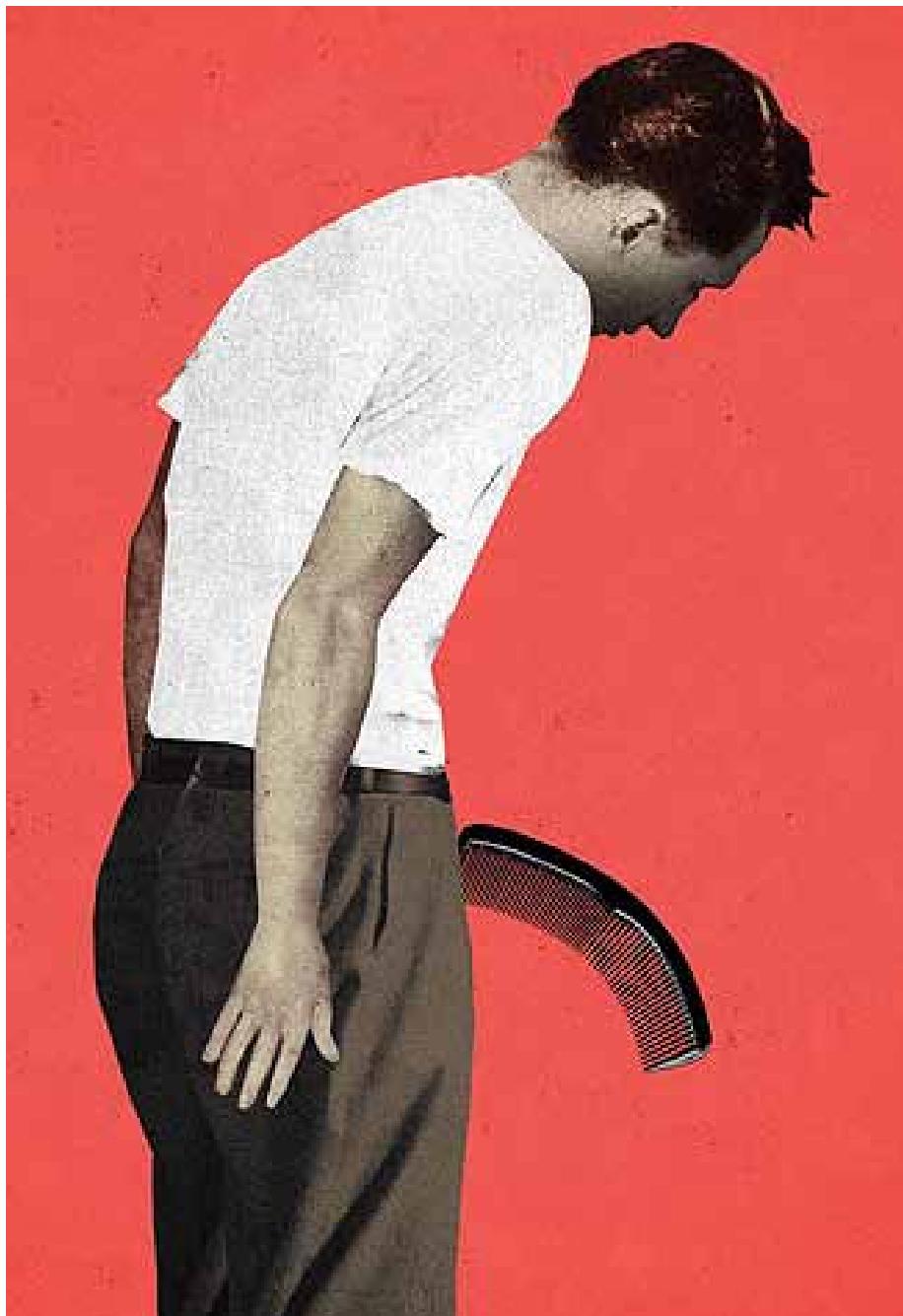


A Hair-Raising Side Effect

It's a common baldness remedy, but its side effects may be more than you—or your girlfriend—can handle

BY JIM THORNTON • ILLUSTRATIONS BY BRIAN STAUFFER



I

F YOU'RE A BIG TEN SPORTS FAN, you've probably seen Charles K. moving up and down the Big House field during Michigan home games. The now 31-year-old didn't play football—he played sax in the Wolverine marching band. Early on, Charles was a "shy band nerd," but over the course of his college career he morphed into another kind of player. "By my senior year," he concedes, "I'd earned something of a reputation among my friends for dating multiple girls at once."

