Cover illustration: Cultured human skin cells infected with varicella zoster virus, stained with acridine orange and photographed under ultraviolet light. Courtesy of Dr. Randall Cohrs, University of Colorado Health Sciences Center.

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Introduction

When the itchy red spots of childhood *chickenpox* disappear and life returns to normal, the battle with the virus that causes chickenpox seems won. But for too many of us this triumph of immune system over virus is temporary. The virus has not been destroyed but remains dormant in our nerve cells, ready to strike again later in life. This second eruption of the chickenpox virus is the disease called shingles or *herpes-zoster*.

Most adults who have the dormant virus in their body never get shingles. The disease occurs when an unknown trigger causes the virus to become activated.

You cannot develop shingles unless you have had an earlier exposure to chickenpox. The disease most often strikes after age 50. But since shingles is so common, affecting an estimated one-quarter of Americans at some point during their lifetime, cases in young people are not rare. Most people who get shingles have it only once, but it is possible for the outbreak to appear again.

* Terms in Italics are defined in the Glossary.
What is Shingles?

Scientists call the virus that causes chickenpox/shingles varicella-zoster virus or VZV. The word “varicella” is derived from “variola,” the Latin word for smallpox, another infectious disease that can resemble chickenpox. “Zoster” is the Greek word for girdle; shingles often produces a girdle or belt of blisters or lesions around one side of the waist. This striking pattern also underlies the condition’s common name: shingles comes from “cingulum,” the Latin word for belt or girdle.

VZV belongs to a group of viruses called herpesviruses. This group includes the herpes simplex virus that causes cold sores, fever blisters, mononucleosis, Epstein-Barr virus involved in infectious mononucleosis, and genital herpes. Like VZV, other herpesviruses can hide in the nervous system after an initial infection and then travel down nerve cell fibers to cause a renewed infection. Repeated episodes of cold sores on the lips are the most common example.

As early as 1909, scientists suspected that the viruses causing chickenpox and shingles were one and the same. In the 1920s and 1930s, the case was strengthened by an experiment in

After a bout of chickenpox, some of the virus particles move into specific nerve cells, where they remain in an inactive form until reactivated years later and cause shingles.
which children were inoculated with fluid from shingles blisters. Within 2 weeks, about half of the children developed chickenpox. Finally, in 1958, detailed analyses of the viruses taken from patients with either chickenpox or shingles confirmed that the viruses were identical.

Virtually all adults in the United States have had chickenpox, even if it was so mild as to pass unnoticed, and could possibly develop shingles later in life. In the original exposure to VZV (chickenpox), some of the virus particles leave the blood and settle into clusters of nerve cells (neurons) called sensory ganglia, where they remain for many years in an inactive (latent) form. The sensory ganglia, which are adjacent to the spinal cord and brain, relay information to the brain about what the body is sensing—heat, cold, touch, pain.

When the VZV reactivates, it spreads down the long nerve fibers (axons) that extend from the sensory cell bodies to the skin. The viruses multiply, the telltale rash erupts, and the person now has herpes-zoster, or shingles. With shingles, the nervous system is more deeply involved than it was during the bout with chickenpox, and the symptoms are often more complex and severe.

Who is at Risk for Shingles?

About 25 percent of all adults, mostly otherwise healthy, will get shingles during their lifetime, usually after age 50. The incidence increases with age so that shingles is 10 times more likely to
occur in adults over 60 than in children under 10. People with compromised immune systems—from use of immunosuppressive medications such as prednisone, from serious illnesses such as cancer or from chemotherapy or radiation treatment, or from infection with HIV—are at increased risk of developing shingles. Shingles is also common in people who are under prolonged stress. These individuals can also have re-eruptions and some may have shingles that never heals. Most people who get shingles re-boost their immunity to VZV and will not get the disease for another few decades.

Youngsters whose mothers had chickenpox late in pregnancy—5 to 21 days before giving birth—or who had chickenpox in infancy, have an increased risk of pediatric shingles. Sometimes these children are born with chickenpox or develop a typical case within a few days (see section entitled “Can Shingles During Pregnancy Harm the Baby?” for more information).

