

# PAIN TOPICS

## Shingles and Postherpetic Neuralgia

Anne Louise Oaklander, MD, PhD, and Julia Campeti, BS  
Partners Nerve Injury Unit at MGH

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### Overview

Shingles (herpes zoster) is a painful, necrotizing rash caused by focal reactivation of latent varicella-zoster virus. The virus, which causes varicella (chickenpox) in naïve individuals, lies dormant in sensory ganglia long after the resolution of chickenpox.<sup>1</sup> The most common locations for a shingles rash are the torso and above the eye, but shingles can occur anywhere on the body.<sup>2</sup> Shingles has the highest annual incidence of any neurological illness<sup>3</sup> and will affect 15% of Americans during their lifetime.<sup>4</sup>

Shingles destroys peripheral sensory neurons and can cause serious complications, of which the most common is postherpetic neuralgia (PHN), the persistence of pain in an area affected by shingles at least three months prior. PHN often resolves within the first six months following shingles, but for some, the pain can last for years or indefinitely. Age is the most significant risk factor for developing shingles and, independently, PHN.<sup>5</sup> At least 50% of shingles patients over age 50 and 75% of those over 70 will be left with PHN.<sup>5</sup> Consequently, shingles and PHN are a major health threat to the elderly. Other at-risk populations include those immunocompromised from illness or medication.

PHN causes combinations of various pain complaints. Some PHN patients will experience *mechanical allodynia*, or pain from light touch, and will go to extremes to avoid contact between their PHN-affected skin and clothing, bed sheets, or even a light breeze. Other PHN patients will be left with *hyperalgesia*, or exaggerated pain following a minimally painful stimulus. Others report sudden paroxysms of stabbing or lightning-like pain known as *lancinating pain*. Another complication of zoster is the chronic itch syndrome known as *postherpetic itch* (PHI).<sup>6</sup> PHI is more common after shingles on the face or neck than torso<sup>7</sup> and seems more resistant to medical treatment than PHN.

### Treatment of established PHN

Immediate treatment of shingles with antiviral medications and tricyclic antidepressants is proven to lessen the likelihood and severity of PHN.<sup>8</sup> Treatment of established PHN is similar to that of other neuropathic pain syndromes, with medications as the most effective therapeutic option. Efficacy and safety have been established in placebo-controlled double-blind studies for four categories of treatments:

1. topical local anesthetics
2. tricyclic antidepressants
3. anticonvulsants
4. opioids

It is difficult to predict who will be helped by which medication, so it is often necessary to try several medications before finding the optimal treatment and dose for a particular patient. As a rule, the medications most likely to be effective should be tried first, titrated to an adequate dose, and then discontinued if ineffective or poorly tolerated. Elderly patients should be treated with attention to potential cognitive side effects, hypotension, constipation, cardiac arrhythmia, and urinary retention.

1. **Topical anesthetics** in patch, cream, and other forms are a promising advance for PHN. Applied to painful skin, topical anesthetics act locally, making them ideal for many patients because of the lack of side effects and drug interactions. The Lidoderm™ patch contains 5% lidocaine and is FDA approved for PHN.<sup>9</sup> Lidocaine in gel, ointment, or spray preparations can help patients with pain affecting mucous membranes, especially by allowing them to engage in specific activities (e.g., chewing). Because systemic absorption

can occur when lidocaine is applied to the mucosa, serum levels should be tested. Topical creams and ointments containing capsaicin, a substance P depletor found in chili peppers, are not widely used because of their intolerable burning sensation upon application.<sup>10</sup> A few small clinical trials of topical non-steroidal anti-inflammatory drugs (NSAIDs) have been conducted<sup>11</sup> with uneven results.

2. **Tricyclic antidepressants** (TCAs) are a mainstay of treatment for PHN and other types of neuropathic pain.<sup>12-14</sup> Noradrenergically active TCAs are effective for persistent ongoing pain,<sup>12-15</sup> lancinating pain, and allodynia as well.<sup>15</sup> However, patients rarely obtain total relief from TCAs and are often unable to tolerate their side effects (cognitive changes, constipation, dry eyes and mouth, and orthostatic hypotension).

Desipramine, given in the morning, and nortriptyline, given at night, are the best tolerated; amitriptyline is contraindicated for patients over 65 because of side effects.<sup>15</sup> Initial doses range from 10–25 mg daily, depending on a patient's age and risk for side effects. Elderly patients should always be started on the lowest dose. Dose escalation should proceed in 10–25 mg weekly increments as tolerated. Most patients achieve pain relief in the dosage range of 60–100 mg/day. If marked relief is not obtained at this level, other therapies should be tried. Rare patients benefit from and tolerate doses ranging from 150–250 mg/day.