After graduating and moving to Chicago, Charles planned on playing the field for at least a few more years. But then something happened that he hadn't counted on: His hair started falling out. "I panicked," he recalls. "Here I was, a single guy just starting life in the big city, and I was going bald. I kept thinking, *If I lose my hair, what chance will I ever have with the ladies?*"

Charles decided to start taking Propecia, the only FDA-approved oral medication for male-pattern baldness. For the next 6 years he tolerated the drug fairly well. But he noticed one odd side effect: a random, intermittent decline in his sex drive. "I'd be with a sexy woman, and there was just no interest at all on my part," he recalls. "If anything, it was almost like I felt mild repulsion." Over time, these unpredictable episodes became less frequent, and he convinced himself that they'd just been some weird hormonal glitch.

By 2009 Charles was in a secure, loving relationship. At this point, his fear of baldness had lost much of its hold on his self-confidence, so he decided to quit Propecia.

For the first few weeks he felt fine. Then, without warning, his libido suddenly vanished; it was almost as if a switch had been thrown. At the same time, he lost all pleasurable sensations in his penis. This one-two punch made achieving and sustaining an erection nearly impossible for him. Trying to stem his panic, he told himself these were just withdrawal symptoms from Propecia, that he'd soon go back to normal.

Only he didn't.

"After a month," Charles says, "I began my long struggle to find out what the hell was going on."

IMAGINE A PILL THAT PROMISES TO SAVE A crowning aspect of a man's youth, something otherwise fated to wither away with each passing year. Imagine, too, that according to the drug's manufacturer, only one man in 50 suffers significant sexual side effects from treatment—and even those side effects lessen with time.

A modest risk, in other words, offered great potential gain: a clear win-win for patients and the drugmaker, right?

Such is the picture that pharmaceutical giant Merck & Co. has long sought to paint for its blockbuster baldness medication Propecia, also known by the generic name finasteride. The male-pattern baldness that Propecia treats is caused when dihydrotestosterone, or DHT—a potent hormone related to testosterone—shuts down genetically vulnerable hair follicles. Thanks to the luck of the DNA lottery, half of all men are destined to turn into bulletheads and/or Friar Tucks with advancing years.

Of course, such pharmaceutical miracles don't come cheap. Brand-name Propecia costs upwards of \$2 a dose; patients must take it daily for as long as they want hair, and most insurance companies won't foot the bill. And yet Propecia still managed to rake in *\$447 million* for Merck in 2010. Clearly, balding men are willing to pay a lot to save their pates.

The question is, what other price could they end up paying?

Researchers have known for some time that finasteride induces "sexual adverse events" in a statistically significant minority of men who take it. Consider one study published back in 2003 in the journal *Urology*. The researchers followed 3,040 men ranging in age from 45 to 78, all of whom suffered from prostate enlargement—another condition finasteride is approved to treat. In the study's first year, 15 percent of the men on finasteride suffered new sexual side effects, compared with only 7 percent of the men on placebos.

"There were real, ill effects from the drug," recalls lead investigator Hunter Wessells, M.D., chairman of the department of urology at the University of Washington school of medicine. "In some men, finasteride caused erectile dysfunction; in others it decreased ejaculate volume; and in others it reduced libido."

For most of the men, the finasteride-induced sexual problems proved tolerable. But for as many as 4 percent of them, the side effects were severe enough that they dropped out of the study altogether.

Merck, for its part, has long urged patients to stick with treatment, arguing that finasteride's rare side effects, when they do occur, generally lessen over time. If there's no improvement, then the company says to go ahead and quit taking the drug. In theory, everything—hair density included—will eventually revert to its pretreatment baseline.

But is that really true? Among the study dropouts, says Dr. Wessells, only half had seen full resolution of their symptoms 6 months after going off the pills. "It was always one of the strange things about that study," he says, "as to why these men didn't get better."

As more and more cases began surfacing of men who'd quit finasteride only to suffer severe and persistent sexual problems afterward, researchers at George Washington University and the Greater Baltimore Medical Center decided to survey a group of those self-

just need to relieve pent-up pressure down there, he clicked on some porn and began a routine familiar to nearly every young man on the planet.

