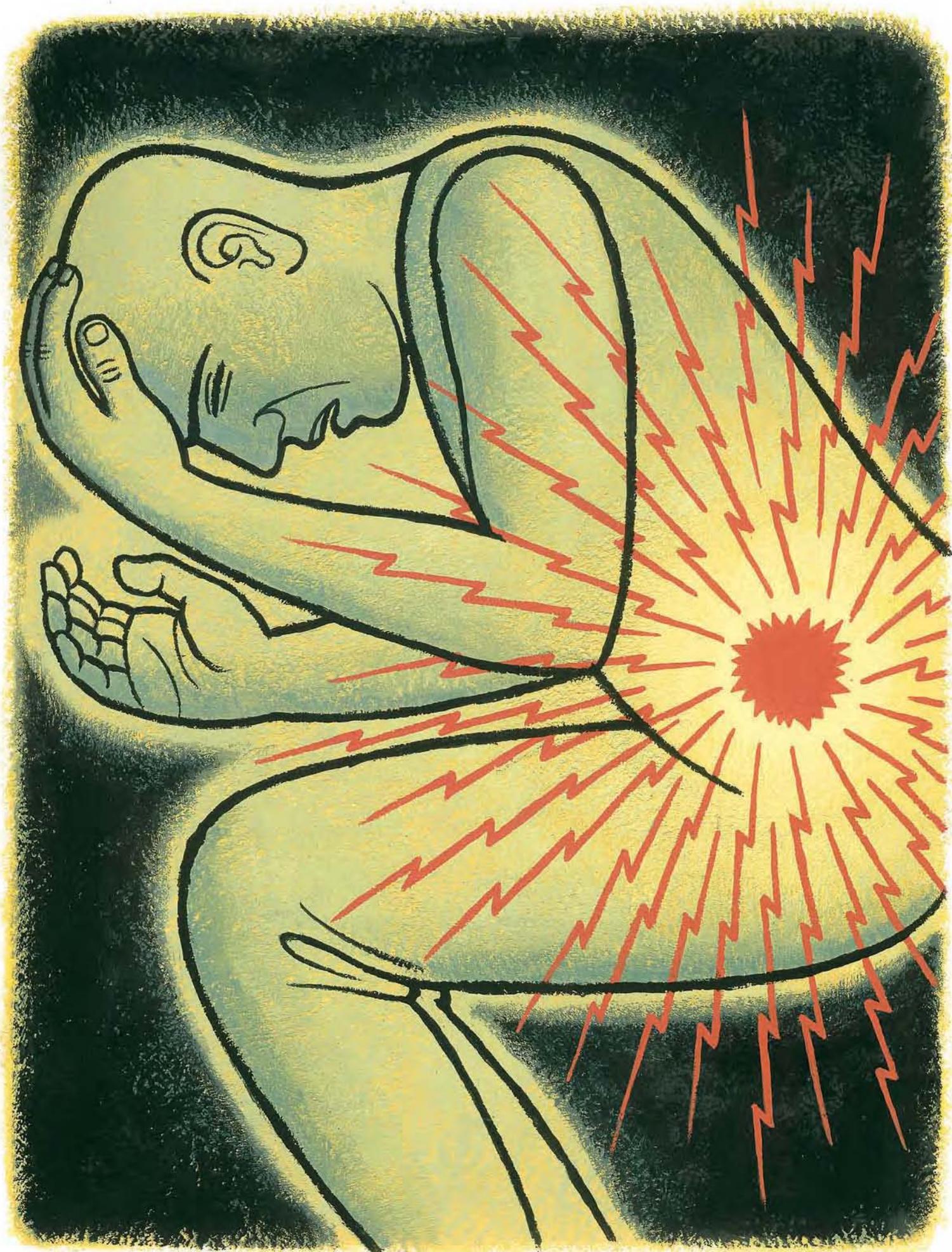
*Nociceptive* or *somatic pain*—a normal response to noxious stimuli—is essential for life. It tells you to pull your hand away from a flame or withdraw your mouth from a cup of hot coffee. If you break an ankle, the pain keeps you from walking around on it, so the bone can heal. Nociceptors are sensory receptors, or nerve endings, that react to mechanical, thermal, and chemical stimuli that may damage tissues. They relay nerve impulses—electrical messages from the site of injury in peripheral tissues such as skin, muscles, and joints—to the dorsal horn, an area in the spinal cord that acts as a switchboard. There, different chemicals determine whether these electrical messages reach your brain, where you actually perceive pain.

from damage to the nerves themselves. Common causes include AIDS, diabetes, and shingles (also known as herpes zoster, a viral infection that produces a blistering rash). Nerve pain is typically a burning sensation, tingling, or numbness, she explains, and is not well localized: you may have burning pain in your hand, but not be able to say which fingers are involved. *Visceral pain* arises from internal organs and is even more difficult to pinpoint. Pain originating in your stomach, for example, may cause discomfort in your back. That's because visceral organs have different types of receptors than other body parts, such as bones and muscles, do. People don't typically break or cut organs. "You feel pain in your stomach not so much when somebody hits your stomach," says Warfield, "but when acid gets into the lining or if your stomach gets distended."

Chronic pain involves the mind and emotions more than acute pain does, and has more to do with chemical disturbances in the spinal cord and brain. Although experts say that chronic pain and depression often coexist, they are still unsure which condition comes first. What they do know is that serotonin and norepinephrine—chemical messengers that help to regulate mood—also modulate pain signals. Doctors treat chronic pain differently from acute pain. Recognizing that people may be living with discomfort for long periods of time, they may prescribe drugs, injections, stimulation techniques, surgery, physical therapy, or psychological interventions.

