

After 4,000 years, scientists are finally solving the mysteries of

PAIN

There are few things worse than chronic pain—the constant pounding, burning or stabbing sensations that can come from any part of the body, often for no apparent reason. Twenty million Americans suffer from the syndrome. Most have headaches or back pain, but arthritis, cancer-related pain, muscle spasms, nerve injuries and general achiness are also common. All this suffering is costly as well as debilitating: The nation spends \$80 billion a year to relieve it.

Yet for a long time doctors took little interest in the subject, dismissing pain as merely an unfortunate symptom of the traumas or diseases that were their primary focus. Now, in the 1990s, a wave of research has led to a more complete understanding of the pain mechanism, to startling revelations about the destructive effects of pain and to a host of novel approaches—involving new technology, medications and clinical practices—to ease the suffering.

Where does it hurt?

Standing at the boundary between physiology and psychology, between body and mind, pain has always been hard for physicians to address. The cause might be physical—a banged head or a stubbed toe—but the pain itself is an emotional response, and as such is nearly impossible to track by conventional methods. "There is no X ray, no picture, no blood test, for pain," says Steven Waldman, M.D., director of the Pain Management Clinic at the Minora Health Center in Kansas City, Missouri. "Only the patient can judge what she's feeling."

Although it can't be measured, pain does serve the crucial function of

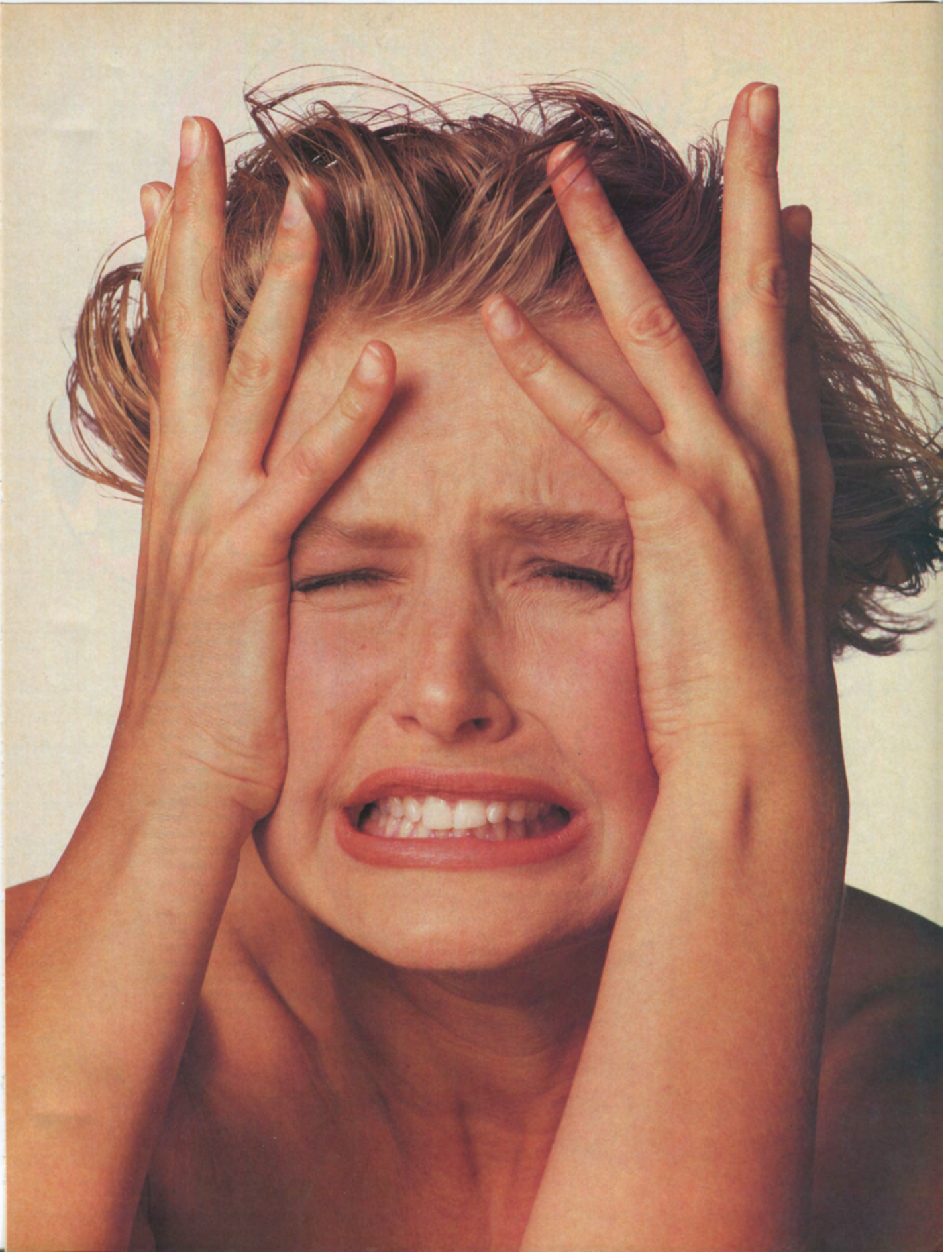
warning us that we are in physical distress. Without it, we would be in constant danger of unwittingly doing ourselves serious harm. For example, there is the case of the woman who, after being hypnotized to ease a chronic pain condition, burned her hand on an iron without realizing it. Perhaps for this reason the medical profession has always assumed that, to a certain degree, pain was simply something to be borne. But doctors are now coming to believe that extreme persistent pain is not just an indicator of disease, but a disease in itself.