What are the Symptoms of Shingles?

The first sign of shingles is often burning or tingling pain, or itch, generally on only one side of the body around the waist. After several days or up to two weeks after the first symptoms are felt, a rash of fluid-filled blisters appears. These are similar to chickenpox but in a cluster rather than scattered over the body. The cluster typically

The small fluid-filled shingles blisters are often limited to a band, called a dermatome, spanning one side of the trunk.
appears in one area on one side of the body. Recent studies have shown that subtle cases of shingles with only a few blisters, or none, are more common than previously thought. These cases may remain unrecognized. Cases without any known lesions are known as *zoster sine herpete*.

Shingles pain can be mild or intense. Some people have mostly itching; some feel pain from the gentlest touch or breeze. The most common location for shingles is a band, called a dermatome, spanning one side of the trunk around the waistline. The second most common location is on one side of the face around the eye and on the forehead. However, shingles can involve any part of the body. The number of lesions is variable. Some rashes merge and produce an area that looks like a severe burn. Other patients may have just a few scattered lesions that don’t cause severe symptoms.

For most healthy people, shingles rashes heal within a few weeks, the pain and itch that accompany the lesions subside, and the blisters leave no scars. Other people may have sensory symptoms that linger for a few months.
How Should Shingles Be Treated?

Currently there is no cure for shingles, but attacks can be made less severe and shorter by using prescription antiviral drugs such as *acyclovir*, *valacyclovir*, or *famcyclovir* as soon as possible after symptoms begin. Early treatment can reduce or prevent severe pain and help blisters dry faster. Antiviral drugs can reduce by about half the risk of being left with *postherpetic neuralgia* (see section entitled “What is Postherpetic Neuralgia?”), which is chronic pain that can last for months or years after the shingles rash clears. Doctors recommend starting antiviral drugs at the first sign of the shingles rash, or even if the telltale symptoms indicate that a rash is about to erupt. Even if a patient is not seen by a doctor at the beginning of the illness, it may still be useful to start antiviral medications if new lesions are forming. Other treatments to consider are anti-inflammatory corticosteroids such as *prednisone*. These are routinely used when the eye or other facial nerves are affected.

Most patients with shingles can be treated at home. People with shingles should also try to relax and reduce stress (stress can make pain worse and lead to depression); eat regular, well-balanced meals; and perform gentle exercises, such as walking or stretching to keep active and stop thinking about the pain (but check first with your physician). Placing a cool, damp washcloth on the blisters—but not when wearing a topical cream or patch—can help blisters dry faster and relieve pain.
Is Shingles Contagious?

Shingles is not contagious—you cannot catch it from someone else. Shingles occurs when an unknown trigger causes the virus hiding inside the person’s body to become activated. Unlike chickenpox, shingles can’t be “caught” from someone else.

But a person with a shingles rash can pass the virus to someone, usually a child, who has never had chickenpox. In this case, the child will develop chickenpox, not shingles. The child must come into direct contact with the open sores of the shingles rash. Merely being in the same room with a shingles patient will not cause a child to catch chickenpox because during a shingles infection the virus is not normally in the lungs and therefore can’t be spread through the air.

Likewise, a person with chickenpox cannot give shingles to someone else—but they can pass the virus to someone who has never had chickenpox. In cases of chickenpox, the virus can become airborne because it is found in the upper respiratory tract.

Can Shingles Be Prevented?

*Chickenpox vaccine*

Immunization with the varicella vaccine (or chickenpox vaccine)—now recommended in the United States for all children between 18 months and adolescence—can protect children from getting chickenpox. People who have been vaccinated against chickenpox are less likely to get shingles.
because the weak, “attenuated” strain of virus used in the chickenpox vaccine is less likely to survive in the body over decades. Not enough data currently exists to indicate whether shingles can occur later in life in a person vaccinated against chickenpox.