But for Mark, there was nothing routine about it this time. Videos that had never failed to turn him on now brought no sense of mental excitement. His penis and scrotum, too, felt strangely numb, as if the nerves were no longer signaling correctly. With no pleasure upstairs or down, achieving an erection proved to be an ordeal. When he finally limped his way

After quitting the drug, one man said he felt like an "asexual zombie."

reported victims of what was being called "post-finasteride syndrome," or PFS.

The investigators recruited a total of 92 men from medical practices and PFS-support websites, and by word of mouth. A board-certified endocrinologist then conducted a standardized interview with each man, ultimately excluding 21 candidates because of pre-existing medical or psychological conditions or the use of other medications, or because their symptoms weren't severe enough.

This left 71 men who'd been deemed completely healthy—physically, sexually, and psychologically—until they took finasteride. For most of the men, the symptoms first appeared while they were on the drug. But for some, it was only after they stopped taking it that their sexual health plummeted.

The researchers acknowledge that their study, which was published earlier this year in the *Journal of Sexual Medicine*, does not conclusively prove that finasteride is the cause of the men's problems. But it certainly bolsters reason for suspicion.

"Before our study, the published research indicated these were largely reversible side effects," says lead researcher Michael Irwig, M.D., an endocrinologist at George Washington University. But in this select population, over 90 percent were suffering from low sexual desire, erectile dysfunction, and decreased arousal—this after being finasteride-free for 40 months on average. One man had still not improved *11 years* after taking his final pill.

"It's a real irony," says Dr. Irwig. "Men took finasteride to stop or prevent hair loss and sometimes to improve their dating lives. And it actually ended up destroying their sexuality and self-esteem."

IN NOVEMBER 2004, MARK J., A 25-YEAR-OLD financial services rep from the Pacific Northwest, had finally lost all patience with the pain in his groin. For 3 days straight his right testicle had ached, punctuated by sharp stabs radiating up from his prostate. Figuring he might

to climax, he produced only a fraction of his typical ejaculate volume.

Nothing even remotely like this had ever happened to him before, but Mark thought he knew what might be going on: Three days earlier he'd taken his first dose of Proscar. This is the brand of finasteride prescribed for prostate enlargement that at the time was also used by doctors as a less expensive substitute for Propecia. Mark had hoped that the drug would be an antidote for the male-pattern baldness that ran on both sides of his family.

"My dermatologist was very happy-go-lucky about prescribing it," Mark recalls. "He told me lots of guys take it, that there hadn't been any issues with the medication, and that if I wanted, he'd prescribe it, no problem. It was almost like handing out candy for him."

Three days later, barely able to ejaculate, Mark wondered if he should quit right then and there. "Instead, I rationalized the symptoms away as a normal adjustment to the drug," he says of the decision that now haunts him years later. At the time, he took solace from the label insert that came with his prescription. The fine print claimed that sexual side effects usually abate over time and disappear entirely in men who stop the drug.

More than anything else, it was this second promise that convinced Mark to stay the course. As collateral damage to his body and psyche mounted, he reassured himself that he could always hit the reset button and resume his pre-finasteride life. It never occurred to him that he might not have a reset button.

On October 1, 2005, after 11 months of continuous daily use, Mark threw away his last pill, unable to tolerate the increasingly severe side effects that he says had begun to include panic attacks and depression. To his relief, within 12 days he began feeling like his old self. "All of a sudden," he says, "I could get it up, no problem. I felt alive again—aggressive, horny, full of drive, and ready to take on the world."

It didn't last. Five days later, he suffered what some doctors have come to describe as

an "endocrine system crash." Old symptoms returned and were more severe than ever, accompanied by strange new ones: hot flashes, extreme fatigue, and visible changes to the structure of his penis and scrotum, both of which literally began shrinking overnight.

His libido vanished entirely. "Forget the fact that I wasn't very horny anymore," he says. "Now there was just no urge for sex whatsoever. I could be with the hottest girl on the planet and nothing would happen, either down there or in my head. It was as if my brain could no longer respond to anything erotic—visual or through touch."

