

The Changing Science of Pain

Millions of aging boomers and the latest generation of wounded soldiers hope the secrets of our most enduring medical foe can finally be unlocked.

By Mary Carmichael

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June 4, 2007 issue - Late into the night of May 2, 1863, a few hours after Thomas (Stonewall) Jackson took two bullets in his left arm at the Battle of Chancellorsville, surgeon Hunter Holmes McGuire sawed off the bleeding limb, trying to save the general's life. With the knife came another medical tool, one fairly new to the battlefield—a rag soaked in chloroform. As he awaited amputation, Jackson, who would die a week later, was as stoic as his nickname suggested. But as he slipped into unconsciousness, it's said he betrayed his vulnerability in the face of pain just once, mumbling that the anesthesia was "an infinite blessing.

For most of the 144 years since then, the military has stuck with similarly crude techniques for treating its soldiers' pain. Morphine, also given to Jackson and many others in the Civil War, is still the Army's most commonly used painkilling drug. It works, but compared with more-modern options, it's one step above chloroform and two above biting the bullet. Now, though, with casualties mounting in Iraq and Afghanistan, the military is being forced to change its strategy. More than 90 percent of wounded soldiers have made it off the battlefield—the highest survival rate in American history—only to overwhelm chronic-pain clinics when they come home. "We're seeing the tip of a tidal wave of pain," says Lt. Col. Chester (Trip) Buckenmaier, an anesthesiologist at Walter Reed Army Medical Center, who has emerged as a sort of pain czar for the Army. After decades of "sucking it up," the military has finally started to respond in new and innovative ways to this escalating pain crisis. Even as the VA hospital system has come under fire for poor care, Army doctors haven't just joined up in medicine's larger war against pain—they're leading the charge.

Winning this medical war is crucial, and not just for the sake of the soldiers, who are far from the only burgeoning new group of pain sufferers. Chronic pain is one of the most pervasive and intractable medical conditions in the United States, with one in five Americans afflicted. Aging baby boomers have reported in surveys more aches and pains than any previous generation. Cancer patients have more treatments to choose from than ever, but more pain, too. Even retired NFL players—a suck-it-up group if ever there was one—have started speaking out about the wear and tear on their bodies. Civilian chronic pain already costs the country \$61 billion in lost productivity and many more in medical fees. Treating the soldiers in the coming years will add at least \$340 billion to the toll.

As the number of patients has grown, though, so has medicine's understanding of what pain is. Scientists once viewed it as merely a symptom of injury, an intuitive idea that resonated with laymen. "The public understanding of pain has been that it's a stubbed toe or a broken bone," says Will Rowe, executive director of the American Pain Foundation. "But that's just one aspect of it. Now there's a growing awareness that pain is a disease of its own."

This is far more than a semantic change, Rowe adds: it's "tectonic." Docs now know that the brain and spinal cord rewire themselves in response to injuries, forming "pain

pathways" that can become pathologically overactive years later. They are trying to sever this maladaptive mind-body connection with a host of new drugs and approaches. Some focus on recently discovered chemical receptors in the brain and muscles. Others pack all the punch of narcotics with less of the specter of addiction. (Patients can still become dependent on a new form of the morphine derivative called Kadian, for instance, but if they crush one of the pills for snorting, its center explodes, releasing a substance that blocks the euphoric high.) New types of electrical stimulators targeting the brain, the spine and the muscles hit the market almost every year. Fentanyl skin patches, first introduced in 1990, have evolved into a patient-controlled, push-button device called IONSYS, available by the end of this year. And complementary and alternative medicine offer a parallel universe of treatments: herbs, yoga, acupuncture, chiropractic, massage and "prolotherapy," which injects various solutions, including cod-liver oil, into ligaments and tendons near the area of pain.