**Shingles vaccine**

In May 2006, the Food and Drug Administration (FDA) approved a VZV vaccine (Zostavax) for use in people 60 and older who have had chickenpox. In March 2011, the FDA extended the approval to include adults ages 50-59.

Researchers found that giving older adults the vaccine reduced the expected number of cases of shingles by half. And in people who still got the disease despite immunization, the severity and complications of shingles were dramatically reduced. The **Shingles Prevention Study**—a collaboration between the Department of Veterans Affairs, the National Institute of Allergy and Infectious Diseases, and Merck & Co., Inc.—involved more than 38,000 veterans aged 60 and older. The purpose was to find out how safe the vaccine is, and if it can prevent shingles. Half the study participants were vaccinated with a more potent version of the chickenpox vaccine, developed specifically for use in adults, and half received a placebo vaccine. Neither volunteers nor researchers knew if a particular subject had gotten active or placebo vaccine until after the end of the study (a double-blind study).
During more than 3 years of follow-up, the vaccine reduced shingles cases by 51 percent; 642 cases of shingles developed in the placebo group compared with only 315 in the vaccinated group. Pain and discomfort were reduced by 61 percent in people who received the active vaccine but still got shingles. The vaccine also reduced the number of cases of postherpetic neuralgia by two-thirds compared with the placebo.

The shingles vaccine is a preventive therapy and not a treatment for those who already have shingles or postherpetic neuralgia.

**What is Postherpetic Neuralgia?**

Sometimes, particularly in older people, shingles pain persists long after the rash has healed. This postherpetic neuralgia can be mild or severe—the most severe cases can lead to insomnia, weight loss, depression, and disability. Postherpetic neuralgia is not directly life-threatening and may get better over time.

Shingles often affects a sharply circumscribed region of the body, as in this case where the blisters are on only one side of the face. When shingles affects the region around the eye, the patient should see an ophthalmologist immediately.
About a dozen medications in four categories have been shown in clinical trials to provide some pain relief. These include:

**Tricyclic antidepressants (TCAs):** TCAs are often the first type of drug given to patients suffering from postherpetic neuralgia. The TCA amitryptiline was commonly prescribed in the past, but although effective, it has a high rate of side effects. **Desipramine** and **nortriptyline** have fewer side effects and are therefore better choices for older adults, the most likely group to have postherpetic neuralgia.

Common side effects of TCAs include dry eyes and mouth, constipation, and grogginess. People with heart arrhythmias (irregular heartbeats), previous heart attacks, or narrow angle glaucoma should usually use a different class of drugs.

People with shingles can pass the virus to individuals who have never had chickenpox, but these individuals will develop chickenpox, not shingles. These hospital aides are carefully cleaning a hospital bed to avoid such a transmission.
Anticonvulsants: Some drugs that reduce seizures can also treat postherpetic neuralgia because seizures and pain both involve abnormally increased firing of nerve cells. The antiseizure medication gabapentin is most often prescribed. Carbamazepine is effective for postherpetic neuralgia but has rare, potentially dangerous side effects. Side effects of the drug include drowsiness or confusion, dizziness, and sometimes ankle swelling.

Opioids: Opioids are strong pain medications used for all types of pain. They include oxycodone, morphine, tramadol, and methadone. Opioids can have side effects—including drowsiness, mental dulling, and constipation—and can be addictive, so their use must be monitored carefully in those with a history of addiction.

Topical local anesthetics: Local anesthetics applied directly to the skin of the painful area affected by postherpetic neuralgia are also effective. Lidocaine, the most commonly prescribed, is available in cream, gel, or spray form. It is also available in a patch that has been approved by the Food and Drug Administration for use specifically in postherpetic neuralgia. With topical local anesthetics, the drug stays in the skin and therefore does not cause problems such as drowsiness or constipation. Capsaicin cream may be somewhat effective and is available over the counter, but most people find that it causes severe burning pain during application.
Postherpetic itch

The itch that sometimes occurs during or after shingles can be quite severe and painful. Clinical experience suggests that postherpetic itch is harder to treat than postherpetic neuralgia. Topical local anesthetics (which numb the skin) provide substantial relief to some patients. Since postherpetic itch typically develops in skin that has severe sensory loss, it is particularly important to avoid scratching. Scratching numb skin too long or too hard can cause injury.
What are Other Complications of Shingles?