In fact, some clinicians regard the body's complex pain mechanism as a kind of bodily organ that is subject to disease no less than is the liver or heart, with serious implications for a patient's physical and emotional well-being. Joel R. Saper, M.D., director of the Michigan Head Pain and Neurological Institute (MHNI), points out that some chronic pain may be caused not by any illness or trauma but simply by a malfunctioning of the brain's pain mechanism. "It's like a smoke alarm that goes off even when there is no smoke in the room," Dr. Saper says. "I call that an illness. It's no different than if your kidneys stopped working." The source of mysterious back pain, then, may not be in the sufferer's back at all, but in her brain.

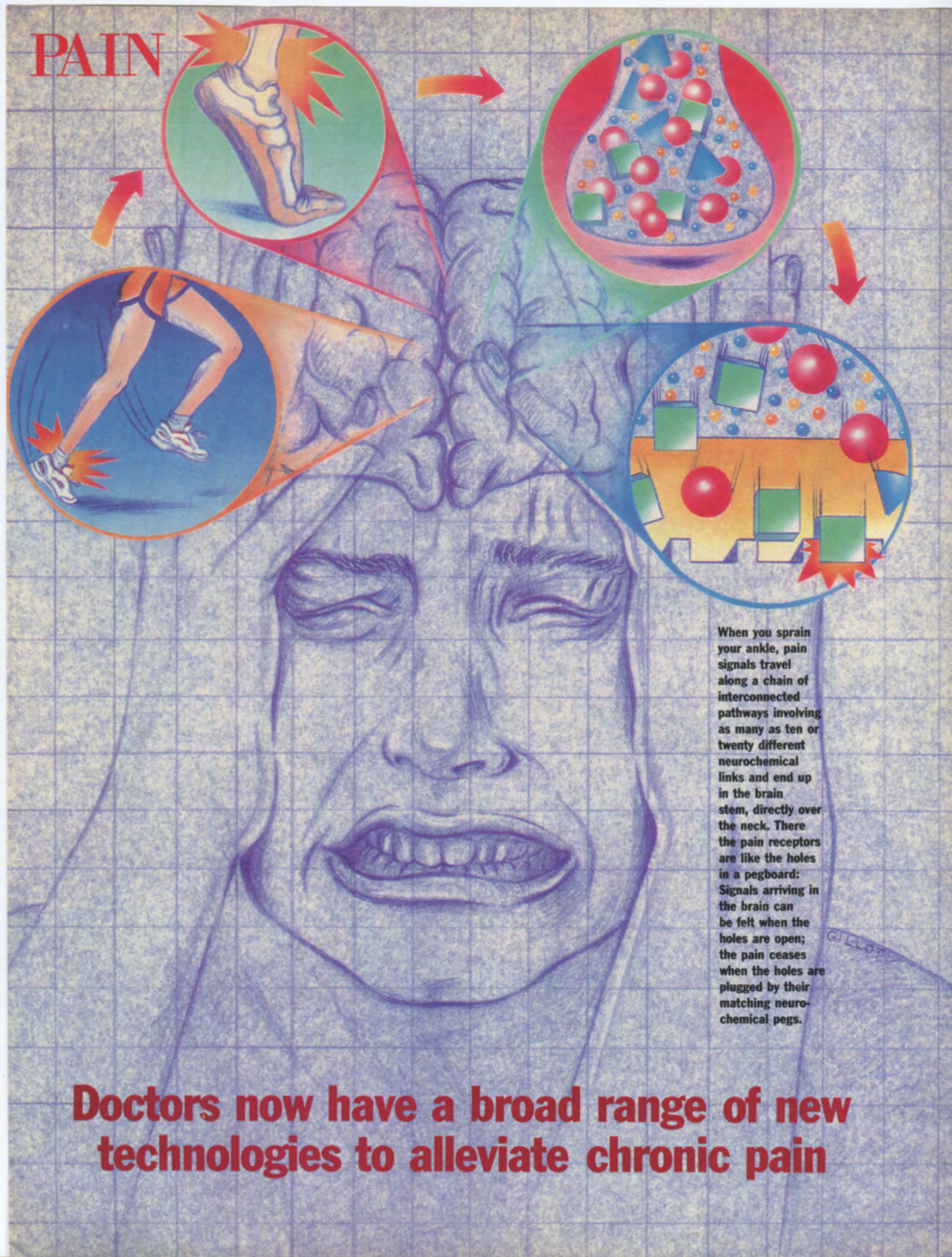
A patient who has this "pain disease" may exhibit drastic hypersensitivity: When her skin is pricked, she feels as if she's been stabbed; if her arm is gently stroked, she feels as if she is being scratched with sandpaper. Many migraine patients report just such heightened sensitivity to pain—also to light, sound and smells—a few hours before their headaches begin. They, too, according to Saper, are suffering from a