Most pain is actually a mixture of types. For example, if a disk—a shock-absorbing cushion between vertebrae—slips out of place and presses on a spinal nerve, the muscles in your back

by Kathleen Koman



may go into spasm in an effort to protect your spinal cord. This is somatic pain; it's short-lived and well-localized. In addition to this somatic pain, however, you may experience the persistent tingling, numbness, or burning of nerve pain, which travels down your leg. Likewise, "If you have a headache, sometimes you can really touch and feel where it's tender," Warfield notes. "On the other hand, you may have some dull sort of pain, some visceral pain in your head that you can't put your finger on."

Acute pain is considered "good" pain because it is an alarm system that warns of injury. Chronic pain is like a faulty alarm. It serves no beneficial purpose and, if ignored, becomes an illness unto itself, causing changes in the nervous system that only result in more pain.

### The Gates of Pain

**I**N THE SEVENTEENTH CENTURY, French philosopher René Descartes proposed that pain signals travel directly along a fixed pathway from the injured site in the periphery of the body to a pain center in the brain. Until the mid 1960s, doctors generally subscribed to this Cartesian theory, believing that the brain was a passive recipient of pain information and that pain intensity rose directly with the amount of actual tissue damage.

But in 1965, Canadian psychologist Ronald Melzack and British neurobiologist Patrick Wall proposed the *gate control theory of pain*, suggesting that nerve cells in the spinal cord acted like gates, opening to allow pain messages to pass through, or closing to prevent them from reaching the brain. "What Melzack and Wall's theory said was that there are different types of nerves that input into the spinal cord," Warfield explains. "There are the pain nerves and then there are the touch and pressure nerves. And once those nerves transmit a message into the spinal cord, it's the balance between the pain nerves and the pressure nerves

that determines whether this gate opens and you perceive pain in your brain." That balance explains

why counter-stimulation may decrease the transmission of pain signals—for example, why rubbing a stubbed toe can make it feel better. Acupuncture and the application of heat or cold are also methods of competing with the pain and closing the gates.

Melzack and Wall further theorized that psychological factors—emotions, expectations, attitudes, and memories—could influence the perception

and experience of pain by affecting the opening or closing of the "gates." Their hypothesis could explain, as Descartes's could not, why amputees often complain of pain in their missing limbs, or why three-quarters of the soldiers seriously wounded while seizing the beachhead at Anzio during World War II felt so little pain in the hours immediately following their injuries that they refused medication—a phenomenon noted by a military physician who was present, Henry K. Beecher, M.D. '32. Beecher was also Dorr professor of research in anesthesia at Harvard Medical School. When he returned to his practice at Massachusetts General Hospital (MGH), he found that civilians with comparable wounds were more likely to require morphine for their pain. Soldiers, he concluded, associated their wounds with survival and escape from a dangerous environment, whereas civilians interpreted an accident as the beginning of disaster. Beecher's observations helped inspire the gate control theory, and illustrated a mind-body connection in the experience of pain.

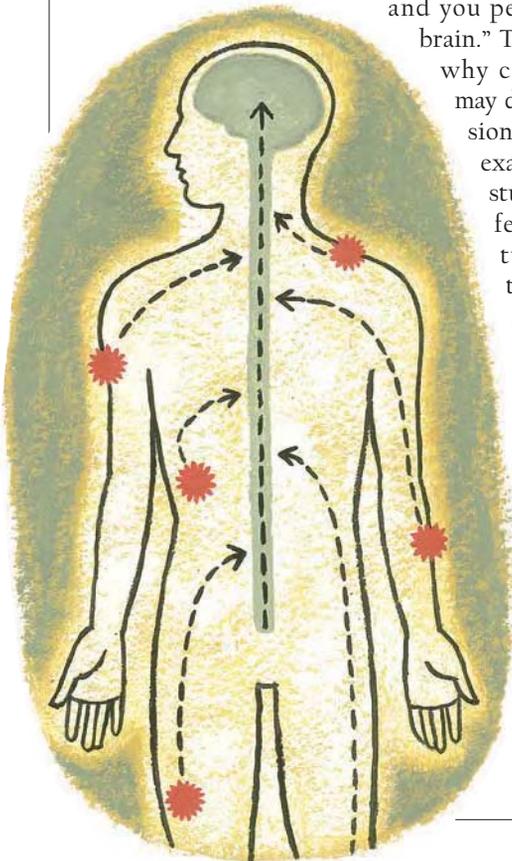
Since the publication of the gate control theory, scientists have elucidated more clearly what it is that sends the pain message to the brain—or doesn't. They now know, for instance, that neurotransmitters (chemical messengers found naturally in the brain and spinal cord) are important in conducting signals from one nerve cell to the next. Neurotransmitters stored in the bulbous end of a nerve cell travel across a junction (synapse) to attach to receptors on the surface of a neighboring cell and thereby either prompt or inhibit a continued electrical impulse along the nerve. Gamma-amino butyric acid (GABA), a naturally occurring amino acid, is an example of an inhibitory neurotransmitter that prevents nerve cells from firing, thus diminishing the sensation of pain. On the other hand, the neuropeptide (an organic compound composed of amino acids in a defined order) known as Substance P. is a neurotransmitter that increases the conduction of the pain stimulus to the brain. Substance P. is released in response to noxious stimuli or injury to tissues, and acts like a spark to speed the pain impulse along the nerves.

