Patched Up

Medicated skin patches are now available for Parkinson's, pain, ADHD, and Alzheimer's.

BY DAN HURLEY

With the approval in July of the first skin patch to treat Alzheimer's disease, the growing number of patches to treat neurological conditions is leading patients and families to wonder: What are the benefits and what are the risks?

Since the first skin patch for delivering a drug into the body went on sale 27 years ago, the options for taking your medicine without the hassle of remembering to pop a pill have expanded to include motion sickness, attention deficit hyperactivity disorder (ADHD), a variety of painful conditions, and Parkinson's disease. If research now underway pans out, a patch to treat migraine headaches could be around the corner, and another to prevent Alzheimer's altogether by delivering a vaccine against the memory-robbing disease could be down the road.

Not all patches are created equal. The lidocaine patch for pain caused by shingles works only in the immediate area of the patch, in the same way that a dentist's injection of novocaine numbs just the part of the mouth being worked on. Transdermal patches, on the other hand, use the skin as a route into the bloodstream, delivering a drug to the entire body.

Even when used correctly, patches can cause a rash, and when misused, they have led to patients' deaths. But they also offer benefits that sometimes cannot be matched by either a pill or an injection.

ROTIGOTINE FOR PARKINSON'S

The primary benefit of the patch containing rotigotine (Neupro) for Parkinson's disease, which was approved in May of this year, is the convenience of applying it once a day, versus the pills already on the market that need to be taken three times a day, says J. Eric Ahlskog, Ph.D., M.D., professor of neurology and chair of the movement disorders section at the Mayo Medical School in Rochester, MN.

Like pramipexole (Mirapex) and ropinirole (Requip), the drug in the new patch increases brain dopamine function and improves the slow movements of Parkinson's. "Patients with mild disease may prefer a once-daily patch to a pill three times daily," Dr. Ahlskog says. Increasing the dose of rotigotine with the patch might also prove easier than increasing the dose of the two pills already on the market, he adds.

But the same nausea and sleepiness that can be caused by the pills can also be caused by the patch, he points out. Skin reactions to the patch, usually mild, have been reported in up to half of patients using it. And once symptoms become moderate to severe, most patients will need to begin taking the drugs carbidopa and levodopa to maintain their usual activity level.

ADHD AGENT

The Daytrana patch for ADHD contains the same stimulant, methylphenidate, as in Ritalin. A U.S. Food and Drug Administration (FDA) scientist initially recommended against approving the patch out of concern that it increased the risk of unwanted side effects, such as insomnia, anorexia, and weight loss. But after that scientist reversed his opinion, the agency approved the patch in April of 2006.

Still, parents should be cautious in considering the patch for their children, says Andrew Adesman, M.D., director of the ADHD Center in the Department of Pediatrics at Schneider Children's Hospital in New York.

One drawback: the patch takes about two hours to become effective, compared to the usual 90 minutes for pills. Also, "About 60 percent of children using it will develop a rash," Dr. Adesman says. "Often it's mild, but other times it's not." The biggest worry is that caregivers might fail to remove it after the prescribed nine hours. Sometimes the parents forget, and sometimes the child isn't at home when the patch is supposed to be removed.

The patch does have advantages. Some children refuse to take pills—or even the tiny sprinkles now available for many ADHD drugs. More importantly, "The patch offers flexibility in decid-

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ing how long you want the drug to be active," says Dr. Adesman. Adults with ADHD might find this flexibility attractive. "With a pill, once you take it, it's going to last the rest of the day. But you can take the patch off after six hours if you want. That's something we haven't previously had," Dr. Adesman notes.

> The options for taking medication without **popping a pill** have expanded.

LIDOCAINE FOR SHINGLES

The pain associated with shingles has sometimes been described as worse than the pain of delivering a baby. But according to Richard M. Dubinksy, M.D., a neurologist at the University of Kansas Medical Center, transdermal lidocaine patches bring only mild to moderate relief.

"They may best be used by patients who are not experiencing severe, incapacitating pain," he says.

Another caution is that in general, the patches should not be applied until after the blisters that first accompany shingles have subsided, says Charles E. Argoff, M.D., assistant professor of neurology at the New York University School of Medicine.

Beyond the skin irritation that they can sometimes cause, however, "The lidocaine patch is almost devoid of major side effects," says Dr. Argoff. "It's among the safest treatments you could ever offer somebody."

FULL-BODY PAIN RELIEF

Unlike the lidocaine patch, the fentanyl transdermal patches deliver the potency of narcotic pain relief to the entire body. When used properly, typically to relieve the kind of severe pain that can accompany some cancer-related or non-cancer-related conditions, it is a convenient way to deliver a steady dose of pain relief, Dr. Argoff says.

But in July of 2005, the FDA reported that 120 patients had died while taking the transdermal fentanyl patches. The deaths resulted from overdoses caused by changing the patches more frequently than every three days, as prescribed.

Dr. Argoff compares the difficulty of trying to increase the dose of the fentanyl patches with the challenge of changing speeds in a Mac truck. "A Mac truck takes a while to build up to a level speed," he says, "but once it does, it takes a long while to slow down. If you try to increase that speed too quickly, the truck can go out of control. The same thing can happen if a patient tries to increase the dose of the fentanyl patch too quickly."

Because of the potential dangers, the FDA urges patients to carefully follow label instructions and their doctors' recommendations.

ALZHEIMER'S, MIGRAINE

In July of this year, the FDA approved a patch containing rivastigmine (Exelon) for the treatment of mild to moderate dementia caused by Alzheimer's disease. The approval was based on the results of the IDEAL study, involving 1,195 patients with Alzheimer's disease given a patch containing either the drug rivastigmine or an inactive placebo. People wearing the patch with the active drug had significantly improved memory and were better able to engage in everyday activities. They had fewer side effects than previously seen in people taking the drug in pill form, and 70 percent of caregivers said they preferred the convenience of the patch over the pills.

But the drug, which has long been available as a pill, does not alter the downward trajectory of the disease. Of greater potential impact is the testing of a vaccine that would prevent Alzheimer's from developing in the first place. Scientists have long known that the protein called beta amyloid is found in the brains of people with Alzheimer's, jamming it up like chewing gum. When researchers tried injecting small amounts of beta amyloid into the bloodstream of older adults to provoke the body's immune system into developing protective antibodies against the protein, it caused an inflammatory reaction in the brains of six patients, who died. Earlier this year, researchers announced that they had tried the same approach in mice using a transdermal skin patch. They reported that the technique successfully cleared the mice's brains of any beta amyloid without producing any apparent side effects.

"Transdermal immunization with beta amyloid does not appear to trigger the toxicities associated with past immunization strategies," says Jun Tan, M.D., Ph.D., director of the Neuroimmunology Laboratory at the Institute for Research in Psychiatry at the University of South Florida College of Medicine. But with studies not even begun yet in humans, the Alzheimer's vaccine remains years away from reaching market.

On June 8, positive results were announced in a small study of a transdermal patch containing sumatriptan, the most widely used drug for treating migraine. The patch worked on average four times longer than a 6 mg injection of sumatriptan, and more than twice as long as a 50 mg tablet of the drug. But the special patch requires an electrical charge (so mild it can't be felt) to get the drug to seep through the skin, and years of testing remain before it can be considered for approval by the FDA.

Promising? Absolutely. But like everything to do with patches for neurological ailments, the devil will be in the details. NN

Dan Hurley's medical articles have appeared in the New York Times, Men's Health, *and* Psychology Today.