POST-HERPETIC NEURALGIA (PHN) is a form of nerve pain that persists after an acute case of shingles. Shingles is an acute viral infection of the peripheral and central nervous system by the herpes zoster virus, which usually affects a single spinal nerve root.

After causing chickenpox in childhood, the herpes zoster virus lies dormant in the dorsal root ganglion cells of the spinal nerves, constantly being suppressed by the immune system. During times of stress (infection, trauma) or immunosuppression, the virus multiplies, being no longer suppressed by the immune system. This leads to an acute attack of herpes zoster and is more likely to occur in the following groups:

- Cancer patients (on chemotherapy, radiotherapy)
- Immuno-compromised (HIV) and immuno-suppressed patients
- Hodgkin’s disease patients
- Kidney transplantation patients
- Chronic corticosteroid users.

The overall incidence of acute herpes zoster is 1.3-48 cases per 1,000 person-years. Children account for 5%-8% of cases, with adults aged 50-70 accounting for 40%.

The highest incidence is in the over 80s, having an incidence of 10 cases per 1,000 person-years.

During an acute attack, the virus spreads from the dorsal root ganglion travelling upwards to the dorsal horn of the spinal cord, and down the spinal nerve towards the skin. When the virus reaches the skin it causes the typical blistersing rash of shingles, which follows a dermatome.

Clinical features of acute herpes zoster

Pain and/or itching typically precedes the appearance of the rash by several days, most frequently over the thoracic dermatomes. Pain has little or no bearing on the severity of lesions (and vice versa).

The viral outbreak can cause local nerve tissue swelling and reduce blood flow, and cause permanent nerve destruction, affecting the dorsal horn sensory processing centre, the dorsal root ganglion, and also the peripheral sensory receptors in the area of skin affected.

 Destruction of these different nerve areas leads to the syndrome of post-herpetic neuralgia (PHN). Whether or not PHN develops after an acute attack of herpes zoster depends on age, being more common in elderly patients.

PHN is simply defined as persisting pain in the area of the
rash over where the herpes zoster lesions have healed. It presents as:
- Extreme sensitivity of the skin in the area affected by the herpes zoster rash, especially to light touch and brushing of clothing
- Spontaneous pain in the area which may be aching or stabbing in nature
- Musculo-skeletal problems (2% muscle and joints) caused by excessive guarding of the affected area.

**Acute herpes zoster (shingles)**
The two most important reasons for treating acute herpes zoster early are:
- To prevent virus multiplication, thereby reducing damage to the dorsal horn, dorsal root ganglion and peripheral sensory receptors in the skin. The early use of antiviral drugs like aciclovir helps to reduce the severity of acute herpes zoster and the incidence and severity of PHN by limiting viral induced damage. These benefits have only been demonstrated in patients who receive the antiviral agents within 72 hours after the onset of the rash. Antiviral agents may be beneficial as long as new lesions are actively being formed, but they are unlikely to be helpful after lesions have crusted
- To prevent excessive degrees of dorsal horn sensitisation, acute herpes zoster pain has both somatic and nerve components. Early pain management with a combination of paracetamol, NSAIDs, opioids and amitriptyline (a tricyclic antidepressant (TCA)) helps to reduce severe pain and therefore reduce sensitisation of the dorsal horn. There is strong evidence that early use of amitriptyline reduces the incidence and severity of post-herpetic neuralgia.

**Tricyclic antidepressants**
TCAs have an analgesic effect independent of their antidepressant effect and historically have been used in the treatment of chronic neuropathic pain. It has been postulated that these drugs relieve pain by blocking the reuptake of norepinephrine, thereby increasing inhibition of the spinal neurons that promote pain perception. Amitriptyline and nortriptyline were shown to provide effective pain relief in subjects who suffer PHN of at least 6-12 months’ duration. Amitriptyline is the most studied TCA and may be preferred when COA is a primary concern, but nortriptyline may have a more favourable side-effect profile and has efficiency equivalent to amitriptyline.

Unfortunately, cardiac (eg. arrhythmias) and other anti-cholinergic adverse effects, eg. dry mouth, dizziness, drowsiness, confusion, urinary retention and postural hypotension, associated with TCAs, as well as their potential for interaction with other drugs, limit their use in the management of those patients among whom PHN is most common, ie. the elderly.

**Anticonvulsants**
Second-generation anticonvulsant agents (eg. gabapentin and pregabalin) have a mechanism of action for modulating neuropathic pain distinct from that of TCAs. Two large trials (one in the US and one in the UK) demonstrated that gabapentin (1,800mg–3,600mg a day) significantly reduces pain in the subjects who have PHN. The most recent anticonvulsant to be specifically licensed for PHN is pregabalin. **Topical capsaicin (0.025% and 0.075%)**
This is an extract of chilli peppers, which can be useful in some patients. It depletes substance P from sensory nerve endings, thereby decreasing the perception of post-herpetic pain.

Because incomplete depletion of substance P may heighten pain perception, capsaicin cream must be applied at least four or five times daily; if used less often it may actually increase pain.

**Lidocaine patch**
A lidocaine patch was the first product to receive FDA approval specifically for the treatment of PHN. It has the advantage of ease of use, safety and evident response within two weeks after treatment initiation. Limited published evidence suggests that lidocaine patch may have some value in reducing zoster associated pain.

**Corticosteroids**
Orally administered steroids are commonly used in the treatment of herpes zoster, even though clinical trials have shown variable results. Prednisolone used in conjunction with aciclovir has been shown to reduce pain associated with herpes zoster; the likely mechanism involves decreasing the degree of neuritis caused by acute infection and possibly decreases residual damage to affected nerves.

**Opioids**
High dose opioids are effective in the treatment of PHN and are commonly used in the management of acute zoster infections. However, concerns about physical dependence, possible abuse and potential side effects and constipation limit their use.

Some clinicians prefer to treat the patient aggressively with gabapentin and TCAs before progressing to long-term opioid analgesic treatment.

**Herpetic scar desensitisation**
Some patients find that infiltrating the depigmented area of skin with local anaesthetic/steroids on several occasions radically reduces hypersensitivity.

**Clonidine**
The high density of alpha-2-adrenoreceptors in the dorsal horn of the spinal cord suggests there should be a role for clonidine in the treatment of PHN. Pain reduction has been reported after this drug has been used epidurally and orally, but there are no properly constructed controlled trials to show benefit is anything more than a theoretical possibility.

**N-Methyl-D-Aspartate (NMDA) antagonists**
Ketamine and dextromethorphan are NMDA antagonists that have been used in the treatment of PHN. It is thought that tricyclics may have NMDA antagonist activity too. Ketamine has helped in selected cases when given orally or by injection.

Herpes zoster and post-herpetic neuralgia are relatively common conditions, primarily in elderly and immunocompromised patients.

Although the diagnosis of the condition is generally straightforward, treatment can be frustrating for the patient and physician. Approaches to management include treatment of the herpes zoster infection and associated pain, prevention of post-herpetic neuralgia and control of neuropathic pain until the condition resolves.

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