Other neuropeptides called endorphins and enkephalins are the body's own painkillers—natural opiates—and work in much the same way morphine does. Endorphins and enkephalins bind with the nerve cell receptors required to send the electrical impulse across the synapse and thus, by closing the pain "gates," block the release of neurotransmitters responsible for increasing pain perception. Research has shown that certain behavioral habits, like regular exercise or positive thinking, can increase levels of endorphins and enkephalins.

### Pain Pathways

**T**HE GATE CONTROL THEORY "had an enormous philosophical impact, in terms of understanding that pain has a neurobiological basis that can be studied," says Patrick Wall's former student Clifford Woolf, Kitz professor of anesthesia research, who chairs anesthesia studies at Harvard Medical School and directs the neural plasticity research group at MGH. Melzack and Wall showed that pain is not just a symptom, but a disease, so their research launched a new multidisciplinary era in the study of pain.

**Psychological factors could influence the experience of pain by affecting the opening or closing of the "gates."**



In 1983, while working in Wall's laboratory in London, Woolf revolutionized the pain field when he discovered *central sensitization*, an increase in the excitability of neurons within the brain and spinal cord to the extent that a normally innocuous stimulus begins to produce pain. This explains why people with rheumatoid arthritis feel pain when they make simple, normal movements with their hands, why people who have had abdominal surgery cringe painfully when they cough, and why people with shingles often complain that clothes or bed sheets feel like scalding water against their skin. In all of these cases, pain has rewired the nervous system into a heightened, distorted sensitivity for prolonged periods, ranging from hours to months. Says Woolf, "It's as if the volume control on the radio has been switched right up so it's blasting away very loud."

Before Woolf made this discovery, doctors typically gave surgical patients a general anesthetic with little or no analgesia. In other words, they rendered them unconscious, but did nothing to shield them from the barrage of pain signals that traveled along their nerves as surgeons cut their skin and ripped through their muscles. Woolf's findings led to the use of preemptive analgesia, the administration of painkillers before patients feel pain. Today, doctors routinely give narcotics, regional nerve blocks, or local anesthetics before surgery. "They now recognize," he says, "that it is morally and ethically and scientifically essential that when patients wake up from surgery, they're not screaming in agony."

Beyond this new therapeutic strategy, other changes since the advent of the gate control theory have profoundly affected the treatment of patients in pain. One is the proliferation of specialized pain clinics throughout the country. "It wasn't until the late 1970s that people started to look at pain as a specialty," says Warfield. Before then, she says, there was no one person who could look at a pain problem and say, "Okay, here's the individualized game plan for you."

Warfield started Beth Israel's pain clinic (now the Arnold Pain Center) in 1980. At first, it was just Warfield treating patients in a small corner of the recovery room. Today, the clinic has about 100 employees who handle a total of 14,000 visits a year from patients with acute and chronic pain. In addition, the multidisciplinary center has a research component and the largest pain fellowship program in the country. The fellowships provide anesthesiologists, physical medicine specialists, and neurologists who have completed residency training in their own specialties



**Carol Warfield notes that one barrier to pain relief is the prevailing attitude toward narcotics.**

with a year of additional training in pain medicine. The syllabus includes training for cancer pain, post-operative pain, back pain, and headache, and in treatments ranging from nerve blocks and medications to acupuncture and psychology.

Debilitating back pain stemming from his car accident as well as hand and arm pain related to his diabetes continue to nag Stephen Fulton daily. But he now finds some relief at the Arnold Pain Center. There, he says, doctors never doubt the severity of his pain. Rather, they "wave a flag in the storm." They have prescribed narcotics and short periods of physical therapy to help him manage his chronic pain and, through counseling, have

taught him coping strategies and ways to alter his “pain behavior.” He’s learned, for instance, to avoid doing things that make him the center of attention because of his pain. “Watch how you walk into a room,” doctors told him. “If you’re acting in a way that results in someone saying, ‘Take this chair,’ you just changed everything in the room.” Fulton acknowledges that being around a pain patient can be very trying. It’s important, he says, to stop using pain as a crutch with other people, “because that breaks up relationships and takes people into hell.”

Like other stressors, pain can also bring out behavioral oddities. In the support groups for pain patients that Fulton used to attend, he says, some participants competed not only over who was in the most pain, but also over whose insurance company provided the most coverage for pain treatments.

In their own way, such debates suggest the growing acceptance of pain medicine. Pain clinics have proliferated, and in 2001, the Joint Commission for the Accreditation of Healthcare Organizations made pain the fifth “vital sign.” “Now, in addition to record-

ing temperature and blood pressure, pulse and respiration, the nurses all have to record pain,” Carol Warfield notes. “That was a great stride in recognizing that pain itself is a problem and that people deserve to have their pain tended to.”

