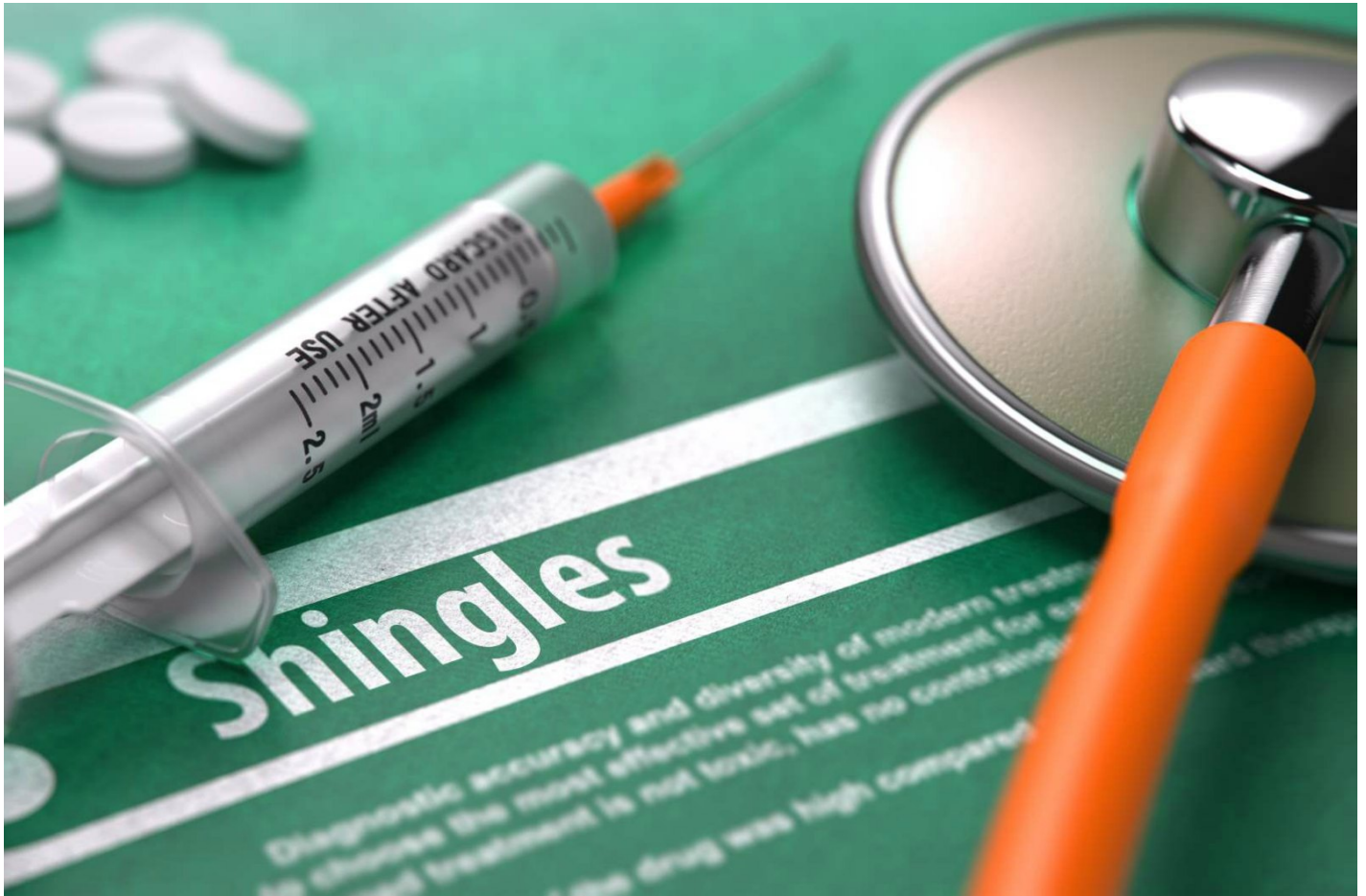


Shingles Vaccine Outwits The Suffering Of A Painful Disease

University of Colorado



Nobody who has shingles forgets the experience — an outbreak of often-painful blisters in a belt-like band on the torso or face. Worse, while the shingles itself may clear up in a matter of weeks, for 1 in 10 victims, the pain can linger for many weeks, even months, the consequence of inflamed nerves.

For some people, the effect can be incapacitating, making actions as simple as walking utterly painful and dictating lengthy confinement in bed. Some victims find their bodies so sensitive to pain that they can't stand to be touched or even to wear clothes.

The irony is that shingles is directly linked to a childhood disease most people remember as having coasted through — chicken pox. In childhood, an attack of the varicella-zoster virus usually meant a couple of weeks with spots all over the body, itching and perhaps a period of “feeling poorly.” And, probably, ice cream.

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But even though the chicken pox clears up, the varicella-zoster virus doesn't go away. It migrates from the skin up the

nerves to nestle in nerve roots, hiding in the body for decades before coming back with a vengeance.

“Even for people who breezed through chicken pox as children, shingles surfaces in as many as 1 in 3 adults who’ve had chicken pox — most of them over 60,” says infectious disease specialist Myron Levin, M.D., a professor of pediatrics and medicine at the University of Colorado Anschutz Medical Campus and the Children’s Hospital in Denver who led development of a vaccine for shingles. That vaccine, Zostavax, was licensed for sales by the U.S. Food and Drug Administration in 2006.