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BY JOHN SEDGWICK



PAIN



When you sprain your ankle, pain signals travel along a chain of interconnected pathways involving as many as ten or twenty different neurochemical links and end up in the brain stem, directly over the neck. There the pain receptors are like the holes in a pegboard: Signals arriving in the brain can be felt when the holes are open; the pain ceases when the holes are plugged by their matching neurochemical pegs.

Doctors now have a broad range of new technologies to alleviate chronic pain

disturbed pain mechanism and not from swollen blood vessels, as has long been believed.

Perhaps pain and the chemicals that communicate it to the brain actually cause disease. "People have always said that pain can't kill you, but our findings show that it can," concludes UCLA's John C. Liebeskind, Ph.D., current president of the American Pain Society. His—and others'—experiments with laboratory rats have revealed that pain suppresses the immune system and encourages the growth of cancerous tumors. Dr. Liebeskind's conclusions have yet to be proved by research on humans, however.

But there is ample evidence from research on humans that chronic pain can lead to debilitating emotional distress, and not just because it's depressing to be in constant pain. "The same chemicals in the body that mediate depression also mediate pain," says Carol Warfield, M.D., director of Beth Israel Hospital's pain center in Boston and an assistant professor of anesthesiology at Harvard Medical School. The result is a vicious circle. "The people who are in chronic pain get depressed, and the people who are depressed feel more severe pain," she says. Antidepressant drugs like Elavil are frequently prescribed as painkillers, but the effects are very different. When used to ease pain, they work in a day or two, whereas it takes weeks for them to affect depression. This discrepancy suggests that the pain receptors may be doing double duty, registering pain at a low concentration of neurochemicals and depression at a higher one.

Pain central

The exact process by which the body records pain is still far from clear. But as researchers now conceive it, pain signals travel along a chain of interconnected pathways involving as many as ten or twenty different neurochemical links and end up in the brain stem at the top of the spine directly over the neck. There, the pain receptors are like the holes in a pegboard: Signals arriving in the brain can be felt when the holes are open; the pain ceases when the holes are plugged by their matching neurochemical pegs.

Several of these neurochemicals have been identified, including the opioids, noradrenaline, choline and serotonin. The receptors for opioids, which are more commonly known as endorphins, are currently believed to register pain most directly and intensely. This explains why opium, first cultivated by the Sumerians, is still

Cayenne pepper may serve as a painkiller by depleting a pain messenger called substance P.

regarded as the single most effective painkiller four thousand years later. Usually given in the form of morphine, natural opium substitutes for the body's version, shutting off the pain. By contrast, codeine, which is chemically similar to morphine, is less effective because it doesn't exactly fit the opioid receptors, and so they remain partly open, allowing some sensation to pass through.

Research has also begun to explore other roles the pain receptors play in the body. Saper believes they may be linked to depression, sleep disturbances and drug abuse. In a study of 615 headache patients at MHNI, approximately 70 percent of them also suffered from depression, and there

was a similar overlap with sleep disturbances and drug addiction.

One study suggests that the pain receptors may even figure in suicidal impulses. An examination of the brains of twelve suicide victims revealed that all had significant changes in their opioid receptors. "I don't buy the idea that people kill themselves because they are too sensitive to pain," says Saper, "but I do believe that the changing chemistry of their brains, as reflected by the changes in their pain receptors, may induce self-destructive acts."

One possible explanation for the apparent overlap in the functions of pain perception, mood modulation and sleep control is that they may all involve the same chemical neurotransmitters. Another is that the controlling receptors share a common location in the brain stem, leading to some spillover effects.

