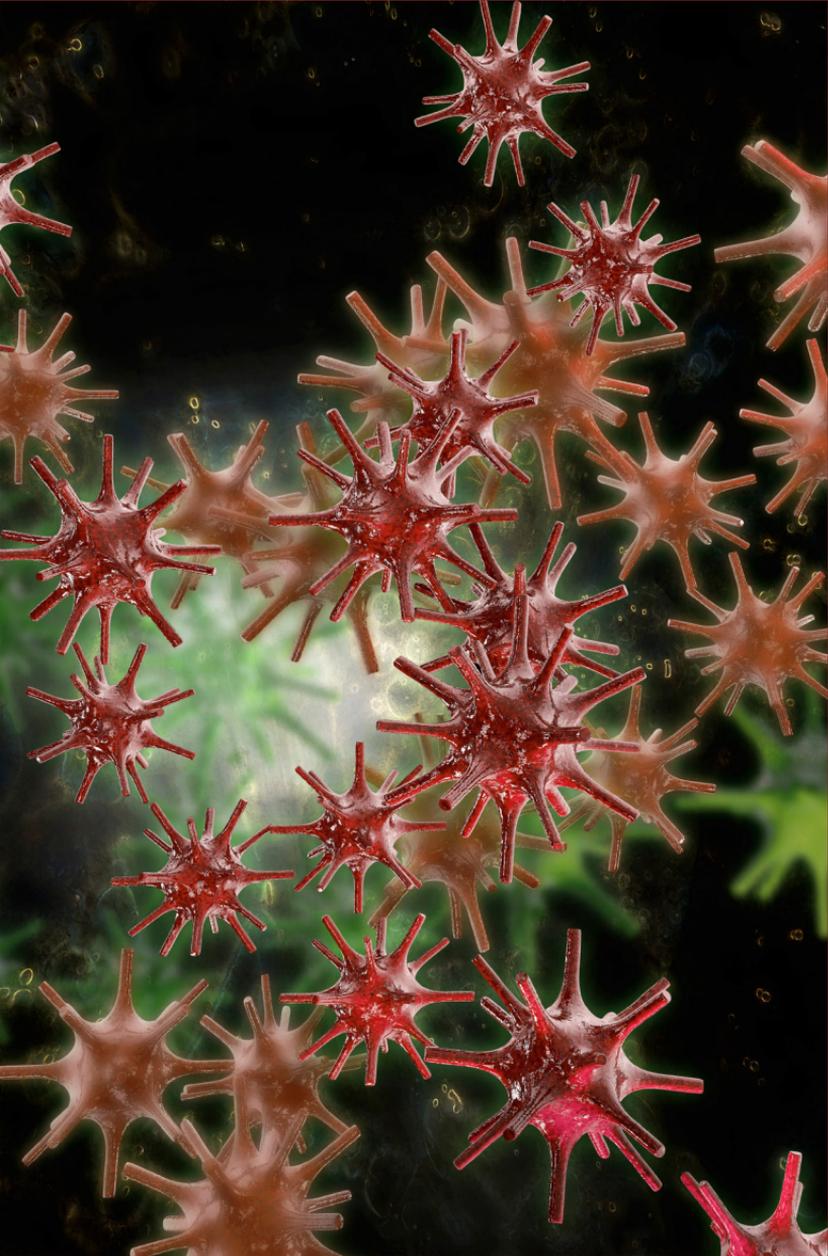


Shingles



**National Institute of Neurological Disorders
and Stroke
National Institutes of Health**

Hope Through Research

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What is shingles?

Shingles is a viral infection that causes pain, burning, or a tingling sensation, along with an itch and blisters that usually form on one side of the body. It is caused by the *varicella zoster virus*, or VZV—the same virus that causes chickenpox. When the itchy red spots of childhood chickenpox disappear, the virus may remain in a dormant state in our nerve cells, ready to strike again in later life. This second eruption of the chickenpox virus is called shingles or *herpes-zoster*.

You cannot develop shingles unless you have had an earlier exposure to chickenpox. Shingles occurs when an unknown trigger causes the virus to become activated. Most adults who have the dormant virus in their body never get shingles.

1

What are the symptoms and signs of shingles?