“Most people who’ve had chicken pox won’t get shingles, but those who do amount to about 1 million sufferers each year,” Levin says. “And for many of them, the misery far exceeds the suffering associated with ‘breezing through’ chicken pox.”

A Migrating Virus

Once the embedded varicella-zoster virus becomes active and moves back along the nerves to the skin to cause blisters, the issue is not so much itching as it is pain, burning, numbness or tingling caused by inflamed nerves.

“More importantly,” notes John Grabenstein, Ph.D., senior medical director of adult vaccines at Merck & Co. Inc., “while a shingles attack — the rash and its accompanying pain — typically lasts three to five weeks, about 10 percent of patients experience postherpetic neuralgia, the intense, chronic pain that can continue long after the blisters have disappeared.” The definition of postherpetic neuralgia is pain of significant intensity that continues at least 90 days after the rash began.

“The pain is the worst part,” Levin adds. “It’s the main reason you want to get the shingles vaccine. The vaccine reduces the prospect of intense pain tremendously.”

There are other potential consequences. Unlike chicken pox, in which the rash is scattered all over the victim’s body, the shingles rash is limited to the area of skin that one nerve is responsible for, usually in a belt-like band on one side of the face or torso (the term shingles comes from the Latin word for belt).

Shingles anywhere presents a danger of bacterial skin infection and a risk of permanent nerve damage that can make the pain resistant to treatment. But shingles on the face compounds this with risks of infections that can cause blindness, hearing and balance problems, and facial paralysis.

Like Disease, Like Vaccine

Just as shingles the disease grows out of chicken pox, the Zostavax vaccine is a legacy of the chicken pox vaccine — the Varivax vaccine — developed by a Japanese physician in the 1970s. Levin was involved in work at Colorado to test the earlier vaccine for its safety before it was approved for use in the United States in 1995.

“He was familiar with the varicella-zoster virus,” notes Rick Silva, Ph.D., director of the Technology Transfer Office at the University of Colorado. “He reasoned that a version of the childhood vaccine could be used in older people to prevent shingles.”

While there are antiviral treatments for shingles, these are imperfect and it’s far preferable to prevent the disease with Zostavax. The duration of a bout of shingles can sometimes be shortened with early antiviral therapy, but such therapy is often delayed, and shingles is difficult to treat once it is established. Painkillers like oxycodone may become necessary.

“For a long time,” Levin says, “it wasn’t clear why the virus resurfaces after so much time, and so often in people over age 60. But we pretty much know that as we age, our cellular immunity to the varicella-zoster virus — as to many other infections — wanes. The likelihood is that the virus is kept quiet by the body’s immune system, and, once the immune protection drops to a certain level, the virus is able to break out as shingles. And, the older you are when you develop shingles, the greater your chance of getting postherpetic neuralgia.”

Similarly, shingles can be a problem for younger patients whose immune systems are compromised by other diseases or treatments.

Same Vaccine, Higher Dosage

The concept for developing the new vaccine was that the chicken pox vaccine could prevent shingles in adults — but that much larger dosages would be necessary.

“The virus in the shingles vaccine is exactly the same as in the vaccine for chicken pox but it’s more potent,” Levin notes. “Our initial study involved 240 adults, focusing, in large part, on testing different amounts of virus in the vaccine.

“This wasn’t easy on the volunteers in the study,” he adds, “since the vaccine we had at the time required as many as four shots at once to give the largest dose tested.” In the end, the dosage for successful shingles vaccine was set at 14 times that of the chicken pox vaccine — in one small shot.

To that point, Levin’s research was supported by National Institutes of Health funding, but he then approached Merck, the only company licensed to produce the chicken pox vaccine for use in the United States.

The next step was a large-scale trial, and Levin proposed partnering with the Veterans Administration’s Cooperative Studies Program in a study that would involve some 38,000 men and women aged 60 or older. The Shingles Prevention Study was also supported by the National Institute of Allergy and Infectious Diseases, and by Merck, which provided the vaccine. The tests began in 1999, but the results weren’t clear until 2005.

“The bottom-line answer was that the vaccine would prevent shingles in about 50 percent of the people who received it,” Levin says. “More importantly, it would prevent or reduce chronic pain by some 67 percent among people who did get shingles.

“That’s a very significant reason to get the shot.”

Larger Benefits

Once approved, the new vaccine was licensed exclusively to Merck. The patent is held jointly by Merck and the university.

“On the individual level, this is an important vaccine,” says the University of Colorado’s Silva. “In broader terms, it holds the potential of reducing shingles-related doctor visits in the United States each year by perhaps 300,000 and hospitalizations by 10,000. That would be a savings of as much as \$100 million spent on shingles related care in the United States annually.”

Because it’s estimated that there are some 50 million people over 60 in the United States, and Merck has shipped more than 6.5 million doses, there’s still a long way to go in protecting the population.

“It’s a general phenomenon,” Grabenstein says, “that other than flu shots, adults don’t give the attention to vaccines

for themselves that they do for their kids or grandkids. They should. Shingles is a miserable illness that can be minimized, possibly prevented.

“People who’ve had chicken pox are vulnerable to shingles and should get the Zostavax vaccine when they reach the appropriate age of 60 years. It can make life better for a lot of them.”

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