Even so, many barriers to pain relief remain. Chief among them is the prevailing attitude toward narcotics. “I’ve had patients who’ve been in Alcoholics Anonymous, for example, and they’ve been told by their sponsors or somebody else that because they’re alcoholics in recovery, they should never take narcotics,” Warfield says. “So they’ll only take aspirin after their gallbladder surgery, which is ridiculous. No data whatsoever support that.” Cancer patients often complain to Warfield that when they try to fill a prescription for narcotics, pharmacists give them dirty looks and treat them like drug addicts. Although the potent narcotic OxyContin can be effective against severe pain, news reports have tended to focus on people who obtain it illegally and chew, snort, or inject it for a quick, heroin-like high. “There are a lot of societal norms out there,” Warfield explains. “You turn on the TV and hear, ‘Say no to drugs,’ and you hear about OxyContin and I think people just assume that anyone on OxyContin is a drug addict. There are a lot of people out there that we could help, but can’t for a variety of reasons.”

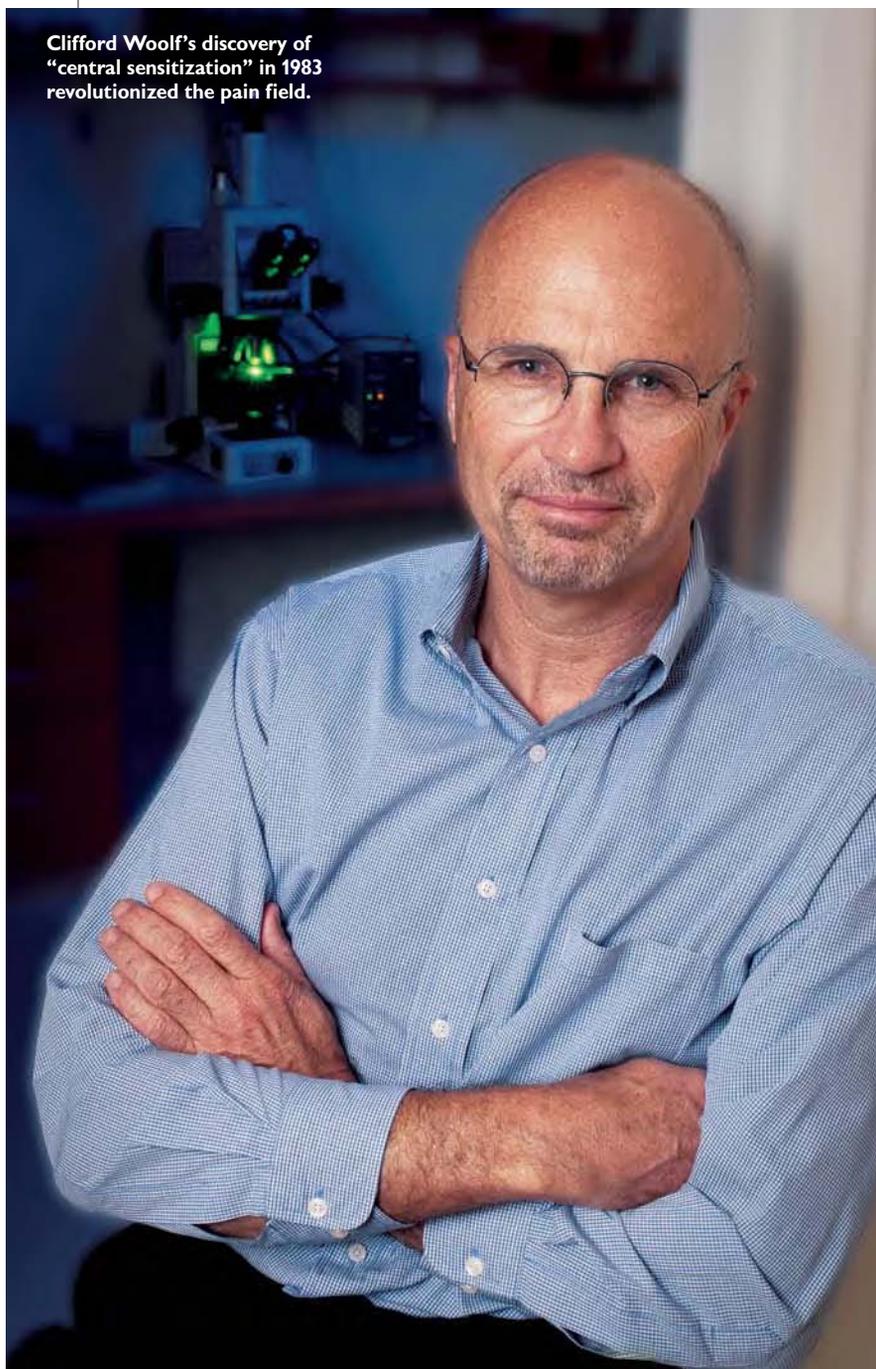
Some insurance companies block patients from getting adequate relief by refusing to cover the expense of pain treatments, adds Warfield—for example, by refusing to pay for implantable pain-relieving devices such as spinal morphine pumps and spinal-cord stimulators. Warfield’s staff used to run a 10-week course that taught coping strategies and relaxation techniques to people in pain, but insurers would not cover these group meetings. “Many insurers don’t cover or would like not to cover pain, and they make you really jump through a lot of hoops to get patients seen on a timely basis in a pain clinic,” says Warfield. Pain is not tangible, she notes, so many insurers claim that it is not life-threatening. But, she says, “Pain *can* kill you.” For one thing, it decreases the body’s immune response, making patients more susceptible to infections and tumors.