The first symptom of shingles is often burning or tingling pain, or itch, generally on only one side of the body around the waist, chest, stomach, or back. Shingles pain can be mild or intense. Some people have mostly itching; some feel severe pain from the gentlest touch, such as bed



One of the first symptoms of shingles may be burning or tingling pain, or itching, around the waist, chest, stomach, or back.

linens or clothing. A few people may have general symptoms of a viral infection, like fatigue, fever, and headache.

After several days or up to two weeks after the first symptoms are felt, a rash of fluid-filled blisters (vesicles) appears. These are similar to chickenpox but in a cluster rather than scattered over the body. The number of vesicles is variable. Some rashes merge and produce an area that looks like a burn. Other people may have just a few small scattered lesions. The clusters most often appear on one side of the body in a band called a dermatome, which contains nerves that branch out from the nerve root exiting the spine. 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, including organs inside the body.

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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.

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. There sometimes are complications or long-lasting effects from shingles, such as continuing chronic nerve pain, called *postherpetic neuralgia*.

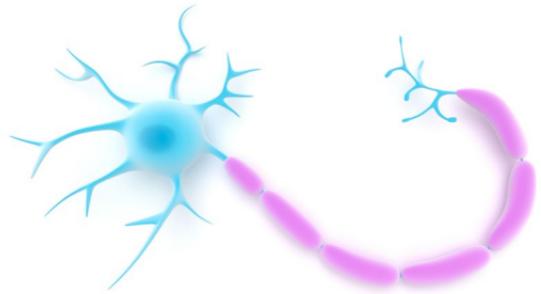
What is the varicella-zoster virus and how does it cause shingles?

The word “varicella” is derived from “variola,” the Latin word for smallpox. “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* (HSV) that causes cold sores, fever blisters, and genital herpes. Like VZV, HSV 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.

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Most adults in the United States have had chickenpox, even if it was so mild as to pass unnoticed, and can possibly develop shingles later in life. In the original exposure to VZV (chickenpox), some of the virus particles settle into nerve cells (*neurons*) of sensory ganglia, where they remain for many years in an inactive, hidden (*latent*) form. The sensory ganglia, which are adjacent to the



During the original exposure to VZV or chickenpox, some virus particles can settle into nerve cells where they remain inactive or hidden for many years. When the virus reactivates, it spreads down the long nerve fibers, called axons, that extend from the sensory cell bodies to the skin.

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 virus multiplies, the tell-tale 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.

How are chickenpox and shingles different?

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When a person, usually a child, who has not received the chickenpox vaccine is exposed to VZV, he or she usually develops chickenpox, a highly contagious disease that can be spread by breathing as well as by contact with the rash. The infection begins in the upper respiratory tract where the virus incubates for 15 days or more. VZV then spreads to the bloodstream and migrates to the skin, giving rise to the familiar chickenpox rash.

In contrast, you can't catch shingles from someone else. You must already have been exposed to chickenpox and harbor the virus in your nervous system to develop shingles. When reactivated, the virus travels down nerves to the skin, causing the painful shingles rash. In shingles, the virus does not normally spread to the bloodstream or lungs, so the virus is not shed in air.

But a person with a shingles rash—which contains active virus particles—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 someone who has shingles will not cause a child to catch chickenpox.



Chickenpox is a highly contagious disease that can be spread by breathing as well as by contact with the rash. The infection begins in the upper respiratory tract, then spreads to the bloodstream, and travels to the skin, producing the familiar rash.

Likewise, a person with chickenpox cannot give shingles to someone else—but they can pass the virus to someone who has never had chickenpox.

Who is at risk for shingles?

Anyone who had previously had chickenpox 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, a natural consequence of aging or 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. Some individuals can also have re-eruptions and some, particularly those with significantly impaired immunity from drugs and diseases, may have shingles that never heals. Most people who get shingles re-boost their immunity to VZV.

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 or at birth harm the baby?” for more information).

Most people who get shingles have it only once, but it is possible for the outbreak to appear again.

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How is shingles 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, 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 person 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.



Keeping active with gentle exercises such as walking or stretching can help reduce stress which can make shingles pain worse and lead to depression.