Desperate for explanations, he stumbled upon an online discussion forum for men reporting "persistent" side effects after quitting finasteride. Mark couldn't believe what he was reading: Hundreds of young men who had, like him, taken a pill to stave off baldness were reporting the same horrific symptoms that now afflicted him. The site acknowledged that these side effects usually resolved within days or weeks, but for some unfortunate men, there'd been no improvement months or even years after their last pill.

"My worst nightmare," says Mark, "was staring back at me from the computer screen."

OVER A DOZEN PFS PATIENTS CONTACTED

by *Men's Health* revealed remarkably similar symptoms to the ones described by Mark J. and Charles K. One man reported that since using and then quitting finasteride, he has been wandering through life in a state of constant "brain fog." Yet another views himself as an "asexual zombie."

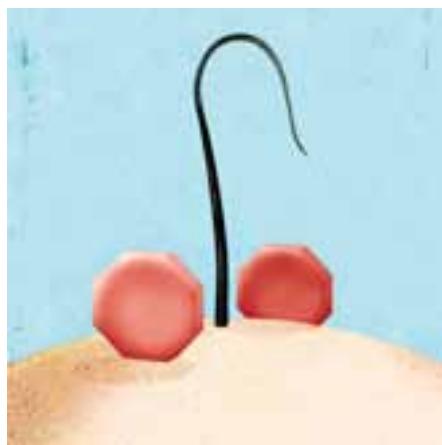
Currently, no one knows for sure how many potential victims exist. One popular online support group for the condition, Propeciahelp.com, claims to have over 2,000 members who regularly visit for updates on a disorder they're convinced they share.

"This probably represents just the tip of the PFS iceberg," says Dr. Irwig. Finasteride, he explains, has become such a popular drug worldwide that even if only a tiny percentage of men who take it are affected, the number of victims could be enormous.

Many of the current victims agree, convinced that legions of fellow sufferers are out there, probably fruitlessly chasing the wrong causes for what ails them.

Charles ran into his own diagnostic dead ends, first with his family doctor and then later with a holistic specialist. He eventually heard about Irwin Goldstein, M.D., one of the nation's premier experts on male sexual function. While visiting friends in San Diego, Charles made an appointment with Dr. Goldstein, who heads the sexual medicine program at Alvarado Hospital.

Charles recalls Dr. Goldstein's pronouncement: "He told me, 'I hate to say this, but it looks like you have what we're calling post-



IS THERE (SEX) LIFE AFTER PROPECIA?

What to do if your hair comes back but now your mojo is MIA

Let's say you're a current or former Propecia user and your erections suddenly stop reporting for duty. Before you blame the pills, see a doctor who treats hypogonadism, a.k.a. clinically low testosterone levels. "Lots of things can cause hypogonadism," says Alan Jacobs, M.D., a New York City-based neuroendocrinologist who specializes in helping men with PFS. "For instance, one man had a pituitary tumor, and when we treated this, his problem went away completely."

The first thing Dr. Jacobs checks is bioavailable testosterone, the form your body can use immediately. "Having low levels of bioavailable T correlates much more strongly with impaired sexuality in men than just low total testosterone," he explains. Next he measures LH (luteinizing hormone), FSH (follicle-stimulating hormone), and estradiol (a potent form of estrogen), each of which plays a key role in the hormonal symphony of sex. If the tests rule out other possible culprits, consider stopping Propecia entirely if you haven't already. Still no improvement? Doctors have reported success with testosterone-replacement therapy—sometimes with a second drug (like Arimidex) added to reduce estrogen levels, or Clomid, which bumps up LH and FSH. —J.T.

finasteride syndrome.' He explained that nobody knows how going off finasteride causes the endocrine system to crash, and that it will probably take researchers a couple of years to figure it out."

What Dr. Goldstein and his colleagues do know with some certainty is that testosterone is a big part of solving the PFS puzzle.

Testosterone is a critical hormone responsible for a wide range of the drives, emotions, and behaviors that make men, well, *men*. It can also be turbocharged into DHT—the more potent form that can cause male-pattern baldness. The conversion of T to DHT, in the body and brain alike, occurs courtesy of a special enzyme known as 5-alpha reductase. Finasteride works

by putting the kibosh on this enzyme, in effect slashing some 70 percent of the DHT that would normally be produced.