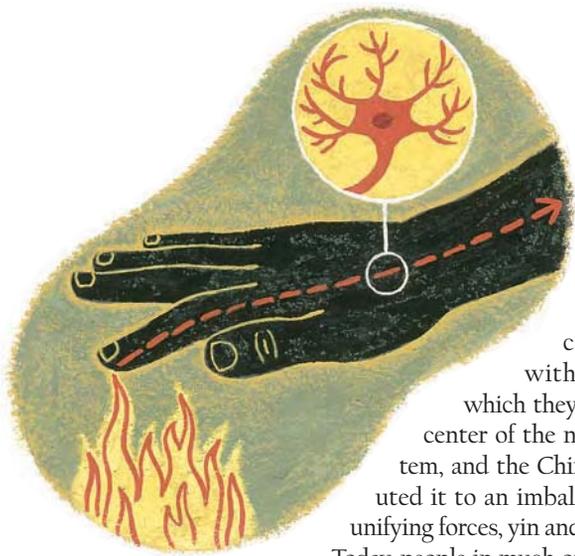
Fulton says that his insurance company initially delayed reimbursement and then slowly began to deny coverage for his pain medications and other treatments. “It became so expensive,” he says. “I hit the wall.” He was so concerned about not getting his treatments that he went into panic mode and began to “awfulize,” or constantly complain to himself—a habit, he says, that makes life miserable. Doctors suggested that he apply for disability payments, but Fulton initially refused because of pride. He finally gave in when he could no longer pay his bills.

### The Meanings of Pain

**P**AIN IS A COMPLEX HUMAN EXPERIENCE that varies according to person, place, and time. In the ancient world, people believed that pain was a punishment from the gods, and every society had its own idea of what caused pain. Buddhists, Warfield says, blamed pain on the frustration of desire. Hindus asso-

Clifford Woolf’s discovery of “central sensitization” in 1983 revolutionized the pain field.





When someone is hurt, the capacity for language gets destroyed—they utter a monosyllable or cry.

ciated pain with the heart, which they saw as the center of the nervous system, and the Chinese attributed it to an imbalance of the unifying forces, yin and yang.

Today, people in much of the nonindustrialized world believe that pain is an inherent component of living and endure it in silence, according to Rabb professor of anthropology and professor of psychiatry Arthur Kleinman. In the United States, however, people tend to equate personal freedom and the pursuit of happiness with a guaranteed

freedom from pain. Too often, they ignore the meaning behind their pain, even though that meaning may be aggravating their illness.

“The meaning of pain is very different from the pathology,” says Kleinman. In *The Illness Narratives: Suffering, Healing, and the Human Condition*, he examines the lives of selected patients and discusses the cultural and psychosocial meanings of their chronic pain. Howard Harris, for instance, is a police lieutenant who has tried almost every orthodox and alternative treatment available for the lower back pain that has plagued him for 20 years. The chief meanings of his pain are transparent, notes Kleinman. “Dominating them all is the sense of extreme vulnerability and the strict self-limitations he has placed on his life in order to prevent serious episodes and complications of the pain,”

## The Character and Language of Pain

THE DIFFICULTY OF TREATING PAIN flows in part from the difficulty people have in expressing and characterizing their painful sensations. In her essay “On Being Ill,” Virginia Woolf observed that literature rarely portrays bodily pain. “English, which can express the thoughts of Hamlet and the tragedy of Lear,” she wrote, “has no words for the shiver and the headache....The merest schoolgirl, when she falls in love, has Shakespeare or Keats to speak her mind for her; but let a sufferer try to describe a pain in his head to a doctor and language at once runs dry.”

Cabot professor of aesthetics and the general theory of value Elaine Scarry says, “We often recognize pain only if we see body damage or the weapon that caused the damage—and, sometimes, not even then.” While researching her book *The Body in Pain: The Making and Unmaking of the World* (1985), Scarry, a participant in Harvard’s Mind/Brain/Behavior interfaculty initiative, studied literature and art, medical case histories, documents on torture, and legal transcripts of personal-injury trials. “Many physicians still look on patients as unreliable narrators,” she says. And this often happens, she believes, because it is enormously difficult to put physical pain into words. “When someone’s hurt, you can see [the capacity for] language being destroyed,” she says. “They utter a monosyllable or cry.”

The unsharability of pain—its ability to destroy language—is a major contributor to unrelieved suffering. “To have pain is to have *certainty*,” Scarry writes. “To hear about pain is to have *doubt*.” When she was working on her book in the late 1970s and early 1980s, Scarry felt optimistic because specialized pain clinics were opening. Yet, over time, she noticed that pain continued to be undertreated.

Medicine has attempted to come to grips with the elusiveness of pain, to help in its treatment. In 1975, 10 years after he and Patrick Wall set forth their gate control theory of pain, Ronald Melzack introduced the McGill Pain Questionnaire.

This diagnostic tool, designed to help patients articulate the character of their pain, measures subjective pain experience to facilitate communication between patient and doctor. Patients are asked to rate the intensity of their pain on a numerical scale and to choose among adjectives such as “pinching,” “pulling,” “burning,” and “vicious” to describe the sensory and affective components they are experiencing. Although it can be a valuable tool, the questionnaire often goes unused—and even when used, it is not enough to convince some doctors that a patient’s pain is genuine.

Many doctors believe that the pathology underlying the pain doesn’t merit the patient’s level of complaint, says Rabb professor of anthropology and professor of psychiatry Arthur Kleinman, who offers an uncomplicated solution. “In the pain field,” he says, “ethics should precede epistemology.” In other words, doctors should first acknowledge that the patient’s pain is real before interrogating him or her about its sources.