Ethan Hill for Newsweek

Determined to Help: Buckenmaier, with his team at Walter Reed, is developing new methods for treating acute pain on the battlefield in the hopes of heading off chronic pain

The military is pioneering its own new approaches. Since 2003, a small but growing number of soldiers in Iraq have been treated at the front with high-tech nerve-blocking devices that are effective but not addictive. They are common in civilian life, but their use on the battlefield is unprecedented. Back at home, many VA clinics are offering extensive and elaborate pain treatments, and they're learning how to get tough guys and girls to soften up and admit they need help. At Walter Reed, Buckenmaier's team is conducting groundbreaking research on the link between acute and chronic pain; his findings, due in the next few years, could revolutionize treatment. "The military needs people to be functioning out on the field," says Rollin (Mac) Gallagher, chief of pain medicine at the Philadelphia VA hospital. "What we're now starting to recognize is that if you control people's pain, they're not liabilities—they're assets."

That's not to say pain is all bad. It's unpleasant, of course, but in an evolutionary sense, it has its uses. Acute pain begins in the peripheries of the body, where sensory neurons are constantly on patrol for signs of damage. They are the mechanisms that alert us to one injury so we can avoid a second one. Touch a hot stove for the first time and you won't be happy, but you'll ultimately be better off—because you'll certainly never want to do it again.

By the time it has become a chronic condition, however, pain is no longer useful. It is, as Rowe says, a disease—specifically, an overactivity of the nervous system. The brain keeps a diary of the injuries the body receives, writing each entry by reconfiguring certain neurons into new, interconnected patterns. In healthy people, these neurons stop

firing once the initial damage is fixed. But in chronic pain, they keep going long after the injury has healed. "The circuits get turned up, and they stay up. They get stuck," says Gallagher. "Most diseases are physiology gone wrong. Pain is one of them."

Scientists don't know why some people develop chronic problems after injuries while others continue on with no pain. It is nearly impossible to answer the question on a wide scale; pain simply has too many causes. Some patients fully recover from massive trauma. Others, like most of the boomers with aching backs and knees, find themselves debilitated by nothing more than the accumulated, mundane strains put on joints, bones and muscles every day. Even soldiers can fall into this second category—if the bullets don't get them, the back pain brought on by months of jumping out of trucks, burdened with heavy equipment, well may.

Complicating the issue even further is pain's inherently subjective nature—we may say we "feel each other's pain," but really, we can't. Doctors don't have any good way of measuring pain from one person to the next. The best they can do is ask patients to rate it for themselves on a scale of 1 to 10, with 10 being the greatest agony of their lives. This is absurdly imprecise. Patients are usually honest (and fakery is fairly easy to spot), but they can exaggerate. A person feeling a 4 may claim a 7 to get aggressive treatment, and a person feeling a 7 may downplay it as a 4 in hopes of looking tough. Robyn Walker, a psychologist at the Tampa (Fla.) VA, says she's seen the latter dynamic in her clinic. "These patients know what a 10 feels like," she says. "But they are active-duty soldiers, and they minimize their problems. Unless you really ask them about their pain, they may be very hesitant to tell you." Doctors are trying to develop new methods of measuring pain, but their most advanced idea so far is to study facial expressions—which aren't much more standardized than the 10-point scale.



John Clark for Newsweek

Wounded in Action: Barbara Canal works with patient Scott Brozena on a physical-therapy regimen for his pain

On top of that, one patient's 7 may be another's 4. "Our bodies are not one-size-fits-all," notes Rowe, "and doctors are finding that this is far more true with pain than they ever imagined." Genes may vastly influence how intensely people feel pain and how much they can withstand—although genetic testing for pain susceptibility is probably decades away. Gender matters, too. Women have up to twice as many nerve fibers in the skin as men do, so they feel some types of pain more intensely. (This doesn't mean they're weaker; it means that, all other factors being equal, their 10 is off a man's chart.) Even

traits that seem unrelated to pain, like vitamin D deficiency, may increase it for reasons no one fully understands. Trying to untangle all these factors is a scientific nightmare.

Regardless of their injuries, their genes, their gender or their background, though, nearly all chronic-pain patients agree on one thing: the hyperactive neurons can make life near unbearable. The cascade of changes in the nervous system can lead to an equally painful cascade of events in a patient's life: memory loss, job loss, marital strife, depression, suicide. And through it all the body hurts like hell. "Imagine somebody holding a knife in your back and twisting it against your nerves continually, never stopping. That's what chronic pain is," says Dan O'Neal, a contractor who herniated two vertebrae in 2003 while cleaning up a job site. "At first you just shut off totally. It's terrible living like that."