Most people 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. Keeping the area clean can help avoid a secondary bacterial infection.

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. (The chickenpox vaccine became available in the United States in 1995.) Not enough data currently exists to indicate whether shingles can occur later in life in a person vaccinated against chickenpox.) People who have been vaccinated against chickenpox are probably 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.

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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.

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



In 2006, the FDA approved a VZV vaccine for use as a preventative therapy in people 60 and older who have had chickenpox. The vaccine is not a treatment for those who already have shingles.

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 received the shingles vaccine, and half received a similar looking, inactive vaccine (placebo vaccine). Neither volunteers nor researchers knew if a particular subject had gotten active or placebo vaccine until after the end of the study (called 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. And in people who received the active vaccine and still got shingles, the severity and discomfort were reduced by 61 percent. The vaccine also reduced the number of cases of long-lasting nerve pain (postherpetic neuralgia) by two-thirds compared with the placebo.

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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 is postherpetic neuralgia, defined as pain lasting three months after onset of the rash. Pain can be mild or severe—the most severe cases can lead to insomnia, weight loss, depression, and disability. There may be other sensations, such as tingling, coldness, or loss of feeling. About 20 percent of people age 70 or greater who develop shingles may have long-lasting

*Postherpetic neuralgia
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lasting three months
after onset of the rash.*

pain. Postherpetic neuralgia is not directly life-threatening and may get better over time.

About a dozen medications in four categories have been shown in clinical trials to provide some pain relief for postherpetic neuralgia. These include:

Tricyclic antidepressants (TCAs): TCAs are often the first type of drug given to people suffering from postherpetic neuralgia. The TCA amitriptyline 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 impaired memory. People with heart arrhythmias (irregular heartbeats), previous heart attacks, or narrow angle glaucoma should usually use a different class of drugs.

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, including drowsiness or confusion, dizziness, and sometimes ankle swelling. Some small studies have shown positive effects using divalproex sodium to treat postherpetic neuralgia.

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 FDA 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. An alternative approach using a high concentration capsaicin patch has been reported to be effective.

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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 individuals. 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?

Complications of zoster are more frequent in people with lesions in or around the eyes, forehead, and nose (ophthalmic shingles), or around the ear and on the face (herpes zoster oticus or Ramsay-Hunt syndrome). People with shingles in or near the eye should see an ophthalmologist immediately, as they can suffer painful eye infections and, in some cases, immediate or delayed vision loss which may be temporary or permanent. Symptoms can include redness and swelling involving just the white of the eye (sclera), the clear front of the eye (cornea), or internal parts of the eye. If the cornea is involved, treatment to avert permanent scarring is important to preventing lasting vision loss. The disease can cause damage to or death of the nerve cells that react to light (called acute retinal necrosis).

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Shingles infections within or near the ear can cause hearing or balance problems as well as weakness of the muscles on the affected side of the face. These

problems can be long-lasting or permanent.

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 ophthalmic shingles (shingles in or near the eye) should see an ophthalmologist immediately as they can suffer eye infections and, sometimes, vision loss.

The varicella zoster virus also may involve blood vessels or provoke an immune reaction irritating the surface of blood vessels (vasculopathy). People with shingles have slightly increased risk of stroke, greatest in the first few weeks after vesicle eruption, but lasting for several months. The risk of stroke is highest in people with eye zoster, perhaps as much as five percent.

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 individuals are helped by taking antiviral medications on a continuous basis. People taking immunosuppressive drugs, or with diseases such as HIV or leukemia, should see a doctor immediately for treatment to avoid possible serious complications.

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Can infection with VZV during pregnancy or at birth harm the baby?

Some infections can be transmitted across the mother's blood-stream 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



VZV infection during pregnancy may pose some risk to the unborn child. If a pregnant woman develops chickenpox between 5 to 21 days before giving birth, her newborn can have chickenpox at birth or develop it within a few days.

chickenpox may, in some cases, lead to congenital malformations (although such cases are rare). 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.

If a mother contracts chickenpox at the time of birth, 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?

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease. The NINDS is a component of the National Institutes of Health, the leading supporter of biomedical research in the world.

The NINDS funds and conducts research on a wide range of neurological disorders, such as shingles, to understand their causes and to develop and improve ways to diagnosis, treat, and prevent them.