But doctors’ medical-school training and the way they have to function in hospitals encourages a sense of doubt, notes Kleinman, drawing on his own clinical experience. “If there is a single experience shared by virtually all chronic pain patients,” he writes in *The Illness Narratives: Suffering, Healing, and the Human Condition*, “it is that at some point those around them—chiefly practitioners, but also at times family members—come to question the authenticity of the patient’s experience of pain.

“This response contributes powerfully to patients’ dissatisfaction with the professional treatment system and to their search for alternatives,” Kleinman continues. “Chronic pain discloses that the training and methods of health professionals appear to prevent them from effectively caring for the chronically ill. Reciprocally, chronic pain patients are the *bêtes noires* of many health professionals, who come to find them excessively demanding, hostile, and undermining of care. A duet of escalating antagonism ensues, much to the detriment of the protagonists.”

## Stimulating the touch and pressure nerves, for instance by rubbing a banged knee, can help relieve pain, so people have developed ways to accomplish this electrically.

Kleinman writes. “Each twinge and cramp is carefully tracked. A minute change is observed assiduously, and so on, so that his entire life is his pain. The pain controls him.”

In Kleinman’s interpretation, the weak spine and vulnerability to falling apart are “metaphors of another set of fears that relate to Howie’s job, his marriage, his childhood experience of growing up with an absent father and emotionally distant mother, his personal fears of inadequacy, inefficiency, and dependence. The illness has taken on these meanings from Howie’s life world.” Kleinman is unsure whether these meanings contributed to the onset of the pain, but he is certain that they influence its course.

Another case study focuses on Rudolph Kristiva, a 38-year-old unmarried accounts clerk, of Bulgarian-Jewish background, with a 15-year history of chronic abdominal pain. “If Howie Har-

ris’s story is life dominated by pain,” writes Kleinman, “Rudolph Kristiva’s is close to the opposite: pain dominated by life.” Kristiva, a homosexual who had led a promiscuous life in France and the United States, is caught up in a cycle of worries—about AIDS, his low-status job, his lack of close friends, and his failure to finish his doctorate. For him, pain is just another source of worry in a life devoted to fears and frustrations. As the stresses in his life worsen, so does the pain. Once, after reading newspaper articles about the spread of the AIDS epidemic, Kristiva’s pain became so severe that he had to visit an emergency room.

In Kleinman’s interpretation, “Chronic pain syndromes, originating in the biology of injury and disease, are worsened and prolonged by these vicious cycles of misery.” Such cycles can begin early in life. Stresses like family discord, anxiety about separating

## Relieving Pain

“**W**HEN we treat pain, the first thing we do is try to eliminate the source of pain, say, by relieving compression on a nerve,” says professor of anesthesiology Carol A. Warfield. “When this cannot be done, we treat the perception of pain, i.e., with drugs that block the pain message in the brain. Or we may block the pathway that brings the perception of pain to the brain, say with a nerve block. However, there is a whole gamut of treatments. For example, if a patient has a cancer that’s growing into or around a nerve, first we would try to get rid of the tumor either by surgery, radiation, or chemotherapy. We may inject steroids to try to decrease the irritation and swelling around the nerve. If that doesn’t work, we try to treat the pain itself with morphine or medications aimed at nerve pain, or we might inject something into the nerve that relays pain from the cancerous area to the brain, or electrically stimulate those areas to interfere with the electrical transmission of pain along the nerves to the brain.”

Here are some of the major modalities of pain treatment.

### Pharmacological

Physicians may prescribe *narcotics* such as morphine and Oxy-Contin for severe pain. Doctors give narcotics by mouth or, in some cases (particularly with patients suffering from cancer),



they may inject them into the spinal area.

These drugs are derivatives of opium and work on the natural narcotic receptors in the brain and spinal cord. Common side effects include constipation and drowsiness. Contrary to earlier beliefs, patients who take narcotics for medicinal purposes rarely become addicted to them.

“When I started doing this 25 years ago, it was absolutely taboo to give narcotics to a patient you expected to have pain for the next 10 years,” says Carol Warfield. “Now the pendulum has swung.” Some patients actually do better on these drugs than on other painkillers, she says. “It’s a matter of whether the narcotics can really restore their function.”

*Nonsteroidal anti-inflammatory drugs (NSAIDs)*, including over-the-counter medications such as aspirin, Advil, and Aleve, are less potent than narcotics. They reduce inflammation by blocking the action of certain enzymes called cyclooxygenase (Cox) 1 and 2, thus helping to treat the source of pain when a person has a condition like a toothache or sprain. But they can also cause stomach ulcers and bleeding. Vioxx and Bextra, newer types of NSAIDs, were pulled off the market after studies showed that they increase the risk of heart attack and stroke.

*Steroids* are powerful anti-inflammatory medications that doctors may inject directly into the area that is the source of pain.

from a parent, school difficulties, and being bullied can lead to both pain and disability in children, says Charles Berde, professor of anesthesiology and pediatrics and chief of pain medicine at Boston's Children's Hospital. But mind-body medicine can help people of all ages; a six-to-eight-session cognitive-behavioral training regimen, aimed at helping patients alter patterns of negative thoughts and dysfunctional attitudes, has proven as effective as any medication for childhood headache, he notes. Migraine, for example, is a very real physiological problem, "but attitude, expectation, attention, and belief can change your physiology."