People with ophthalmic shingles—lesions in or around the eye and forehead—can suffer painful eye infections, and in some cases immediate or delayed vision loss which may be temporary or permanent. People with shingles in or near the eye should see an ophthalmologist immediately. Shingles infections within or near the ear (herpes zoster oticus or Ramsay Hunt syndrome type II) can cause hearing or balance problems as well as weakness of the muscles on the affected side of the face. In rare cases, shingles can spread into the brain or spinal cord and cause serious complications such as stroke or meningitis (an infection of the membranes outside the brain and spinal cord).

People with shingles need to seek immediate medical evaluation if they notice neurological symptoms outside the region of the primary shingles attack. People who are immunosuppressed, whether from diseases such as HIV or medications, have an increased risk of serious complications from shingles. Most commonly, they get shingles that spreads to involve more parts of the body, or shingles rashes that persist for long periods or return frequently. Many such patients are helped by taking antiviral medications on a continuous basis.

Can Infection with VZV During Pregnancy Harm the Baby?

Many mothers-to-be are concerned about any infection contracted during pregnancy, since some infections can be transmitted across the mother’s bloodstream to the fetus or can be acquired by the
baby during the birth process. VZV infection during pregnancy poses some risk to the unborn child, depending upon the stage of pregnancy. During the first 30 weeks, maternal chickenpox may, in some cases, lead to congenital malformations. Such cases are rare and experts differ in their opinions on how great the risk is. Most experts agree that shingles in a pregnant woman, a rare event, is even less likely to cause harm to the unborn child.

If a pregnant woman gets chickenpox between 21 to 5 days before giving birth, her newborn can have chickenpox at birth or develop it within a few days. But the time lapse between the start of the mother’s illness and the birth of the baby generally allows the mother’s immune system to react and produce antibodies to fight the virus. These antibodies can be transmitted to the unborn child and thus help fight
the infection. Still, a small percent of the babies exposed to chickenpox in the 21 to 5 days before birth develop shingles in the first 5 years of life because the newborn’s immune system is not yet fully functional and capable of keeping the virus latent.

What if the mother contracts chickenpox at the time of birth? In that case the mother’s immune system has not had a chance to mobilize its forces. And although some of the mother’s antibodies will be transmitted to the newborn via the placenta, the newborn will have little ability to fight off the attack because its immune system is immature. If these babies develop chickenpox as a result, it can be fatal. They are given zoster immune globulin, a preparation made from the antibody-rich blood of adults who have recently recovered from chickenpox or shingles, to lessen the severity of their chickenpox.

What Research is Being Done?

Because of nervous system involvement, the chickenpox/shingles virus is studied by the National Institute of Neurological Disorders and Stroke, a part of the National Institutes of Health. The National Institute of Allergy and Infectious Diseases, the National Cancer Institute, the National Institute on Aging, and the National Eye Institute also support research on shingles.
Medical research on shingles has two main goals. The first is to develop drugs to fight the disease and to prevent or treat its complications, especially postherpetic neuralgia. The second is to understand the disease well enough to prevent it, especially in people at high risk. Scientists need to learn much more about the VZV, particularly how it becomes latent in the body and what induces it to become active again. Scientists suspect that the VZV DNA is inserted into one of the chromosomes of the nerve cell—the units that house the cell’s own genetic material.

A healthy immune system protects against all kinds of diseases, but people with weakened immunity are vulnerable to many illnesses, including shingles. Antibodies, one of the immune system’s major defense mechanisms against infection, are not very
helpful against shingles. The immune cells that appear to combat shingles are two types of white blood cells: T lymphocytes and macrophages. Scientists are trying to find ways to boost the activity of these cells—especially in patients at high risk for severe or disseminated shingles (a rare condition in which the virus spreads to other areas of the body, sometimes vital areas such as the blood or the lungs).

