Shingles: An Unwelcome Encore

Shingles (herpes zoster) has joined the ranks of vaccine-preventable diseases. In October 2006, the advisory panel to the Centers for Disease Control and Prevention voted unanimously to recommend the routine immunization of all adults aged 60 years and older (including those with a prior history of shingles) with the only licensed herpes zoster vaccine (Zostavax, Merck & Co., Inc.). The shingles vaccine is safe and effective in providing protection against shingles and associated chronic pain.

During their lifetime about 25% of people develop shingles, with the majority of cases occurring in those older than 50 years of age. In the United States, there are about one million cases of shingles per year. The complications from shingles include uncomfortable rash, eye and skin problems, scarring, nerve paralysis, pneumonia, encephalitis, and death. Excruciating pain from post-herpetic neuralgia (PHN) can last for months or years.

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In Italy, shingles also is called St. Anthony’s fire, a fitting name for a disease that has bedeviled saints and sinners throughout the ages. Caused by the same varicella-zoster virus that causes chickenpox, shingles (also called herpes zoster) most commonly occurs in older people. Treatment was once limited to wet compresses and aspirin. Today’s treatments provide a variety of ways to shorten the duration of a shingles outbreak and to control the associated pain. Sometimes, however, shingles leads to a chronic painful condition called post-herpetic neuralgia (PHN) that can be difficult to treat.

Initial Symptoms

After an attack of chickenpox, the varicella-zoster virus retreats to nerve cells in the body, where it may lie dormant for decades. But under certain conditions, usually related to aging or disease, the virus can reactivate and begin to reproduce. Once activated, the virus travels along the path of a nerve to the skin’s surface, where it causes shingles. Shingles’ symptoms may be vague and nonspecific at first. People with shingles may experience numbness, tingling, itching, or pain before the classic rash appears. In the pre-eruption stage, diagnosis may be difficult, and the pain can be so severe that it may be mistaken for pleurisy, kidney stones, gallstones, appendicitis, or even a heart attack, depending on the location of the affected nerve.

The Outbreak

Pain may come first, but when the migrating virus finally reaches the skin—usually the second to the fifth day after the first symptoms—the rash tells all. The virus infects the skin cells and creates a painful, red rash that resembles chickenpox. Doctors can distinguish shingles from chickenpox (or dermatitis or poison ivy) by the way the spots are distributed. Since shingles occurs in an area of the skin that is supplied by sensory fibers of a single nerve—called a dermatome—the rash usually appears in a well-defined band on one side of the body, typically the torso; or on one side of the face, around the nose and eyes. (Shingles’ peculiar name derives from the Latin cingulum, which means girdle or belt.) If a diagnosis is in doubt, lab tests can confirm the presence of the virus.

The rash usually begins as clusters of small bumps that soon develop into fluid-filled blisters (vesicles). In turn, the blisters fill with pus (pustules), break open, and form crusty scabs. In about four or five weeks, the disease runs its course, the scabs drop off, the skin heals, and the pain fades. Most healthy
individuals make an uneventful, if not particularly pleasant, recovery.

Not everyone sails through without incident, however. Although it’s difficult to resist scratching the itchy rash, it’s better to keep hands off, as the damaged skin may develop a bacterial infection requiring antibiotic treatment. After such an infection, the skin may be left with significant scarring, some of it serious enough to require plastic surgery. Another complication called the Ramsay Hunt syndrome occurs when the varicella-zoster virus spreads to the facial nerve, causing intense ear pain. The rash can appear on the outer ear, inside the ear canal, on the soft palate (part of the roof of the mouth), around the mouth and on the face, neck, and scalp. The hearing loss, vertigo, and facial paralysis that may result are usually, but not always, temporary.

Occasionally, the rash will appear as a single spot or cluster of spots on the tip of the nose, called Hutchinson's sign. This is not good news. It means that the ophthalmic nerve is probably involved and the eye may become affected, possibly causing temporary or permanent blindness.

“My husband was undergoing chemotherapy treatment for prostate cancer,” says Julia Hershfield, of Kensington, Md., “when he developed shingles in his right eye. The pain was so bad that he lost all will to live. Shingles finished him." In people whose immune systems are extremely weakened, the shingles virus can also spread to the internal organs and affect the lungs, central nervous system, and the brain, sometimes causing death.

**Chickenpox Redux**

Like other members of the herpes family (such as the herpes simplex viruses that cause cold sores and genital herpes), the varicella-zoster virus that causes chickenpox never completely leaves the body. Most people don’t get chickenpox a second time. However, anyone who has had chickenpox has the potential to develop shingles, because after recovery from chickenpox, the virus settles in the nerve roots.