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. The second is to understand the disease well enough to prevent it, especially in people at high risk. To achieve these goals, scientists need to learn much more about VZV and its effects, including how it becomes latent in nerve cells (neurons), what induces it to become active again, and how such reactivation can lead to postherpetic neuralgia and other complications.

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NINDS supports basic research on a wide range of neurological disorders, including shingles, to understand their causes and develop ways to treat and prevent them.

For example, the NINDS supports research on the interplay between the viral proteins and virus defense mechanisms in neurons to understand why the varicella-zoster virus establishes latency uniquely in neurons and not in other cell types. Other studies focus on how VZV travels along sensory nerve fibers, or axons, and its role in latency and viral reactivation. Scientists also hope to identify molecular mechanisms that regulate the expression of latent viral genes, which may lead to targeted therapy to prevent re-activation.

Research on postherpetic neuralgia includes a study in a new animal model of the condition, to better understand cellular changes that lead to persistent pain. These changes may represent future targets in the form of improved vaccines, new medicines, or even gene therapy.

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How can I learn about or participate in clinical research?

Clinical trials are research studies on humans that are designed to answer specific questions about vaccines or new therapies, to test new ways of using known treatments, or to find out more about a disorder. Clinical studies and trials involving the zoster virus and postherpetic neuralgia may lead to better understanding of shingles and identify potential treatments. Both healthy individuals and people with disorders are needed to advance the understanding of diseases and how to treat them. For more information about clinical trials and how you may participate in a study, see

ClinicalTrials.gov
(www.clinicaltrials.gov)
provides information
about ongoing and
completed federally
and privately supported
clinical studies for a
wide range of diseases
and conditions,
including shingles.



Clinical studies help researchers answer questions about vaccines or therapies, test new treatments, and learn more about diseases such as shingles.

**NIH Clinical Research
Trials and You** (www.nih.gov/health/clinicaltrials/)
provides information about clinical trials, why
they matter, and how to participate, including
links to search for a trial or enroll in a research
matching registry.

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Where can I find more information about research on shingles?

In addition to the NINDS, several other NIH organizations support research relevant to understanding, treating, or preventing shingles and its complications, including the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute on Aging (NIA).

NIH RePORTER (<http://projectreporter.nih.gov>) is a searchable database of current and previously funded research supported by NIH and some other federal agencies. RePORTER also includes links to research results such as patents and publications citing support from these projects.

PubMed (<http://www.ncbi.nlm.nih.gov/pubmed/>) allows users to search millions of journal article abstracts in biomedical research fields. The full text of many articles describing research funded by NIH and other sources is also freely available through **PubMedCentral** (www.ncbi.nlm.nih.gov/pmc/)

Where can I get more information?

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information network (BRAIN) at:

BRAIN

P.O. Box 5801
Bethesda, MD 20824
800-352-9424
www.ninds.nih.gov

Information on shingles also is available from the following organizations:

American Chronic Pain Association

P.O. Box 850
Rocklin, CA 95677-0850
916-632-0922
800-533-3231
www.theacpa.org

National Shingles Foundation

603 W. 115th Street, Suite 371

New York, NY 10024

212-223-3390

www.vzvfoundation.org

National Institute of Allergy and

Infectious Diseases

National Institutes of Health/DHHS

6610 Rockledge Drive, MSC 6612

Bethesda, MD 20892-6612

301-496-5715

www.niaid.nih.gov

National Institute on Aging Information Center

National Institutes of Health/DHHS

P.O. Box 8057

Gaithersburg, MD 20898-8057

800-222-2225

www.nia.nih.gov

National Library of Medicine

National Institutes of Health/DHHS

8600 Rockville Pike

Bethesda, MD 20894

301-594-5983

888-346-3656

www.nlm.nih.gov

Glossary

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

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 people.

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 on-set.

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 individuals.

postherpetic neuralgia—a condition characterized by pain that persists for at least three months after healing of a shingles rash; caused by damage to the nervous system.

prednisone—an anti-inflammatory corticosteroid drug routinely given to individuals who have shingles 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 on-set.

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.



National Institute of
Neurological Disorders
and Stroke

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