Other researchers are studying how VZV infects neurons. In particular, they are looking at how the virus assembles in and exits out of nerve cells, with the goal of blocking this important step. In another study, researchers are developing animal models to evaluate VZV vaccines. Their findings may lead to improved vaccines that protect against varicella or prevent it from establishing latent infection or reactivation to cause shingles and postherpetic neuralgia.

Other research is aimed at finding new methods for identifying the biological differences between people who suffer from or escape long-term postherpetic neuralgia pain after shingles. The goals of this research are to identify ways to reduce the risk of postherpetic neuralgia after shingles.
**Glossary**

*acyclovir*—one of three available antiviral drugs that can reduce the severity and duration of a shingles attack if given soon after onset.

*capsaicin*—an active ingredient in hot chili peppers used in topical ointments to relieve pain. It appears to work by reducing a chemical substance found at nerve endings and involved in transmitting pain signals to the brain. While somewhat effective for postherpetic neuralgia, it can cause severe burning in some patients.

*carbamazepine*—a drug that works both as an anticonvulsant and a pain reliever.

*chickenpox*—an acute contagious disease that usually occurs in children and is caused by the varicella-zoster virus.

*desipramine*—an antidepressant often prescribed to help reduce the pain from postherpetic neuralgia. Doctors often prescribe it because it has fewer side effects than some other antidepressants.

*famcyclovir*—one of three available antiviral drugs that can reduce the severity and duration of a shingles attack if given soon after onset.

*gabapentin*—an antiseizure medicine that is also used as a pain reliever.

*herpes zoster*—the medical term for shingles; an infection caused by the varicella-zoster virus, one of the herpesviruses family of viruses.
**Herpes Simplex**—the medical term for a related but different virus that causes repeated mild blisters of the skin or mucous membrane. Herpes simplex rashes can return many times, whereas shingles usually appears no more than once or twice in a person’s lifetime.

**Herpesviruses**—a large family of viruses that cause a number of related conditions including, but not limited to, oral and genital herpes simplex, varicella (chickenpox), and herpes-zoster (shingles).

**Immunosuppressed**—having a weakened immune system. Common causes are certain illnesses (HIV, some cancers) or use of certain drugs such as prednisone.

**Latent**—hidden, dormant, inactive. The virus that causes chickenpox remains hidden in the nervous system after the initial attack of chickenpox is over. When it becomes reactivated, usually many years later, the virus can cause shingles.

**Lidocaine**—a pain-killing drug sometimes used for treating postherpetic neuralgia. It is available in an adhesive fabric patch that can be placed on the skin directly over the site of the pain.

**Neuron**—the functional cell of the brain and nervous system.

**Nortriptyline**—an antidepressant often prescribed to help reduce the pain from postherpetic neuralgia. Doctors often prescribe it because it has fewer side effects than some other antidepressants.
**postherpetic itch**—severe, painful, and difficult to treat itching that sometimes accompanies postherpetic neuralgia. Topical local anesthetics provide relief to some patients.

**postherpetic neuralgia**—a condition characterized by pain that persists more than 3 months after healing of a shingles rash; caused by damage to the nervous system.

**prednisone**—an anti-inflammatory corticosteroid drug routinely given to shingles patients when an eye or other facial nerve is involved.

**valacyclovir**—one of three available antiviral drugs that can reduce the severity and duration of a shingles attack if given soon after onset.

**varicella-zoster virus**—a virus that causes two distinct diseases, chickenpox and shingles. It is a member of the herpesvirus family. “Varicella” is Latin for little pox; “zoster” is the Greek word for girdle. Medically, zoster is sometimes used as a synonym for shingles.

**zoster sine herpete**—a case of shingles in which there are no blisters or other signs of the illness on the skin.
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