To further complicate matters, 5-alpha reductase comes in various subtypes, each specializing in making DHT in different body tissues. More detailed explanation at this point requires a degree in biochemistry and a case of Red Bull. Suffice it to say that finasteride works its magic primarily, though not exclusively, on the 5-alpha reductase in two areas: the prostate and the hair follicles. Outside these locations, Merck has long contended, the drug's effects are clinically insignificant. The FDA agreed, awarding Merck approval to market finasteride as Proscar for an enlarged prostate in 1992 and as Propecia for male-pattern baldness in 1997.

But in the years since its debut, finasteride's reputation as a laser-focused med has taken some hits. Not all investigators have been willing to accept Merck's word that the drug's effects are so cleanly confined.

In a 2011 study review in the *Journal of Sexual Medicine*, lead researcher Abdulkhaled Traish, Ph.D., and his colleagues outlined extensive cause for concern. They concluded that animal and human studies strongly suggest that finasteride isn't limited to its target tissues but in fact can reduce DHT in many tissues, potentially affecting not only nerve-signaling pathways in the penis but also the ratio of male-to-female hormone levels circulating through a user's body. One study Traish cites found that men taking 1 milligram of finasteride daily had significantly higher levels of estradiol—the predominant female sex hormone—than men taking a placebo.

Just as worrisome as the possible effects in body tissue is the growing evidence that finasteride can enter a man's brain and disrupt key chemicals therein. As Traish's study review details, once finasteride reaches brain tissue it affects the production of more hormones than just DHT. At particular risk, Traish believes, are neurosteroids—brain chemicals that play a role in reducing anxiety, enhancing memory, regrowing brain cells, and helping us sleep.

There's yet another issue for men who already find themselves battling feelings of despair over their dissipated sex lives: At least two studies have shown that finasteride may cause the onset of depressive symptoms. And last year, researchers in Germany found that the drug inhibits the growth of new neurons in the brain's hippocampus; this type of neurological "failure to thrive" has also been documented in people who suffer from clinical depression.

"The percentage of affected men may be small," acknowledges Traish, a researcher in the biochemistry and urology departments at Boston University's school of medicine, "but our research definitely concludes that PFS is real. For a subset of these men, the damage

persists—maybe forever—even after they go off the drug. We don't fully understand why, but it is as if something shuts off biologically, and stays that way."

OUTSIDE THE U.S. MARKET, THE POSSIBILITY

of PFS has been taken seriously for several years. In 2008, for instance, Swedish authorities compelled Merck to adjust Propecia's official prescribing label to include patient reports of "persistent erectile dysfunction" after stopping the drug. Italy and the United Kingdom soon followed suit, requiring similar language as a condition of further marketing of the drug within their borders.

In recent years, the FDA has required Merck to add several new "adverse event" reports to the postmarketing section of Propecia's official label. These include male breast cancer as well as depression. One large study found that breast cancer, while still exceedingly rare in men, was nearly 200 times more common in men taking finasteride than in the general male population. While still not conceding that finasteride can cause either condition, Merck nevertheless agreed to at least report that some users have experienced those effects while on the drug.

Unlike in European countries, however, one adverse-event report had long been conspicuously absent in the U.S. and Canadian markets: persistent sexual side effects after discontinuing the drug. To many PFS sufferers, the refusal to even acknowledge this hallmark symptom of their condition has long been infuriating. If consumers in Sweden, Italy, and England are given this information, why should patients and doctors alike in the United States and Canada be kept in the dark?

To the surprise of virtually no one, anger over Merck's actions has bubbled its way into the legal system. At least two class-action lawsuits—one in the United States and one in Canada—have been filed on behalf of PFS patients seeking damages for the harm they say Propecia has caused them.

"We are aware of the lawsuits," Merck spokesman Ron Rogers said last March, "and we intend to vigorously defend against them."

Despite repeated questioning by *Men's Health* during the reporting of this story, Merck officials declined to explain the inconsistencies between the drug's international and domestic labels. For whatever reason, the company would not concede to U.S. consumers any association between Propecia and persistent harm to a man's sexual health.

But then, on April 19, 2011—in the wake of the new research, publicity about class-action lawsuits in the United States and Canada, and this magazine's continued requests for additional information—Merck suddenly reversed course, officially updating the label to include "reports of erectile dysfunction that continued after discontinuation of Propecia."