Among chronic-pain patients, O'Neal is actually one of the lucky ones. He, at least, knows why his pain started; some patients are denied even that knowledge. Chronic regional pain syndrome, for instance, is a rare disorder that can begin with something as trivial as a skinned knee. The scrape heals, but the nervous system does not. Within a few years the knee that was skinned feels like it is on fire, even though nothing is outwardly wrong. Similarly, fibromyalgia assails the bones, muscles and joints, but has no obvious bodily causes and doesn't show up on X-rays. Growing evidence now suggests that it is in part a brain disorder that sets the pain pathways afire, responding to imaginary wounds—as if the brain's diary of injuries has suddenly filled up with wild, untrue stories. The pain itself is not imaginary. But because it is hard to pinpoint and even harder to treat, for years many doctors used to write it off as such. Andrea Cooper says that's all doctors did when she first developed fibromyalgia, which afflicts 6 million Americans. "There was a bunch of 'We can't figure out what's wrong with you, therefore there's nothing wrong with you'," she says. "People don't like to hear about symptoms that they can't do anything about."

Some fibromyalgia patients may be helped by standard pain treatments. Others aren't. In that, at least, fibromyalgia patients are just like all other pain patients: relief can come for them, but it is often hard-won. Cooper, who is now on fentanyl and Kadian, compares her current pain to "the roar of the faraway interstate, as opposed to being in traffic." But to get to her current regimen she had to go through nearly everything else—antidepressants, anticonvulsants, muscle relaxers, acupuncture and six operations that probably made the pain worse.

Some of the most promising pain treatments of the past decade have turned out to be disappointments. Studies of some radiofrequency therapies show they work no better than placebos. Spinal-fusion surgery, a recent review found, has "no acceptable evidence" to support it. And if a treatment does work, says Edward Covington, a pain specialist at the Cleveland Clinic, "for most people, the effect is temporary." There is no cure for chronic pain, period.

There's not even any "single drug or technology alone" that can treat all the types of pain, says Eugene Viscusi, director of acute-pain management at Thomas Jefferson University Hospital in Philadelphia. Most people need two or three therapies in combination. Scientists' new understanding of pain's broad effects on many levels of the nervous system explains why: a multipart syndrome requires multipart therapy. Viscusi notes that patients under anesthesia still have elevated levels of the pain enzyme Cox-2 in their spinal fluid following surgery. They may not feel pain, but some parts of their brains still think they're in it. For any treatment to work long term, it will have to address not just the immediate sensation of pain but the other, subtler aspects—and there are surely some of those that scientists don't know about yet.

At the American Pain Society's annual meeting in May, a panel drew attention to what seems like the best option pain medicine currently has to offer: "multidisciplinary pain centers," essentially rehab clinics that employ doctors, nurses and therapists from a variety of fields. They prescribe a tough-love regimen of physical therapy (as well as the psychological kind), and many also make a point of cutting down on drug use. Pain specialists have been singing their praises for the past three decades. Data show why: they help many debilitated patients get back to work. But multidisciplinary clinics are on the wane. There are no statistics, but Covington says he suspects their numbers have dwindled by about 90 percent in the past 30 years. The problem is that a lot of patients just don't like them. "Americans love deep brain stimulation, replacement discs, things that are sexy and magical and frequently hyped," Covington notes. Multidisciplinary clinics are a much harder sell. They're not a quick fix, and their emphasis on exercise strikes fear in some people who are already worried about injuring themselves.

Insurance companies also sometimes balk at multidisciplinary clinics, which are costly. They'll cover them, Covington says, but usually "only enough so they lose just a little bit of money on them every year." Insurers say they sometimes have trouble determining how legitimate the clinics are or how much of a service they'll provide, since there are no national guidelines for what the clinics should encompass.

