peace of mind

Contrary to what friends, colleagues, and even some doctors think, the debilitating nature of migraines isn't just in your head. Now a new generation of drugs works before the pain starts. Will it banish headaches forever? Daryl Chen reports. Photographed by Irving Penn.

Janice Levy is the rare kind of person you'd be happy to sit next to on a plane. A vivacious professor in her 40s, she chairs the photography department at a college in upstate New York. She teaches classes and frequently exhibits her work, one of her most recent collections consisting of striking portraits of people in Madagascar paired with proverbs from Malagasy village elders. She talks fast, listens closely, and laughs often.

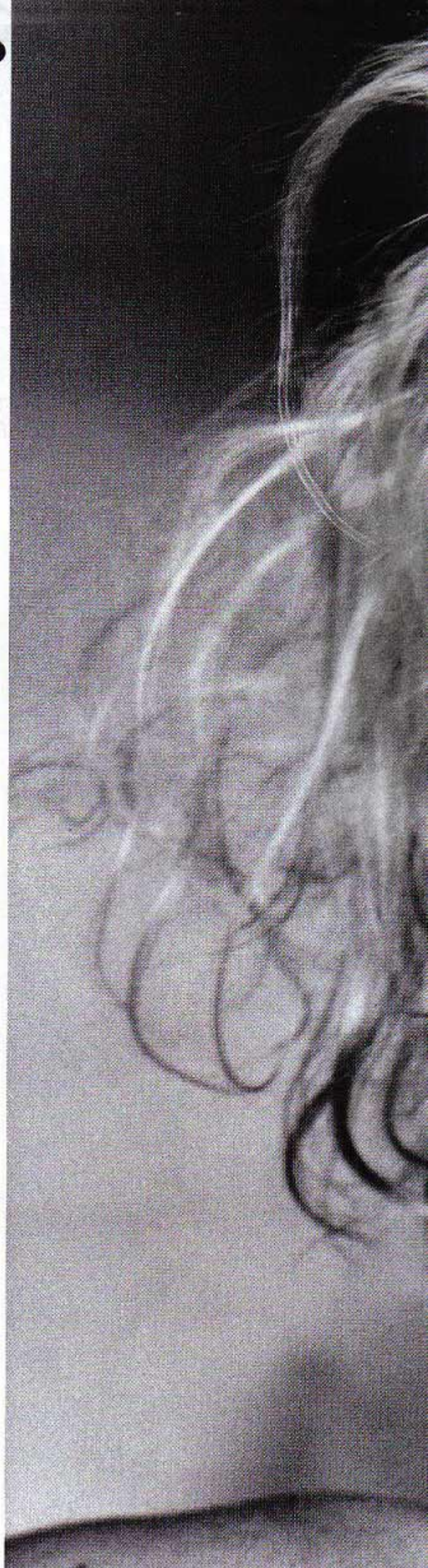
So it's almost impossible to believe that the night before, she was in the emergency room, begging the staff for relief—Toradol, Demerol, morphine—*anything* to stop the pain drilling mercilessly into her right eye. Levy suffers from migraine, a condition that affects 28 million people, 75 percent of whom are women. Anxious for a reprieve, she and her husband have driven six hours to see headache specialist Alexander Mauskop, M.D., at his Upper East Side clinic.

Mauskop starts by posing questions to her in his calming,

DAMSEL IN DISTRESS

Seventy-five percent of migraine sufferers are women. Hair, Oribe at Oribeagency.com; makeup, Peter Phillips. Details, see In This Issue.

Sittings Editor: Phyllis Posnick.



Russian-accented English. He's careful not to interrupt; Levy has much to say. She has four decades' worth of headache stories to tell him—the scores of drugs that promised improvement only to fail to deliver; the three visits to the ER in the last three months; the medical leave from her job last year. "I'm really at my wits' end," she says to the neurologist at one point. "I'm being robbed of my life."

Fifteen years ago, Mauskop would have just been able to prescribe pills that work by essentially knocking users out. But today Levy has reason to be hopeful, because today a new generation of treatments—from disciplines as varied as dermatology, cardiology, and psychiatry—is not only soothing migraine pain but preventing it before it strikes.

