

# Challenges in NEUROPATHIC PAIN Newsletter

## LITERATURE REVIEW

Yildirim K, Şişecioglu M, Karatay S, et al. The effectiveness of gabapentin in patients with chronic radiculopathy. *Pain Clinic* 2003;15:213-218.

This randomized, placebo-controlled study was performed in 50 patients with lumbosacralgia secondary to L<sub>5</sub> or S<sub>1</sub> radiculopathy. Patients in group 1 (n=25; mean age, 38.0 years; mean duration of radiculopathy, 69.3 months) received gabapentin 900 mg/day to 3,600 mg/day in 3 divided doses, while patients in group 2 (n=25; mean age, 40.5 years; mean duration of radiculopathy, 67.7 months) received placebo for the 8-week study period. At baseline, a standard neurological assessment and a radiological examination were performed. Pain location and severity, muscle strength, spinal flexion, straight leg raise, stretch reflexes and sensory assessments were made at baseline, 1 month and 2 months.

At baseline, clinical parameters were similar between the 2 treatment groups. Spinal MRI demonstrated that patients had bulging and/or protrusion at the level of L<sub>4</sub>-L<sub>5</sub> (75%) and L<sub>5</sub>-S<sub>1</sub> (40%). Significant improvements were seen in all parameters, except stretch reflexes, in the gabapentin treatment group. While improvements were also seen for a number of clinical parameters in patients treated with placebo, they were significantly less than the changes observed with gabapentin. The authors concluded that patients with chronic radiculopathy treated with gabapentin had a significantly better response than those treated with placebo.

## WEB SITES ON NEUROPATHIC PAIN

Various Web sites are devoted to neuropathic pain or pain management and provide useful information for clinicians and patients.

The International Research Foundation for Reflex Sympathetic Dystrophy/Complex Regional Pain Syndrome ([www.rsdfoundation.org](http://www.rsdfoundation.org)) is dedicated to research and education on reflex sympathetic dystrophy (RSD), which is also known as complex regional pain syndrome (CRPS). The site provides practice guidelines for clinicians and a video on the impact of this chronic neurological condition in children.

The Pain Relief Foundation ([www.painreliefoundation.org.uk](http://www.painreliefoundation.org.uk)) is a charity in the UK that funds research on chronic pain and promotes education on pain management. The site provides an overview of a range of painful disorders, including neuropathic pain syndromes such as postherpetic neuralgia, trigeminal neuralgia, CRPS/RSD and phantom limb pain, and links to other Web sites for further information on each of the conditions.

## CONFERENCE CALENDAR

MEETING	25 <sup>th</sup> Annual Scientific Meeting of the Australian Pain Society	The 1 <sup>st</sup> Asian Pacific Conference Against Stroke	7 <sup>th</sup> International Conference on the Mechanisms and Treatment of Neuropathic Pain
LOCATION	Canberra, Australia	Hong Kong	Madrid, Spain
DATE	7-10 March 2004	17-18 April 2004	13-16 May 2004
CONTACT DETAILS	Conference Secretariat: DC Conferences Pty Ltd PO Box 571 Crows Nest NSW 1585 Australia Tel: (+61 2) 9954 4400 Fax: (+61 2) 9954 0666 E-mail: APS2004@dcconferences.com.au Web site: <a href="http://www.apsoc.org.au/conference/index.php">www.apsoc.org.au/conference/index.php</a>	Conference Secretariat: The Federation of Medical Societies of Hong Kong 4/F, Duke of Windsor Social Service Building 15 Hennessy Road, Wan Chai, Hong Kong Tel: (+852) 2549 8898 Fax: (+852) 2866 7530 E-mail: cos@fmshk.com.hk Web site: <a href="http://www.stroke.org.hk">www.stroke.org.hk</a>	Conference Secretariat: 7 <sup>th</sup> International Conference on the Mechanisms and Treatment of Neuropathic Pain c/o Kenes International 17 rue du Cendrier, PO Box 1726 CH-1211 Geneva 1, Switzerland Tel: (+41 22) 908 0488 Fax: (+41 22) 732 2850 E-mail: <a href="mailto:neuropathic@kenes.com">neuropathic@kenes.com</a> Web site: <a href="http://www.kenes.com/neuropathic/">www.kenes.com/neuropathic/</a>

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A Leader of Research and Education in Pain Management



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Welcome to the sixth issue of Challenges in Neuropathic Pain, a newsletter brought to you by the members of the Multidisciplinary Panel on Neuropathic Pain. The Panel celebrates their second birthday in December 2003. Since its inception, the Panel has developed a wide range of projects, including recommendations on neuropathic pain, a patient information leaflet and poster, a certificate course on neuropathic pain and, of course, this newsletter.

In this issue, recommendations on the management of poststroke pain are presented, as well as an interesting case on acute transverse myelitis. Regular features, including a literature review, Q&A, useful Web sites and a calendar of upcoming conferences, will keep Hong Kong clinicians informed of the latest news on neuropathic pain.