Researchers are not sure exactly what triggers the virus to spontaneously start reproducing in nerve cells later in life and reappear as shingles. However, they do know the virus may reactivate when the immune system is weak.

Certain factors can cause the immune system to let down its guard. Age is one of them. Immunity declines with aging, so susceptibility to disease increases. The incidence of shingles and of resulting PHN rises with increasing age. More than 50 percent of cases occur in people over 60. Older people may also lack exposure to children with chickenpox, thereby losing an opportunity to boost immunity and prevent virus reactivation. Although most people have only one attack of shingles, about 4 percent will have further attacks.

People who have had chickenpox cannot “catch” shingles from someone who has it. However, people who’ve never had chickenpox can be infected with chickenpox if exposed to someone with an active case of shingles. The rash sheds the varicella-zoster virus and can be contagious. A caregiver or other person who lacks immunity developed from a prior case of chickenpox or the vaccine must avoid coming into contact with the rash or contaminated materials.

Also at risk for shingles are people with leukemia, lymphoma, or Hodgkin’s disease, and those whose immune systems have been weakened because they are HIV-positive, or have undergone chemotherapy, radiation, transplant surgery with immunosuppression, or treatment with corticosteroids. Moreover, about 5 percent of people with shingles are found to have an underlying cancer, about twice the number of people in the population expected to have undiagnosed cancer.

It pays to be vigilant when unexplained symptoms occur. “New development of a rash or pain, especially when it occurs on only one side of the chest or face, should prompt a visit to the healthcare provider,” says Therese A. Cvetkovich, M.D., a medical officer in the Food and Drug
Administration’s Center for Drug Evaluation and Research (CDER).

Controlling the Outbreak
Although viral diseases can’t be cured, doctors can prescribe oral antiviral medications, such as Zovirax (acyclovir), Famvir (famciclovir) and Valtrex (valacyclovir) that help control the infection by hindering reproduction of the virus in the nerve cells. "Antiviral therapy may shorten the course of an episode of shingles," says Cvetkovich. “However, therapy must be started as early as possible after symptoms develop—with 48 hours—in order to have aneffect.”

To relieve pain, the doctor may recommend over-the-counter analgesics (pain-relieving drugs), such as ibuprofen and naproxen, or prescription drugs, such as indomethacin, all members of a class of medications known as nonsteroidal anti-inflammatory drugs. Acetaminophen is also commonly used to relieve the pain. If pain is severe, doctors may add stronger analgesics, such as codeine or oxycodone.

When the Pain Persists
In some patients, the misery continues long after the rash has healed. Many of the 1 million people who develop shingles each year experience a complication called post-herpetic neuralgia (PHN). This term refers to pain that is present in the affected area for months, or even years, afterward. Although the acute pain of shingles and the chronic pain of PHN (called neuropathic pain) both originate in the nerve cells, their duration and the reaction to treatment is different.

Pain that occurs with the initial outbreak responds to treatment and is limited in duration. In contrast, PHN lasts longer, is difficult to treat, and can be incapacitating. Furthermore, for unknown reasons, older people suffer more from this debilitating pain than younger people. In many individuals, the skin is so sensitive that clothing or even a passing breeze cannot be tolerated on the affected area. Described by PHN sufferers as agonizing, excruciating, and burning, the pain can result in an inability to perform daily tasks of living, and lead to loss of independence and, ultimately, depression and isolation.

“I would rather have ten babies than the pain I’ve endured for the past ten years,” says 87-year-old Etta Watson Zukerman of Bethesda, Md., who has lost partial use of her right arm and hand due to nerve damage from PHN. “Nothing my doctor prescribed helped. I even went to a sports medicine specialist who recommended exercises. They didn’t help either.” Many PHN sufferers receive no relief at all, no matter what medications or therapies they use. And what works for one doesn’t necessarily work for another.

Treating the Pain
Doctors use other methods to alleviate pain with varying degrees of success. “One of the relatively new medications that I’m enthusiastic about is the Lidoderm patch,” says Veronica Mitchell, M.D., director of the pain management center and inpatient pain service at Georgetown University Hospital, Washington, D.C. “It’s the transdermal form of lidocaine and it’s been studied in the PHN population with very good results,” adds Mitchell. “We prescribed the Lidoderm patch for a patient who had intolerable side effects with oral medications—and no relief—and she’s had about a 50 percent-plus improvement in pain relief. It’s one of my first-line therapies.”

The medication contained in this soft, pliable patch penetrates the skin, reaching the damaged nerves just under the skin without being absorbed significantly into the bloodstream. This means that the patch can be used for long periods of time without serious side effects.

