How Common is Shingles?

Interview with Theresa Lowry Lehnen (GPN, RNP, PhD) Clinical Nurse Specialist and Associate Lecturer South East Technological University (SETU)

Shingles is an infection of a nerve and the area of skin around it. It is caused by the herpes varicella-zoster virus, which also causes chickenpox.

Most people have chickenpox in childhood, but after the illness has gone, the virus remains dormant in the nervous system. The immune system keeps the virus under control, but later in life it can be reactivated and cause shingles.

It is uncertain exactly why the shingles virus is reactivated at a later stage in life like this. It may be due to having lowered immunity as a result of aging, stress or of an immuno-compromising condition.

It is estimated that about 3 people in every 1,000 have shingles in the UK every year. The figure for Ireland is likely to be similar.

Shingles can occur at any age, but is most common in people who are over 50 years of age.Among people who are over 80 years of age, about 11 people in every 1,000 have shingles each year.

It is much less common in children.

We recently spoke to Theresa Lowry Lehnen, Clinical Nurse Specialist and Associate Lecturer South East Technological University to find out more about this condition, and what community pharmacies need to be aware of in helping to manage and treat this population.

"When the immune system is compromised the virus can re-activate. When reactivated, the virus travels along the affected sensory nerve to reach the corresponding dermatome in the skin where a vesicular rash develops," Theresa explains. "Prior to the rash appearance, the frequent prodromal itching or pain can lead to erroneous and delayed diagnosis. The vesicles pustulate and then scab, usually within 2–4 weeks, but residual scarring is common."

Once the virus activates, it can lead to a painful, blistery rash and the pain can last for months to years. Worryingly, she adds that more than 10% of patients who develop shingles will experience a complication, including blindness, neuropathic pain, and cerebrovascular events. Postherpetic neuralgia is the most common complication, occurring in about one in five patients.

Pathophysiology

VZV is a double stranded DNA human neurotrophic alphaherpes virus. Theresa adds, "Any person who contracted varicella infection (chicken pox) through natural infection by the varicella zoster virus (VZV) or the varicella vaccine can develop herpes zoster. Once the VZV primary infection resolves, it forms a lifelong latency within the cranial or dorsal root ganglia. Herpes zoster infection occurs after reactivation of the latent VZV. The cause of reactivation of VZV is not fully understood, but risk factors include advancing age, stress and immunocompromised status from conditions such as HIV-1 infection, lymphoma, leukaemia, bone marrow transplant, solid organ transplant, and immunosuppressive medications. Other risk factors include Caucasian race, female sex, physical trauma, diabetes mellitus, a prior history and family history of HZ."

During latent varicella, specific varicella zoster memory T cells are produced, suppressing the virus in the sensory root ganglia cells. Over time, the memory T-cell immunity begins to weaken and decline. This decline below the "zoster threshold" leads to reactivation of the virus and development of the herpes zoster infection. Reactivation occurs when VZV is able to overpower immune controls and spreads through the affected ganglions and nerves to reach the skin and manifest as HZ.

Risk factors

The immune system becomes less effective with age and ageing increases the risk of a person developing herpes zoster. She adds, "Depression increases the risk of developing HZ because it affects the immune system. Statins are known to affect the immune system and increases the risk of HZ by 13%. In people with diabetes; the rate of herpes zoster is higher among statins users. People who have taken statins in the past have a higher risk of developing HZ than those who have not."

Diseases such as human immunodeficiency disease (HIV), and lymphoma and medications such as steroids depress the immune system and increase the risk of HZ and other infections.