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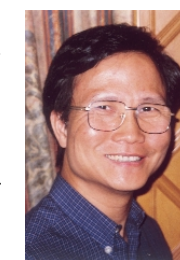
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## RECOMMENDATIONS FOR THE MANAGEMENT OF POSTSTROKE PAIN

One of the key initiatives of the Multidisciplinary Panel on Neuropathic Pain is the development of treatment recommendations for a number of common neuropathic pain syndromes. The recommendations will better assist general practitioners to recognize the signs and symptoms of neuropathic pain, and to initiate appropriate treatment. In this issue, a summary of the recommendations for managing poststroke pain is presented. Dr Wong Chun Por was the project leader for these recommendations.



### Pathophysiology, Prevalence and Symptoms

Several types of pain can occur following a stroke. Pain caused by stroke-related damage to the central nervous system is termed 'central pain'. Pain may also arise from rigidity and reduced mobility, or from pre-existing conditions, such as osteoarthritis, which should be differentiated from central pain. Central poststroke pain (CPSP) is a neuropathic pain syndrome characterized by constant or intermittent pain following stroke. CPSP was initially termed 'thalamic syndrome' as the lesions caused by the stroke were thought to be located in the thalamus, but CPSP may also arise from extrathalamic lesions. Nociceptive pain (eg, frozen shoulder) may also occur in CPSP patients.

The incidence of CPSP has been reported at 8%, with moderate-to-severe pain reported by 5% of all stroke patients.<sup>2</sup> The onset of pain occurs within 1 month in over half of all CPSP patients; however, in some patients, CPSP can take more than 6 months to develop.<sup>2</sup> CPSP tends to affect younger stroke patients. Typical symptoms of CPSP are outlined in Figure 1. Pain may be unilateral, or it may only affect small areas. Pain intensity may also vary within the affected area. Furthermore, symptoms can be exacerbated by stress and reduced by relaxation.

Figure 2: Differentiating central poststroke pain from nociceptive pain<sup>3</sup>

- Test sensation to sharp and blunt objects in the affected area
- Test the sensation to warmth (eg, touch with a finger) and coolness (eg, a metal instrument) in the affected area
- If a patient is unable to differentiate between sensations in either or both of the above tests, CPSP is a probable diagnosis

Figure 1: Typical symptoms of central poststroke pain<sup>3</sup>

- Burning or freezing pain sensation
- Difficulties distinguishing sharp from blunt and warm from cool in the affected area
- Allodynia (pain sensation from a normally nonpainful stimulus)

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## Diagnosis

Because the onset of CPSP can occur several months after a stroke, primary-care physicians involved in poststroke care and responsible for follow-up must be alert to the possible development of pain. All stroke patients reporting pain should be assessed for CPSP. Techniques for differentiating CPSP from nociceptive pain are described in Figure 2.

## General Management of Poststroke Pain

### Nociceptive pain

1. Differentiate nociceptive pain from CPSP, and treat nociceptive pain appropriately.
2. Nociceptive pain (such as frozen shoulder) should be treated with analgesic agents (eg, nonsteroidal anti-inflammatory drugs, COX-2 inhibitors or opioids), intracapsular injection and physiotherapy. Physiotherapy should be commenced as soon as possible after a stroke.

### Central poststroke pain

1. Record the CPSP baseline (or pretreatment) pain intensity to allow comparison with posttreatment pain. A visual analogue scale (VAS) is one of the simplest means of assessing pain. Patients rate their pain on a scale from 0 mm (no pain) to 100 mm (excruciating pain).
2. Counsel patients in relaxation techniques, as stress can exacerbate pain.
3. Commence treatment with a tricyclic antidepressant (TCA), such as amitriptyline, as a first-line agent. Lamotrigine can be considered as an alternative first-line agent. Gabapentin may also be effective in CPSP. If pain relief is unsatisfactory with first-line agents, mexiletine may be used as an adjunct. Early treatment improves outcomes for CPSP patients. Conventional analgesics, including opioids, tend not to be effective in treating CPSP.<sup>3</sup>
4. Consider referral to a multidisciplinary pain centre if a patient remains refractory to pharmacotherapy after 2 to 3 months of treatment.

## Pharmacological and Nonpharmacological Treatment of CPSP

Relatively few clinical trials have investigated the treatment of CPSP. TCAs or anticonvulsants are the usual first-line treatments. Pharmacological management should be supplemented with physical and psychological interventions.

Recommendations for pharmacological treatments are based on published clinical evidence and current clinical practice; however, some of the agents may not be approved for use in neuropathic pain syndromes. Clinicians should consult local prescribing information before initiating treatment.