Yet another method used to treat PHN is transcutaneous electrical nerve stimulation, or TENS. A device that generates low-level pulses of electrical current is applied to the skin’s surface, causing tingling sensations and offering some people pain relief. One theory as to how TENS works is that the electrical current stimulates production of endorphins, the body’s natural painkillers.

TENS is not for everyone. “TENS didn’t help at all,” says Einar Raysor of Rockville, Md. “I found there was a problem in fine-tuning the administration of the electrical current. Low doses of the electrical current didn’t do anything for me. When the
technician increased the current, it gave me a painful response. After this happened a couple of times, we dropped the treatment."

As a last resort, invasive procedures called nerve blocks may be used to provide temporary relief. These procedures usually entail the injection of a local anesthetic into the area of the affected nerves. "We have controversial results in the terms of the efficacy of nerve blocks," says Mitchell. "I do consider nerve blocks in treating PHN and I would perform them because there’s some evidence that they work, but the real efficacy is to catch and treat the patient in the acute shingles phase. As PHN presents mostly in the elderly, and the older patient often is unable to tolerate some of the medications we use, I find nerve blocks useful in these cases."

Injection directly into the spine is another option for relief of pain that is not easily treated. A Japanese clinical study published in the New England Journal of Medicine found that an injection of the steroid methylprednisolone combined with the anesthetic lidocaine reduced pain by more than 70 percent in one patient group compared with groups that received lidocaine alone or an inactive substance.

Prevention, Almost Perfect
Before the FDA approved the chickenpox vaccine in 1995, about 95 percent of the U.S. population developed chickenpox before age 18. Since then, more than 60 percent of American youngsters have been vaccinated against chickenpox.

“The vaccine is a live attenuated strain of the chickenpox virus,” says Philip R. Krause, M.D., lead research investigator in the FDA's Center for Biologics Evaluation and Research. “However, it’s a weaker form so it gives rise to a milder infection. But in the course of giving rise to this milder infection, it induces enough immunity to prevent people from getting the natural infection.” It is estimated that the vaccine is between 75 and 85 percent effective in preventing chickenpox. "But the important thing," says Krause, "is that it is almost completely effective in preventing severe cases of chickenpox."

Now that we have a chickenpox vaccine, are shingles and PHN on their way out? Although the FDA hasn’t evaluated the effects of the vaccine on shingles, Krause believes that “in the long term, if you can prevent enough people from getting the wild (natural) type of chickenpox, you’re likely to see a beneficial effect on the incidence of shingles and post-herpetic neuralgia. But it may take several generations for this to happen."

People who have had chickenpox (varicella zoster) in their youth can develop shingles (herpes zoster) in later years. During an acute attack of the chickenpox virus, most of the viral organisms are destroyed, but some survive, travel up nerve fibers along the spine, and lodge in nerve cells where they may lie dormant for many years. A decrease in the body’s resistance can cause the virus to reawaken decades later. It then travels back down the nerve fibers to the skin’s surface.

The reawakened virus generally causes a vague burning sensation or tingling over an area of skin. A painful rash usually occurs two to five days after the first symptoms appear. A cluster of small bumps turns into blisters that resemble chickenpox lesions. The blisters fill with pus, break open, crust over, and finally disappear. This process takes four to five weeks.

A painful condition called post-herpetic neuralgia can sometimes occur. This condition is thought to be caused by damage to the nerves, and can last from weeks to years after the rash disappears.

Shingles Prevention Study
For many years, physicians could shorten the episodes of shingles, but they have had no means to prevent the disease, which affects up to one-half of all people who reach the age of 85. Now, this void in the medical armamentarium may change as a result of a major study of an experimental vaccine conducted by the Department of Veterans Affairs in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID) and Merck & Co.

The study, whose outcome was announced in June, 2005, was launched in 1999 and included 38,546 participants 60 years of age or older. The volunteers'
average age was 69, 7 percent were older than 80, and 40 percent were women. Half of the subjects were injected with a highly potent version of VZV, Merck's chickenpox vaccine for immunization of children, and half received a placebo.

By the end of the randomized, double-blind trial, 642 (3.3 percent) of the placebo recipients but only 315 (1.6 percent) of those treated with vaccine were diagnosed with shingles. The difference in the incidence of postherpetic neuralgia was even greater: the painful condition affected 80 study subjects on placebo, but only 27 of those who had been vaccinated.

“A preventive shingle vaccine would be an enormous boon for the health and quality of life of seniors,” said Anthony S. Fauci, M.D., director of the NIAID. “We are extremely gratified that the public-private partnership has led to these exciting results, which have the potential to greatly benefit seniors in years to come.”

By Evelyn Zamula

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