3. **Anticonvulsant medications** decrease neuronal sodium ingress and excitability. They work against PHN as well as epilepsy because both are associated with excess central neuronal firing. First-generation anticonvulsants, such as carbamazepine, have been shown effective in relieving pain,<sup>16</sup> but gabapentin, with fewer serious side effects, is now preferred. Because of its relatively benign side-effect profile and paucity of drug interactions, gabapentin has become a first-option treatment for neuropathic pain. Moreover, its tolerability allows for higher dosing for treating pain than necessary for epilepsy. With no need to monitor blood tests, the drug is also easy to manage. Gabapentin is effective against different pain qualities in PHN.<sup>17,18</sup>

Initial dosing is 100–300 mg nightly in geriatric patients, increased by one pill (i.e., 100 mg or 300 mg) daily toward 1,800–3,600 mg daily. The most common side effects include mild sedation, dizziness, and edema of the extremities. Gabapentin is expensive, as are other new anticonvulsants (e.g., lamotrigine, topiramate) that have not yet been evaluated in clinical trials for PHN.

4. **Opioids** were once avoided in the treatment of neuropathic pain because of concerns about lack of efficacy and risk of abuse, but they have been shown effective and safe for PHN in several double-blinded placebo-controlled trials.<sup>19,20</sup> Risk of abuse is particularly low among geriatric patients, unless there is prior history.<sup>19</sup> Raja et al.'s recent study compared opioids to TCAs for treatment of PHN and found that both provided effective pain relief but patients preferred opioids.<sup>21</sup> Neither treatment significantly impaired cognitive function.<sup>21</sup>

These data confirm that opioids are a first-line treatment option for geriatric patients. While extended-release opioids are generally preferable for chronic pain, shorter-acting agents may lessen cognitive side effects and accumulation of metabolites in older PHN patients. Methadone is a useful option: long lasting, inexpensive, and available in minute doses adequate for treating smaller or elderly patients. Prescriptions for the opioid must be labeled with the notation "for pain" in order to be filled at most pharmacies around the country.

## Other treatment options

**Intrathecal steroids:** A Japanese group has documented efficacy of intrathecal methylprednisolone for PHN.<sup>22</sup> Subjects were carefully selected and followed for two years. A 90% rating of good or excellent global pain relief was reported, higher than for any other known PHN treatment. However, it is difficult to obtain approval for the intrathecal administration of methylprednisolone, and intrathecal local anesthetics in the mix can potentially cause spinal block and hypotension. Confirmation of these data is awaited.

**Surgery:** Although surgery be effective in some neuropathic pain conditions, it is not an option for PHN. Neurosurgical options should be considered only in rare patients with longtime pain unresponsive to all available medical options. Ablative procedures that sever pain pathways are rarely helpful and sometimes cause additional pain or neurological problems. Most experts in the surgical treatment of PHN discourage ablative procedures.<sup>23</sup> In

rare cases, patients with limited life expectancies may be candidates for ablative techniques that can produce a pain-free interval of a few months.

**Augmentative therapies:** Treatments that augment the function of remaining neurons, such as nerve or spinal cord stimulators, have proven very effective for treating other types of neuropathic pain.<sup>24</sup> Unfortunately, there are few studies in PHN patients. A recent report<sup>25</sup> supports efficacy but requires confirmation by other groups.

**Comprehensive treatments:** An interdisciplinary approach to caring for patients disabled by chronic pain should address the psychosocial burdens and functional impact. Supportive counseling can help some patients and their families. This can encourage safely increasing physical activity and foster reacting to pain in ways that are less negative and self-defeating. Physical and occupational therapies can address loss of strength and range of motion, and maximize function and minimize secondary problems associated with disuse.

## Conclusion

PHN can be a devastating consequence of shingles, a serious and common neurologic disease. The elderly and people with immune systems weakened by disease or medication are at a higher risk of developing PHN than the population in general. Clinicians should be aware of the importance of treating zoster early and aggressively with antivirals, analgesics, and TCAs to lessen complications as well as to provide symptomatic relief. For patients with established PHN, there are four classes of medications documented in clinical trials to be effective and safe.

To learn more about treating shingles, PHN, and other zoster-related complications, please visit the websites of the [Center for Shingles and PHN at MGH](http://www.shingles.mgh.harvard.edu) and the [VZV Research Foundation](http://www.vzvfoundation.org).

## Links

Center for Shingles and PHN at MGH: <http://www.shingles.mgh.harvard.edu>

VZV Research Foundation: <http://www.vzvfoundation.org>

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