Fast Facts and Concepts

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Postherpetic Neuralgia #272

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Background

POSTHERPETIC NEURALGIA (PHN) is a syndrome described as zoster-associated pain persisting for more than three months after resolution of an initial herpes zoster (HZ) rash ('shingles'). This *Fast Fact* discusses PHN.

Epidemiology

Inconsistencies in diagnosis and data collection make the incidence of HZ and PHN difficult to estimate. PHN develops rarely in those under 50 years. However, it occurs in 20% of persons 60 to 65 with HZ, and its incidence rises to 30% in persons over 80 years old. Fish factors for PHN include severe acute shingles-related pain, rash severity (i.e., more than 50 lesions), increasing age, and immunocompromised status. A

Pathophysiology

In acute HZ, reactivation of the virus from the dorsal root ganglia of spinal or cranial nerves causes inflammation and damage to the affected nerve tissue, resulting in acute pain. Subsequently, primary afferent neurons responding to the acute neuronal damage of zoster reactivation can cause sensitization of the nociceptive dorsal horn neurons, resulting in a prolonged exaggerated response to nonnoxious stimuli. This central sensitization is thought to be a key mechanism in the development and maintenance of the pain of PHN.

Natural History

Most HZ patients experience resolution of the rash and acute HZ pain within two months. For those who develop PHN, prolonged severe disabling symptoms rarely remain beyond six months. A small subset may experience irre-

versible damage to skin and sensory abnormalities that can result in ongoing pain for years. For all patients with acute HZ and/or PHN, physical and emotional quality of life can be affected. $^{6-8}$

Prevention

In adults over 60 years old, live vaccination against the zoster virus reduces overall incidence of HZ by 50% and PHN by two-thirds. It is contraindicated in patients with immune deficiencies (primary or acquired, such as patients with leukemia), including patients taking immunosuppressants or high dose corticosteroids. Initiating antiviral drugs within 72 hours of rash onset reduces acute and chronic pain associated with HZ. There is no clear benefit to initiation after this window. ^{10–12} Best available evidence does not support the routine use of glucocorticoids in preventing PHN. ¹⁰

Pain Management Strategies

PHN is a quintessential neuropathic pain syndrome and the approach to treatment is similar to other neuropathic syndromes. Recent guidelines cite strong evidence for using tricyclic antidepressants (TCAs), gabapentinoids (gabapentin, pregabalin), opioids, lidocaine 5% patch, and capsaicin 8% patch to manage PHN. (See *Fast Facts* #49, 148, 255, and 271 for more information about these drugs.) Strong evidence also supports combined therapy of gabapentin plus opioids or TCAs. Second-line therapies include topical salicylate and topical capsaicin 0.075% cream. To date, evidence demonstrates that epidural steroid injections and acupuncture are no better than placebo. While serotonin norepinephrine reuptake inhibitors such as duloxetine are commonly used for neuropathic syndromes (see *Fast Fact* #187), there are currently no published trials regarding their use for PHN.

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Cost

There is limited literature regarding cost effectiveness among commonly used agents. The following table provides current information regarding starting dose, effective dose, and cost.¹⁵

Drug	Starting dose (cost in USD/month)	Typical effective dose (cost/month)
Gabapentin 300 mg capsule	900 mg/day (\$19)	1800 mg/day (\$99)
Pregabalin 50 mg capsule	150 mg/day (\$180)	450 mg/day (\$180)
Desipramine 25 mg tablet	25 mg/day (\$38)	100 mg/day (\$99)
Nortriptyline 50 mg capsule	50 mg/day (\$20)	75 mg/day (\$20)
Lidocaine 5% patch	1 patch per 12 hours (\$217)	1 patch per 12 hours (\$217)
Capsaicin 8% patch		1 patch per 90 days (\$265)

References

- Delaney A, Colvin LA, Fallon MT, et al.: Postherpetic neuralgia: From preclinical models to the clinic. Neurotherapeutics 2009;6:630–637.
- Watson P: Postherpetic neuralgia. Clin Evid Handbook 2011;301–303.
- Nagasako EM, Johnson RW, Griffin DR, Dworkin RH: Rash severity in herpes zoster: Correlates and relationship to postherpetic neuralgia. J Am Acad Dermatol 2002;46(6):834.
- Jung BF, Johnson RW, Griffin DR, Dworkin RH: Risk factors for postherpetic neuralgia in patients with herpes zoster. Neurol 2004;62(9):1545–1551.
- 5. Thyregod HG, et al.: Natural history of pain following herpes zoster. Pain 2007;128:148–156.
- Johnson RW, Bouhassira D, et al.: The impact of herpes zoster and post-herpetic neuralgia on quality of life. BMC Med 2010;8:37.
- 7. Weinke T, Edte A, et al.: Impact of herpes zoster and post-herpetic neuralgia on patients' quality of life: A patient-

- reported outcomes survey. Z Gesundh Wiss 2010;18(4): 367–374.
- Drolet M, Brisson M, Schmader KE, et al.: The impact of herpes zoster and postherpetic neuralgia on health related quality of life: A prospective study. CMAJ 2010;182(16): 1731–1736.
- JPM16.9_Cebula_2013-9491.docxCenters for Disease Control and Prevention: Herpes Zoster Vaccination for Health Care Professionals. 2013. www.cdc.gov/vaccines/vpd-vac/shingles/ hcp-vaccination.htm. (Last accessed March 6, 2013.)
- Thakur R, Philip AG: Treating herpes zoster and post herpetic neuralgia: An evidence based approach. J Fam Pract 2012;61(S9):S9–S15.
- Dworkin RH, Schmader KE: Epidemiology and natural history of herpes zoster and postherpetic neuralgia. In: Watson CPN, Gershon AA (eds): Herpes Zoster and Postherpetic Neuralgia. 2nd ed. New York: Elsevier Press, 2001, pp. 39–64.
- Tyring S, Barbarash RA, Nahlik JE, et al.: Famciclovir for the treatment of acute herpes zoster: Effects on acute disease and postherpetic neuralgia. A randomized, doubleblind, placebo-controlled trial. Ann Intern Med 1995;123: 89–96.
- Attal N, Cruccu G, et al.: EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. Eur J Neurol 2010;17:1113–1123.
- 14. Dubinsky RM, Kabbani H, El-Chami Z, Boutwell C, Ali H: An evidence based report of the quality standards subcommitee of the American Academy of Neurology. Neurol 2004;63:959–965.
- 15. Drugstore.com Online Pharmacy: www.drugstore.com. (Last accessed February 22, 2013.)

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