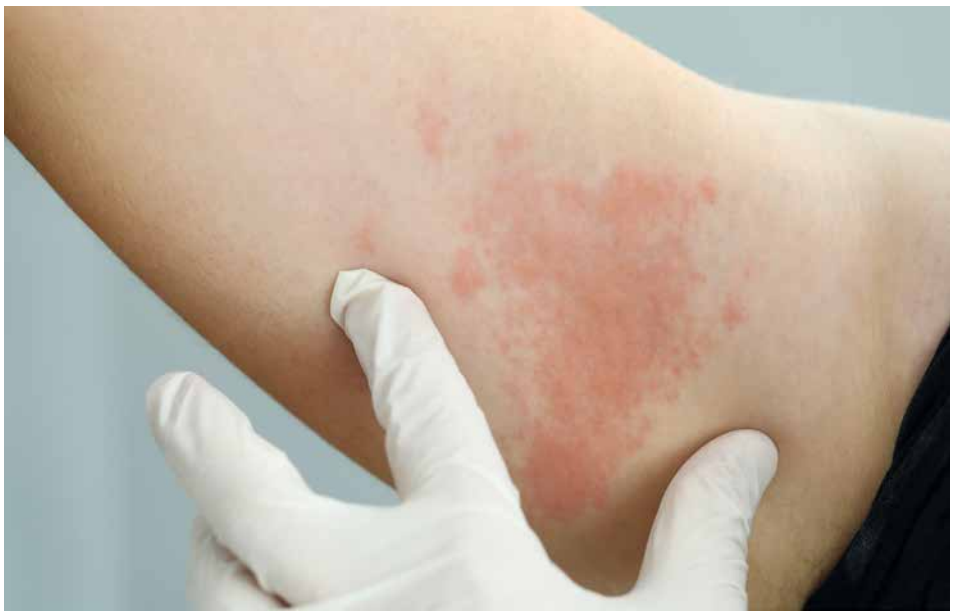
Symptoms, Presentation and Diagnosis

Early symptoms of herpes zoster including headache, fever and malaise are nonspecific, and may result in an incorrect diagnosis. These symptoms are commonly followed by sensations of burning pain, itching, hyperesthesia, or paraesthesia. Pain can be mild to severe in the affected dermatome with sensations such as stinging, tingling, aching, numbing or throbbing interspersed with quick stabs of agonizing pain.

"After one to two days, but sometimes as long as three weeks, the initial phase is followed by the appearance of the characteristic skin rash. The pain and rash most commonly occur on the torso but can appear on the face, eyes, or other parts of the body," Theresa explains.

"A dermatome is an area of skin that is mainly supplied by a single spinal nerve. Usually limited to one (sometimes two) dermatome, a maculopapular rash occurs in a stripe or belt-like pattern on one side of the body and does not cross the midline. Later the rash becomes vesicular, forming small blisters filled with a serous exudate, as the fever and general malaise continue. The painful vesicles eventually become cloudy or darkened as they fill with blood and crust over within seven to ten days. Usually the crusts fall off and the skin heals, but sometimes, after severe blistering, scarring and discoloration remain. Less commonly, the rash can affect three or more dermatomes (disseminated zoster).

"A prodrome of tingling of the forehead may occur. In addition to the painful forehead rash, signs and symptoms may include severe ocular pain; marked eyelid oedema; conjunctival, episcleral, and circumcorneal conjunctival hyperaemia; corneal oedema; and photophobia. Zoster of the trigeminal nerve should be considered in a patient with a prior history of



varicella presenting with blurred vision and a painless red eye. Urgent ophthalmological opinion should be sought."

Around 10% of people with shingles develop ophthalmic complications. In HZO the skin of one side of the forehead and scalp is affected, along with the eye on the same side. "Any part of the eye can be involved, but most commonly it is the eye surface, including the conjunctiva and the cornea," she adds. "The cornea reacts to the infection in various ways; the most serious long-term effects result from damage to the corneal nerves, causing loss of sensation. A small number of people who develop eye complications or neurological complications may not have a rash. Anti-viral treatment should be prescribed as soon as possible. People with moderate to severe HZO should be seen by an ophthalmologist.

"Herpes zoster is diagnosed clinically, based on history and symptom presentation. If necessary, diagnosis can be confirmed from a swab of vesicular fluid by culture or biopsy for electron microscopy. Serology is also available and can be used to demonstrate immunity. A typical history for herpes zoster can include neuropathic pain for around three days followed by a vesicular rash in a dermatomal distribution. The hallmark zoster rash is unilateral, vesicular, and pruritic on an erythematous vesicular base that does not cross the midline. The prodrome period typically precedes the hallmark rash by a few hours to several days. The prodromal symptoms include pain, fever, malaise, headache, itch, and paraesthesia."

Herpes Zoster Vaccines

Herpes zoster vaccines are licensed for individuals aged 50 years and above to reduce the risk of developing zoster and PHN. "It is not necessary to determine whether patients have a history of varicella or zoster prior to vaccination because waning antibodies in previously exposed patient's particularly older adults may lead to negative results despite past infection," Theresa says.

There are two licensed zoster vaccines. Zostavax® and Shingrix®. Zostavax® live attenuated vaccine (designated zoster vaccine live [ZVL] is indicated for prevention of herpes zoster and herpes zoster-related PHN in individuals aged ≥50 years. Shingrix®, non-live recombinant glycoprotein E vaccine (designated recombinant zoster vaccine [RZV] is indicated for prevention of HZ and PHN in adults aged ≥50 years, however, it is currently not freely available in Ireland.