Why has this shift in thinking about headaches taken so long? Part of the problem is that people who have never experienced migraines have no concept of how badly sufferers need help. The medical definition of a migraine is a one-sided headache with pulsing pain, of moderate to extreme intensity, accompanied by heightened sensitivity to light and sound and, frequently, nausea and vomiting. The human definition is something close to hell on earth. As Levy and her fellow sufferers insist, a migraine is nothing like a bad headache. The pain is constant and omnipotent. In 2000, the World Health Organization characterized severe migraine as a disease that's as disabling as quadriplegia, dementia, or psychosis. "That no one dies of migraine seems, to someone deep into an attack, an ambiguous blessing," wrote Joan Didion in her 1968 essay "In Bed."

Even doctors, often in specialties outside neurology, have been known to tell migraine sufferers, "Get over it." Levy's own mother failed to realize how bad her daughter had it until recently. "I was throwing up, screaming in pain, hitting my head against the wall, then trying to run cold water on it," remembers Levy. "She thought I was having an aneurysm. She was completely horrified. The next morning she was all shook up and said, 'I owe you an apology. All those years that you said you had a headache, I never quite believed you.' "

Such attitudes drive many migraine sufferers (or migraineurs) to be in denial themselves. An estimated 31 percent have never seen a doctor about their condition, and 49 percent don't use a prescription drug—either because they don't realize help exists or because they are convinced by others that maybe it *is* their imagination.

Levy knows better, however. She has the dubious distinction of belonging to the small percentage of migraineurs who have headaches fifteen or more days per month. When they appear, her zest for life dissolves into depression and anger. In the throes of an attack, she paces the floor, her body hurting too much to rest on a surface. Her migraines have driven her to reschedule classes, rearrange department meetings, cancel plans with friends. They have strained romantic relationships (although happily she is now a newlywed, having met a man who had dated a woman with the condition in the past). As a result, she has blazed through a myriad of prescription drugs, some of which brought miraculous relief for a few golden months, but all of which inexplicably stopped working. The solution she's settled on is an unsatisfactory combination of willpower, narcotics, antinausea suppositories, and ER visits.

After taking in her story, Mauskop suggests Botox. Ironically, just as antiaging specialists are discovering the possible negative cosmetic effects of the injection (see "Botox Backlash," Beauty, page 211), neurologists are beginning to appreciate the drug for its powerful ability to subdue the muscular spasms exacerbating migraines. In small studies, Mauskop says, more than 70 percent of the subjects have reported fewer days marred by headaches. Botox is still undergoing clinical trials as a headache treatment, and it's still not covered by many insurance plans, but anecdotal testimonies have been so positive that doctors are using the injections off-label.

Levy is eager to try it—"I could definitely use some help with my wrinkles," she jokes—and hops up onto the examining table. The doctor takes a tiny needle and injects her 20 times: over her nose, over each eye, in her temples, in her scalp, above her ears, and at the base of her neck. He uses one vial of Botox—four to five times the amount injected by dermatologists for frown lines. The shots are shallow, and tiny bubbles of the medication can be seen bulging under her skin but disappear within seconds. She'll notice improvement in two weeks, and a treatment lasts for twelve. Levy can't wait. "I'm so desperate right now," she says as she leaves the office.

> Treating a migraine only after it strikes is like treating cardiovascular disease post–heart attack—it makes more sense to stop it before it happens at all

The prospect of banishing migraines completely comes not a moment too soon. With brain-imaging techniques, doctors have discovered that severe headaches affect not only the activity of the brain but also its structure. Treating a migraine only after it strikes is almost like treating cardiovascular disease post–heart attack—it makes much more sense to take measures to stop it before it happens in the first place. "We believe that migraine is a disorder of the hyperexcitable brain," says neurologist Stephen D. Silberstein, M.D., director of the Jefferson Headache Center at Thomas Jefferson University in Philadelphia, and president-elect of the American Headache Society. Women are thought to suffer from it so much more than men because of fluctuations in estrogen. Countless triggers—among them red wine, changes in the weather, chocolate, too little sleep, flashing lights—seem to stimulate what's called the trigeminal nerve, causing the sensation of pain to be conveyed across the face, over the eyes,

and into the brain. Neurotransmitters are released, making blood vessels dilate. The engorged blood vessels then press against the endings of other nerves, amplifying the pain. Silberstein compares the effect to having hives in the lining of the brain.

In 1993, triptans were introduced—a class of fast-acting drugs such as Imitrex, which, when taken at the onset of a headache, affect the trigeminal nerve and intercept those painful messages. "Everybody thought they were the answer," says Silberstein, who, like Mauskop, is a pioneer in preventive migraine research. "They're wonderful drugs, but there are still many patients that have very frequent headaches."