Aahhh, relief

So to control chronic pain, depression, sleeplessness, drug abuse and suicidal impulses, the prescription seems obvious: Boost the opioids, either by tricking the body into manufacturing more of its own or by developing a drug that mimics the opioids' effect. Finding this drug has not been easy. After four millennia, the best painkiller is still morphine, in spite of such side effects as constipation, nausea, drowsiness and addiction.

Researchers have developed new delivery systems that minimize some of these. Anesthesiologists at Massachusetts General Hospital, for example, capitalized on the discovery of opioid receptors all down the spinal column to devise an epidural that injects morphine directly into the lower spine, thereby avoiding the constipation, nausea and drowsiness that stem from the upper body's involvement. In one version of the technique, a four-month

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In a study of 46 migraine patients, 17 percent said that having sex brought moderate to complete relief.

Help a friend

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We each need to develop our own personal definitions of responsibility, irresponsibility and overresponsibility, says Dr. Fredman. And each of us must be prepared to take action based on what we believe.

My own code no longer requires me to extend myself on behalf of friends whose behavior I find unacceptable. Several years ago, a friend became involved with a woman in our office, despite the fact that he was married and had a small child. I knew, and liked, all the players in this triangle, and found that listening to Bill's stories of deception made me feel as if I were betraying his wife as well. I tried to withdraw discreetly from our usual coffee breaks, but found that the more I tried to avoid them, the more eagerly he would push for our morning confessionals.

Finally, I admitted that I was uncomfortable talking about his affair. He accused me of not being a real friend to him, and even of being a prude. I answered, "I'm not being a friend to myself if I continue to support your situation. I care about both you and your wife, and knowing what's happening makes me feel like a liar each time I talk to her."

We were never close again, even after his romance ended. We had each learned something disappointing about the other. Bill had discovered that my friendship wasn't unconditional, and I'd learned too much about his talent for deception.

Helping a friend through a time of trouble can take many forms—from providing chicken soup to emotional support to a temporary place to stay. Still, no matter what a friend needs, empathy will always be the crucial element when it comes to offering real assistance. If a friend knows that someone really understands her feelings, she won't feel so isolated by her despair, and her problems won't seem quite so unbearable. □

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Pain

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supply of morphine is implanted under the skin for the patient to release as needed by touching a subcutaneous valve at her waist. And several hospitals are beginning to try patient-controlled analgesics (PCA)—bedside morphine pumps that the patient can regulate herself. When these systems are used, the patient takes less medication than when it is administered by others. But nothing has eliminated all of the side effects, most notably the problem of addiction.

Scientists are also looking for nonopioid receptors. One development is the discovery of the cannabinoid receptors. Just as the opioids deliver the euphoria of opium, the cannabinoids produce the high of cannabis, better known as marijuana, and with it a distinct analgesic, or painkilling, effect. Drug companies are expressing little interest in developing a cannabinoid painkiller, however. "They're afraid of the stigma of marijuana," says Miles Herkenham, Ph.D., chief of functional neuroanatomy at the National Institute of Mental Health. They may also be discouraged by the fact that while the cannabinoids may not be as addictive as opioids, they do produce some of the side effects of marijuana-smoking, including red eyes, dry mouth and dizziness.

Surprisingly, cayenne pepper, long known to have a numbing effect when applied directly to nerve endings, may also serve as an analgesic because it depletes a pain messenger called substance P. Dr. Waldman has found that a topical cream heavily spiced with cayenne pepper provides significant pain relief for patients with nerve damage caused by diabetes or shingles.

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Among the most promising treatments for pain are those that stimulate production of the body's own opioids. Most pain specialists are now willing to admit that acupuncture, for example, is useful in treating patients who suffer from arthritis or persistent aches in the lower back. And a kind of high-tech version of acupuncture, known as Transcutaneous Electrical Nerve Stimulation, or TENS, has proven to be effective against such localized pain as pinched nerves and chronic muscle spasms.

Exercise also stimulates the endorphins, and it may be for this reason that sex eases some headaches, making the words "Not tonight, dear; I have a headache" a

thing of the past. According to a study of forty-six migraine patients by James R. Couch, M.D., Ph.D., chairman of neurology at Southern Illinois University School of Medicine, 17 percent said that having sex brought moderate to complete relief.

No single one of these medical developments is likely to do away with all chronic pain. But, taken together, they offer real hope for those who suffer from it. While doctors once relied on morphine at one extreme, aspirin at the other and very little in between, they now have a full array of medications and techniques with which to treat pain. It has become standard practice, for example, for a hospital's pain clinic to offer such formerly esoteric treatments as acupuncture, hypnosis and biofeedback, and many are adding the new morphine delivery systems, TENS and other pain-alleviating techniques as well. With these innovations and most doctors' new commitment to reducing suffering, patients are more likely than ever before to find lasting relief from the misery of chronic pain. □

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