Insurers usually prefer to pay for single therapies, like opioids, the narcotics that block messages in the brain and make patients care less about their pain. The drugs are hugely widespread; almost 200 million opioid prescriptions get written in America each year, most of them for Vicodin, OxyContin and various forms of fentanyl. But "widespread" doesn't mean "effective," nor does it mean "popular." In opioid trials, fewer than a third of patients on average report relief, and more than a third drop out of the same trials rather than deal with the side effects, which include nausea, constipation and trouble breathing. "Most of the soldiers I treat say they don't want to take these strong medications," says Walker, the Tampa VA psychologist. "They say, 'These things make me groggy. I want to get back to my life'."

Opioid users also run two parallel risks: that they will become addicted, and that they will suffer the stigma of addiction even if they're not abusing the drugs. Steven Passik, a pain specialist at Memorial Sloan-Kettering Cancer Center, notes that "the issue of addiction doesn't lie in the drugs," but in a complex interaction between the chemicals and biological predispositions. Still, many patients struggle. Brooks Bono, 28, was born with a tumor on his spine and has spent his whole life in pain. At one point he was on so much OxyContin that "the dosages would have killed someone else," says his mother, Kadie Dempsey. He sees Passik now for counseling, and a few months ago he switched to methadone. It's not as addictive, says Bono, but it does little to dull the pain and it brings its own problems. "I went to about 20 different pharmacies," he says, "and they told me, 'We don't treat drug addicts here'."



Gregg Segal for Newsweek

In Search of Relief: Dr. Marc Darrow administers prolotherapy to Mitch Abrams

No one wants to avoid an epidemic of drug abuse more than the military. Addicted Vietnam vets still wander into VAs, and as Gallagher notes, "if our soldiers can't get pain relief in the medical system, they'll turn to other ways." Many VA clinics make a point of cutting down on soldiers' use of opioids and other drugs. At a congressional hearing on pain in December 2005, Capt. John Pruden said he'd talked with one of his old buddies, who had been wounded in Iraq. "As we were talking, he bragged how he was not using his pain meds," Pruden told the audience. "But unfortunately it turns out he was self-medicating with alcohol to cope with the pain."

The military is now pursuing a new pain strategy: stop the trouble before it starts. Historically, wars have led to medical advances, and this one is no different; the notion of a kind of pre-emption has captured the interest and excitement of the entire pain-medicine community. Treat acute pain early, the thinking goes, and you stop the brain from responding to it. You might just wipe out chronic pain in the process.

This is where Buckenmaier's research comes in. His team is responsible for bringing those high-tech nerve blocks to the battlefield. Since 2003, hundreds of injured soldiers have received anesthetic pumps within hours of their injuries. Buckenmaier and Gallagher are jointly tracking these soldiers over the next year and beyond. If the ones who got pumps quickly have less chronic pain—and animal studies suggest they will—the research will not only point the way to new treatments, says Gallagher: for civilians and soldiers alike, "it will be a revolution." It may mean that injuries will be treated much more aggressively. That sprained ankle that only registered a 4 on the pain scale? If you want to avoid chronic pain later, you might need serious therapy, and right away.

It's too soon to say what will ultimately become of the Walter Reed study, though the hospital believes in Buckenmaier's work: despite being short-staffed and underfunded, it decided two weeks ago to fully finance his vision for a new acute-pain-management service, one that may remain in place after the war is over. There is much else left to do. Buckenmaier's nerve-block program needs to be expanded; thousands of soldiers injured in Iraq still don't get the advanced treatment. And, he says, on the battlefield there's

usually "no one in charge" of pain in any given unit. The VA system, like the rest of the country, needs more pain specialists, not to mention mental-health professionals. Indeed, there's call for change at every level of a lumbering bureaucracy that, as has been amply documented in NEWSWEEK and elsewhere, lets too many soldiers fall through the cracks.

But Will Castillo, a 27-year-old Army sergeant, is not one of these soldiers. Like Stonewall Jackson, he is an amputee. Iraqi insurgents shot him in the head—twice—and as he lay on the ground, an IED blew his leg off. It is a horrible story, but sitting in his hospital bed with his leg covered, Castillo shows no sign that it even happened. He is one of the soldiers who have nerve-blocking pain pumps. He feels good, he says, and once he gets a prosthetic leg, he might even consider going back to Iraq for another round. It's hard to believe it, but yes: this is a man who feels infinitely blessed.

With Samantha Henig, Dan Ephron and Julie Scelfo