Only in the past few years have neurologists begun to see migraine not as an episodic illness like PMS but as a chronic, progressive disorder. They've noticed a significant and troubling subset of sufferers who start out experiencing a few headaches a month but, like Levy, shift over time to having a few every week. As the latest research suggests, pain seems to beget more pain. "The more frequently you have attacks, the more frequent your attacks get," says Richard Lipton, M.D., professor of neurology at the Albert Einstein College of Medicine in New York City. Worse, doctors have noticed that at a certain point, lesions begin to emerge in the brain, which might make patients even more vulnerable to further progression of the disease.

"A lot of people are getting good relief from a triptan, and they're saying, 'This is fine. I can carry this with me and use it when I need it,' " says Andrew M. Blumenfeld, M.D., chief neurologist of Kaiser Permanente San Diego. "But what the recent data are starting to point to is this may be a foolish approach. They may be putting themselves at risk down the line to do worse." He and other neurologists are urging patients who have headaches three or more days a month to start taking preventive medications.

Still, whether these drugs are as effective as they seem—and whether they're right for everyone—remains hotly debated. In 1996, the Food and Drug Administration approved the epilepsy treatment Depakote to prevent migraines, but Levy has shied away from it because of side effects that include weight gain, hair loss, drowsiness, and liver failure. Other preventive options used off-label by physicians are the antidepressant Elavil and a clutch of beta-blockers, which were created to lower blood pressure. Since September 2002, Janice has taken topiramate, another epilepsy drug and one of the most promising migraine prophylactics to be used thus far. In a recent clinical trial, 46 to 48 percent of participants given the drug at the therapeutic dose showed a decrease in headache days and a reduction in use of acute remedies like triptans, according to a *Journal of the American Medical Association* report published in February.

For the first two months, Levy experienced two common side effects: nausea and memory problems (some call the drug "Stupimax," a play on Topamax, the brand name of topiramate). Regardless, she says, "it was a miracle drug." To her shock, she was free of any head pain for six to eight months. Shortly after her August wedding, however, her migraines came roaring back. "It's been the worst headache period in my life," she says. Will Botox work?

"Headache clinics end up with the most difficult cases. Overall, though, 90 percent of patients can be helped"

I check in with Janice one week after her visit to the headache clinic. She is in a foul mood. She called Mauskop to say that the Botox wasn't working. He told her that she needed to give it another week. That night, she woke up at 1:00 A.M. with an excruciating migraine, popped a sample of Relpax, a triptan he had given her, and walked around her house for a few hours until the pain receded to a dull ache. Mauskop is not ready to give up, however. "Headache clinics end up with the most difficult cases," he says. "Overall, though, 90 percent of patients can be helped."

He points to the case of Cathy Engdahl, a straight-talking New Yorker who works for a brokerage firm and is also in her 40s. She has had migraines since she was a teenager. They were so bad that before seeing Mauskop for the first time back in November 2002, she had been in the emergency room, vomiting and dizzy with pain, eleven times in one year.

Mauskop weaned her off all drugs and told her to cut out caffeine. He had her go for biofeedback sessions to learn to relax her body and put her on supplements of magnesium and feverfew. Nothing worked. So about five months later, he injected Botox. Exhausted by years of suffering, Engdahl hoped for a slight improvement at most—but the results stunned her: "I didn't get another headache until the middle of May," she says proudly. And unlike her previous migraines, that incident was easily quelled by medication. She's had three more Botox treatments since then over the course of nine months, and zero headaches. "I'm thrilled," she says. "I would drink that stuff if they'd let me."

As more physicians in all specialties begin to realize how crippling migraines can be, perhaps more solutions will emerge from outside the confines of conventional neurology—and more patients will share Engdahl's experience. After all, dermatologists discovered Botox's efficacy against migraines when their patients reported fewer headaches along with fewer wrinkles. Researchers are experimenting with other new preventive drugs besides Botox and topiramate, as well as trying to identify the risk factors that exacerbate migraines. So far, obesity and excessive caffeine intake seem to be culprits in the chronic worsening of the disease. Like polio and scarlet fever, migraine might someday soon become a disease of the past. What would a world rid of head pain be like? Calmer, happier, more creative? Levy cannot wait to find out.

Almost two weeks after her appointment with Mauskop, Levy says, "I feel really good. I feel energized." She hasn't had a migraine in five days. Since she recently upped her dosage of topiramate, she's unsure whether it's the pills, the Botox, or a combination of the two that is responsible for her improvement. "Will I get a headache next week?" she wonders. "That will be the real test." For now, though, she has her life back, and that's all that matters. □