"HZ vaccines should be stored at +2 to +8 degrees C and protected from light. After reconstitution the vaccine should be used immediately and any vaccine unused after 30 minutes should be discarded. The dose of Zostavax is 0.65ml administered IM or SC, preferably in the upper arm.

"Herpes zoster vaccination may be considered in those aged 50 years and above, due to the greater burden and severity of disease in this age group. The vaccine may be given to those who have had zoster. It is preferable to defer vaccination for 12 months after the zoster has resolved so that the vaccine can produce a more effective immune response."

Treatment

The treatment of herpes zoster has three major objectives notes Theresa; treatment of the acute viral infection, treatment of the acute pain associated with herpes zoster and prevention of postherpetic neuralgia. "Early identification and prompt treatment of HZ with antiviral drugs and analgesics frequently reduces acute rash and pain and may prevent some complications. Antiviral drugs have been shown to reduce acute pain and rash severity, accelerate rash resolution and reduce duration of pain. However, many patients experience PHN despite antiviral drug use.

"Herpes zoster can be treated with antiviral medications acyclovir, valacyclovir, or famciclovir, most effective when started within 72 hours after the onset of the rash. Acyclovir, the prototype antiviral drug, is a DNA polymerase inhibitor. Major drawbacks of orally administered acyclovir include its lower bioavailability compared with other agents and its dosing frequency of five times daily.

"Valacyclovir, a prodrug of acyclovir, is administered three times daily. Compared with acyclovir, valacyclovir may be slightly better at decreasing the severity of pain associated with herpes zoster, as well as the duration of postherpetic neuralgia. Valacyclovir is also more bioavailable than acyclovir, and oral administration produces blood drug levels comparable to the intravenous administration of acyclovir.

"Famciclovir is also a DNA polymerase inhibitor. The advantages of famciclovir are its dosing schedule of three times daily, longer intracellular half-life compared with acyclovir and its better bioavailability compared with acyclovir and valacyclovir.

"The choice of which antiviral agent to use is individualised. Dosing schedule and cost may be considerations. All three antiviral agents are generally well tolerated. The most common adverse effects are nausea, headache, vomiting, dizziness and abdominal pain.

"The addition of an orally administered corticosteroid can provide modest benefits in reducing the pain of herpes zoster. Glucocorticoids are an adjunct to antiviral therapy. They reduce acute pain and promote early healing, however, they do not reduce the incidence of postherpetic neuralgia and should not be used without antivirals.

"Paracetamol alone or in combination with a weak opioid such as codeine is frequently used as analgesia. Although postherpetic neuralgia is generally a self-limited condition, it can last indefinitely and patients with PHN may require narcotics for adequate pain control. Addition of drugs active against neuropathic pain e.g. tricyclic antidepressants such as amitriptyline; α-2-δ ligands such as gabapentin or pregabalin or strong opioids such as oxycodone are used for resistant pain but older adults often experience adverse effects. Generally, systemic drugs are poorly effective for the treatment of PHN and have significant side effects. The potential harms of systemic therapies for postherpetic neuralgia should be considered before treating older patients or those with comorbidities. Capsaicin, lidocaine patches and nerve blocks can also be used in selected patients.

"Tricyclic antidepressants can be effective adjuncts in reducing the neuropathic pain of postherpetic neuralgia. These agents most likely lessen pain by inhibiting the reuptake of serotonin and norepinephrine neurotransmitters. Tricyclic antidepressants commonly used in the treatment of postherpetic neuralgia are best tolerated when they are started at a low dosage and given at bedtime. The dosage is increased every two to four weeks to achieve an effective dose. Tricyclic antidepressants share common side effects, such as sedation, dry mouth, postural hypotension, blurred vision and urinary retention. Nortriptyline and amitriptyline appear to have equal efficacy, however, nortriptyline tends to produce fewer anticholinergic effects and is therefore better tolerated.

"Ocular herpes zoster is treated with orally administered antiviral agents, mydriatics and corticosteroids. Although most patients with ocular herpes zoster improve without lasting sequelae, some may develop severe complications, including loss of vision. When herpes zoster involves the eyes, ophthalmologic consultation is recommended. Early treatment with acyclovir 800 mg orally 5 times/day or famciclovir 500 mg or valacyclovir 1 g orally 3 times/day for 7 days reduces ocular complications."