## Images of Pain

**W**HEN DAVID BORSOOK WAS DIRECTOR of the pain center at MGH, he saw the need for better methods to assess and treat chronic pain, so he embarked on a study to track brain activity in response to pain. Using functional magnetic resonance imaging (fMRI), he viewed the brains of eight healthy volunteers as he heated their hands enough to produce a burning pain without damaging the skin. The results, which appeared in *Neuron* in 2001, showed that pain and pleasure activate

For example, in the case of sciatica, where one of the nerves in the back is inflamed, doctors often inject steroids into the epidural space, the sac that surrounds nerve roots and contains cerebrospinal fluid. If taken over long periods, steroids can make bones brittle and can suppress the body's own production of cortisone. Other possible side effects include thinning of tissues and elevation of blood sugar.

Doctors frequently prescribe *antidepressants* for people in pain because they increase the supply of a neurotransmitter, serotonin, that helps activate the body's natural pain-relief system. For instance, doctors often use antidepressants as the first line of treatment for shingles. In addition to dizziness and sleepiness, antidepressants can produce dry mouth, abnormalities of the heartbeat, and inability to urinate.

*Anticonvulsant* or *antiepileptic drugs* can also be effective for nerve pain. If you have a seizure, your brain has a spontaneous discharge of electricity, which these drugs soothe, notes Warfield. The drugs act in the same way against pain when a peripheral nerve suddenly sparks and sends an electrical message, she says. But anticonvulsants often cause drowsiness and dizziness.

## Stimulation-induced analgesia

Stimulating the touch and pressure nerves, for instance by rubbing a banged knee, can help to relieve pain (see "The Gates of Pain," page 48), so people have developed many ways to accomplish this electrically. "The Egyptians [took] electric catfish out of the Nile and, unbeknownst to them, what they were probably doing was electrically stimulating the tissues to stimulate those touch and pressure fibers," says Warfield. Now, there is *transcutaneous electrical nerve stimulation (TENS)*, a method of applying low-voltage electricity within tissue using a beeper-sized, battery-powered device with leads connected to electrodes attached to the skin. Acupuncture is another type of stimulation-induced analgesia.

## Behavioral/psychological interventions

Cognitive behavioral therapy can help patients view their pain as manageable rather than overwhelming, and become actively

involved in their own treatment and rehabilitation, according to Robert Jamison, a clinical psychologist who "coaches" pain patients at Brigham and Women's Hospital. This type of therapy teaches patients to substitute positive thoughts for the negative ones that perpetuate feelings of hopelessness. *Relaxation strategies* such as diaphragmatic breathing and guided imagery can help lessen pain by relaxing tense muscle groups, reducing anxiety, and increasing the patient's sense of control over physiological responses, notes Jamison.

## Surgical Interventions

Doctors generally recommend *surgery* only after more conservative approaches have failed to relieve pain. For instance, in some cases of unrelenting sciatica due to a herniated intervertebral disk, surgeons may remove a portion of the patient's damaged disk through an incision in the back.