In an e-mail to *Men's Health*, spokesman Rogers explained that the company did this proactively and not because the FDA had required it. "Merck made this change by submission to the FDA through a process which, in certain circumstances, allows Merck to change the label without prior approval from the FDA. With this change, the U.S. and EU labels for Propecia are harmonized."

To date, the drugmaker continues to contend that no "causal relationship" has been established between Propecia exposure and persistent ED, and that no one—neither the

company or anyone else—can reliably estimate how many men may be affected.

No matter how heavily couched in uncertainty the label remains, some PFS sufferers say they're glad for any official acknowledgement and that they are at last being heard. Charles K., for his part, hopes anybody contemplating Propecia treatment now will read the package insert—especially the information he never had the opportunity to see.

After Charles was diagnosed with PFS, Dr. Goldstein was able to restore his hormone levels back to about normal. But while some of the sex drive and sensation he'd lost has returned, Charles isn't hopeful that he'll ever feel like his pre-finasteride self.

"If anyone had warned me that there was even a small chance of permanent side effects from this drug, there's no way I would have taken it," he says. "I wish I could just take the time machine back."

As for Mark J., he hopes this will prove to be the beginning, not the end, of Merck's involvement in unraveling the mystery of PFS. Six years after his final pill, he no longer endures bouts of anxiety or depression, but many of his other symptoms persist.

Among other problems, Mark still suffers from a lack of nocturnal erections, genital numbness, and dulled orgasm. His libido has flatlined altogether, along with his zest for life. His once-defined musculature has given way to breast enlargement, atrophied arms, and female-pattern fat distribution in his hips—"this," he says, "despite keeping the same diet and exercise levels I had before ever taking the drug." He has recently joined a class-action suit—not for personal gain, he says, but in the hope that continuing pressure will convince Merck to fund further research into PFS.

"Money is not a factor for me and never has been," Mark says. "The scientific community holds the key to unlocking the cause of these persistent side effects." He believes that the company whose product has caused so much hurt needs to step up now and fund the search for solutions.

In fairness to Merck, PFS remains a controversial diagnosis. Skeptics argue that all sorts of other possibilities, from aging to psychosomatic illness, are just as likely to be culprits behind these men's ongoing suffering. At this point, even those researchers most convinced of finasteride's dark side aren't calling for its removal from the market.

"What we do want," says Dr. Irwig, "is for patients and doctors alike to understand the potential risk of persistent problems that may not, in fact, be reversible when you stop this drug. Even if there's only one chance in 300 that it could happen to you, it's like playing with fire. If you're one of the 299 who don't have problems, that's great. But if you're the one who does, you're going to be kicking yourself for ever taking this medicine." ■

THE OTHER BALM FOR BALDNESS

How to make the most of minoxidil

For balding guys who are gun-shy about Propecia, it makes sense to try the topical treatment minoxidil first. The problem is that minoxidil (brand name Rogaine) is only somewhat effective—unless you give it a boost. Paul J. McAndrews, M.D., a hair-restoration specialist based in Los Angeles, has found that the following strategies can maximize the power of minoxidil, though clinical trials are still needed. "Do I think these approaches can work? Yes," he says. "But I tell my patients we don't have proof yet, and I let them decide whether they want to try them."

INCREASE THE DOSE

Over-the-counter minoxidil comes in a regular 2 percent formulation and a more effective 5 percent "extra strength" version. But what about a still higher dose? It can be even better, says Dr. McAndrews. Pharmacists are able to mix minoxidil at strengths of 12 percent or higher, though you'll need a prescription.

ADD TRETINOIN

There's some evidence that this topical form of vitamin A increases minoxidil's penetration into the scalp, says Dr. McAndrews. It may also decrease the conversion of T into DHT, the hormone that tells your follicles to produce peach fuzz instead of robust hairs. You'll need a script for the combined drug.

SKIP THE FOAM

The first preparations of minoxidil contained propylene glycol, which not only caused dermatitis and dandruff in many users but also left their hair feeling greasy and flat. A more tolerable foam form soon followed, though no one knows if it's as effective. If the foam isn't cutting it, give the original a try.

SCRUB YOUR SCALP

Try a dandruff shampoo containing ketoconazole. A small Belgian study found that ketoconazole can slightly thicken hair, presumably by blocking androgen receptors within hair follicles. "Maybe it will help, but I don't know for sure," says Dr. McAndrews. "I do use it myself, though. It's my witchcraft medicine." —J.T.