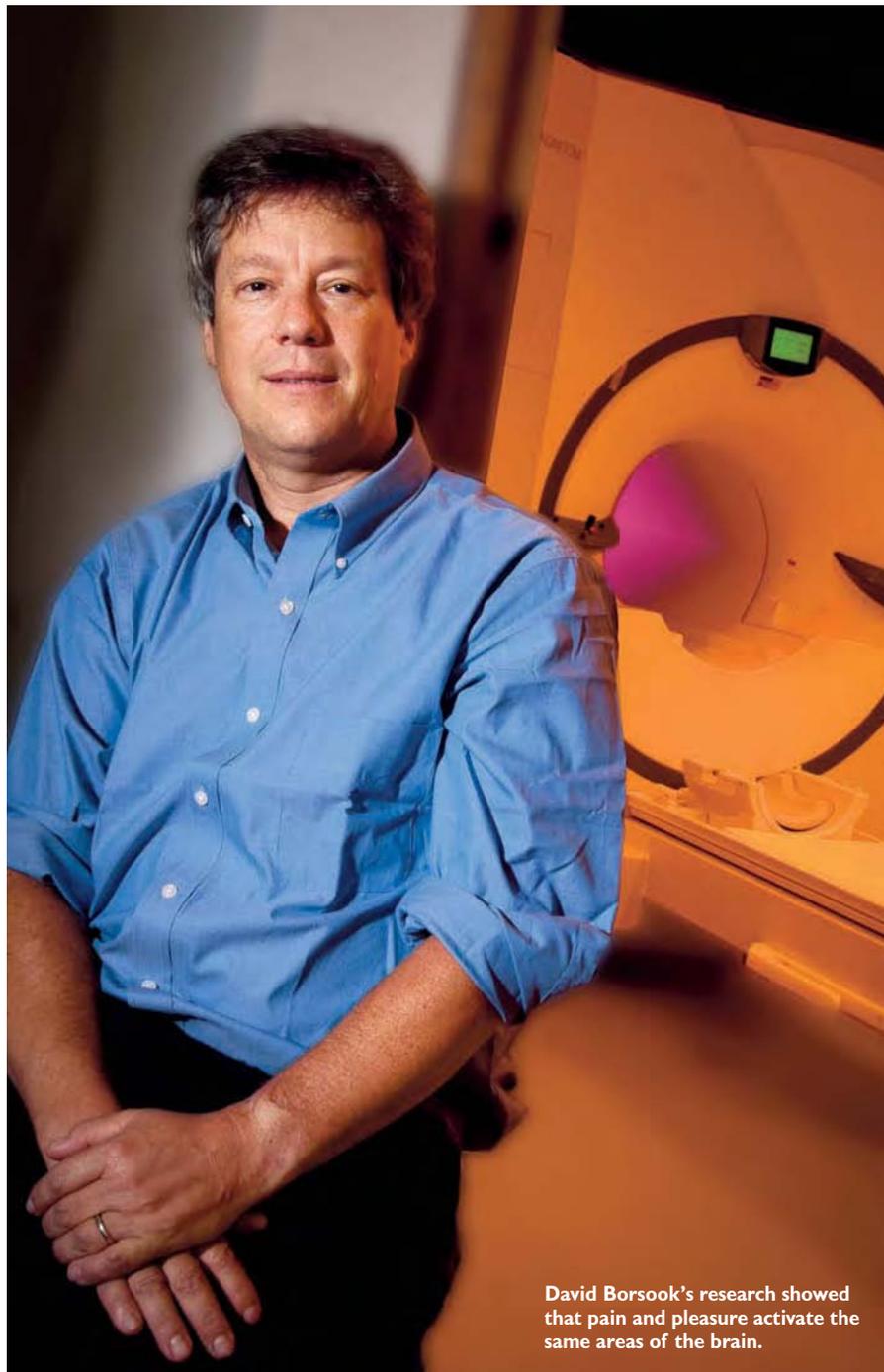
## Physical measures

*Regular exercise* improves muscle tone, strength, and flexibility, and may increase levels of endorphins, which are endogenous opiates (natural painkillers). *Physical therapy* may improve movement and function after a painful injury. *Massage* can reduce stress and tension and improve blood flow to tissues.

## Innovative treatments

Recently, doctors at the Arnold Pain Center began using *nucleoplasty* for disk disease. In this procedure, they insert a needle into an intervertebral disk, then place a special radiofrequency probe through the needle to vaporize the disk's gelatinous core. "It kind of cooks the disk material so it doesn't leak anymore and cause pain," says Warfield.

Soon, they will use *vertebroplasty* for some patients who have compression fractures due to osteoporosis. In this minimally invasive procedure, doctors insert a hollow needle into the vertebral bone and inject a cement mixture, which acts as a glue to stabilize the vertebrae and treat the pain of the compression fracture.



David Borsook's research showed that pain and pleasure activate the same areas of the brain.

## Borsook expects current research to foment a fundamental pharmacological revolution.

tions meant to stimulate the release of natural painkillers.

Now, as director of the P.A.I.N. (pain and analgesia, imaging and neuroscience) Group at McLean Hospital in Belmont, Massachusetts, Borsook continues to map the pathways of pain. With Charles Berde of Children's Hospital and other colleagues, he is using fMRI to look at changes in the brain's pain circuitry in children with complex regional pain syndrome, or reflex sympathetic dystrophy, a debilitating disorder affecting seven million Americans of all ages that causes severe pain, hypersensitivity to touch, and neurovascular symptoms like coldness and poor circulation. The ultimate goal is still finding medications that are safe and effective for chronic pain conditions. Borsook expects current research

to foment a fundamental pharmacological revolution.

Clifford Woolf is helping to lead that revolution. He and his research team at MGH are looking for genes activated in pain-related conditions. Using fluorescent dyes and a special scanner, scientists can analyze the expression of thousands of genes simultaneously, quickly determining whether those arrayed on a glass platform light up under certain conditions, such as when nerve cells respond to pain.

Woolf and his colleagues have already identified hundreds of pain-related genes. Scientists may eventually use some of them as targets for testing completely new classes of analgesics that will perform in ways totally unrelated to the processes by which today's morphine and Cox inhibitors act (see "Relieving Pain," page 52). Until now, doctors have largely used pain medications to control symptoms, says Woolf. "That's what morphine does," he explains. "It doesn't treat the underlying cause of pain; it just suppresses the sensation the person has. But now, I think, as a result of our progress in understanding the mechanisms that operate to produce pain, we are at a transition where we can actually target the treatment to those mechanisms." He believes pain medications will change profoundly within the next 10 to 15 years.

In addition to dissecting pain mechanisms at a molecular level, Woolf and his team have just designed an approach in which they can statistically analyze certain information about patients, including medical histories and results of physical examinations, to derive a cluster of signs and symptoms, a "fingerprint," for the likely mechanisms causing their pain. The investigators hope to develop a new diagnostic tool that reveals the different kinds of pain a patient may have—central sensitization, for example, or abnormal expression of a particular gene—so that doctors can then select the appropriate form of therapy. "We're moving away from seeing pain just as an element of suffering and an unpleasant sensation, to a situation where it has a clear underlying neurobiological mechanism, one that we are beginning to understand and elucidate," says Woolf. "This is revealing targets for the development of very specific forms of treatment. That's where the hope comes."

Sixteen years after his car accident, Stephen Fulton still suffers excruciating pain. Pain medications make him nauseous and dizzy and have become less effective over time. Physical therapy is difficult because there are days when he can barely move his body. Surgery is risky because of his diabetes. "I hope that I will get better, but I'm realistic that that probably won't be the case," he says. His doctors have hinted that new drugs are on the horizon—drugs that may do more to ease his pain and have fewer side effects than his current medications. They may be right, he says, but for now, "I can only wait." And he will do his best to cope with the daily pain, because "if you give up and let the pain take over, you're gone." ▽

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