1. Amitriptyline controls pain in CPSP patients more effectively than carbamazepine and is better tolerated.<sup>4</sup> TCAs, such as amitriptyline or nortriptyline, should be considered as first-line therapy. To minimize side effects, patients should begin with a low dose and titrate to a higher maintenance dose. In elderly patients, amitriptyline should be commenced at 25 mg daily and titrated to 75 mg daily, or the maximum tolerated dose. In frail or very elderly patients who are often sedated by TCAs, consider a lower starting dose of amitriptyline (eg, 10 mg daily).
2. Lamotrigine is an alternative first-line treatment.<sup>5</sup> Lamotrigine should be titrated from 25 mg daily to a maximum dose of 200 mg

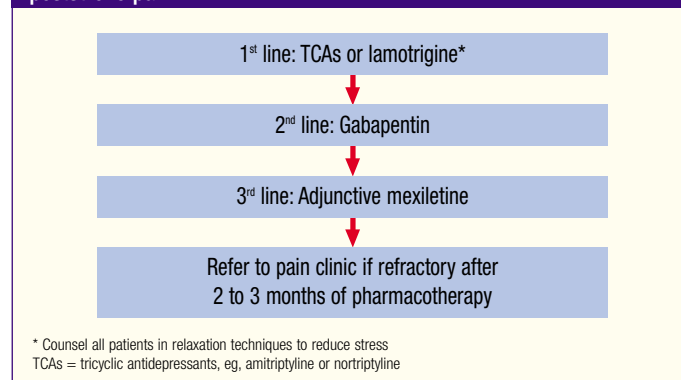


daily, or the maximum tolerated dose. However, a rare, but potentially life-threatening, complication of lamotrigine is Stevens-Johnson syndrome.

3. Gabapentin is approved for the treatment of neuropathic pain and may be effective in treating CPSP.<sup>6</sup> Gabapentin should be commenced at 300 mg at bedtime and increased by 300 mg every 3 days up to a dose of 1,800 mg daily after 1 week (given in 3 divided doses). If higher daily doses are required for maintenance, the maximum recommended dose is 3,600 mg daily (a lower dose is recommended in patients with renal impairment). For elderly patients or patients susceptible to side effects, the recommendation is to increase the gabapentin dosage by 300 mg each week, or to begin with a lower dose (eg, 100 mg).
4. Mexiletine is an antiarrhythmic agent and may be used as an adjunct to TCAs when patients do not respond to TCAs alone.<sup>3</sup>
5. Intravenous lignocaine may provide pain relief in some patients.<sup>7,8</sup>
6. Surgical interventions can be considered for patients unresponsive to pharmacological therapy; however, these treatments have associated morbidity and mortality. Precentral cortex stimulation, spinal cord stimulation and stereotactic mesencephalic tractotomy may benefit selected CPSP patients.<sup>9,10</sup>

Patients should be referred to a multidisciplinary pain centre for treatment if pain continues for 2 to 3 months despite pharmacological therapy. CPSP tends to be persistent and can be difficult to treat.

Figure 3: Pharmacological treatment options for central poststroke pain



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## CASE PRESENTATION

In each issue, a case study is presented on a relevant neuropathic pain syndrome. Reviewing case studies will help to improve your diagnostic approach to neuropathic pain and increase your understanding of how to select treatment strategies based on presenting symptoms. In this issue, a case of acute transverse myelitis is discussed.

## Acute Transverse Myelitis

### Presenting Symptoms

A 38-year-old man presented to the Accident & Emergency Department with acute onset of numbness on the left side of his body that had persisted for 3 days. He was admitted to the Medical Department with the diagnosis of sensory stroke.

### Medical History

The patient had enjoyed good health in the past and denied any history of drug abuse. He had had a mild viral infection 2 weeks before the acute onset of paraesthesia and reported reduced sensation on the left side of his body from the neck down, including the limbs. The symptoms slowly worsened during the few days before admission. The patient also complained of very mild weakness in his left arm and leg. Vision, speech, swallowing and sphincter function were normal.

### Clinical Examination

Physical examination upon admission showed that the patient was fully conscious with normal cognitive function. All cranial nerves were intact. Hypoaesthesia to pinprick, temperature and touch was found on the left side of his body below the T<sub>2</sub> level. The patient's left hand and medial aspect of the left arm were also affected. Vibration and proprioception sensations were intact in all limbs. The tone in both lower limbs was mildly increased. All tendon reflexes were normal and the plantar response was flexor on both sides. There was minimal weakness in his left-sided limbs. The Romberg test was negative and his gait was normal. A noncontrast computed tomograph brain scan was normal on the day of admission.

Over the next 2 days, the patient complained that the abnormal sensations were becoming more unpleasant and had spread to the right side of his body. A magnetic resonance

imaging (MRI) scan of the spine showed a T<sub>2</sub> hyperintense signal, while gadolinium enhancement of the spinal cord from level C<sub>2</sub> to mid-C<sub>4</sub> revealed mild cord expansion (Figure 4). Brain MRI, cerebrospinal fluid and blood tests were unremarkable.

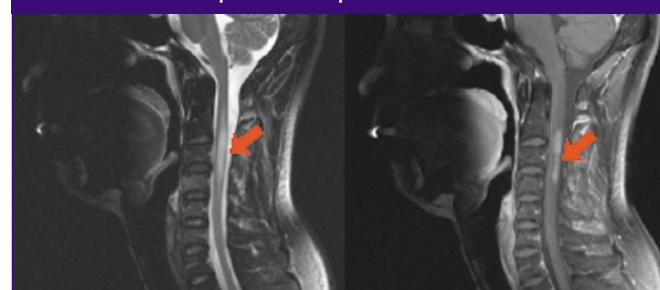
### Interpretation

Typical clinical features of complete spinal cord syndrome include symmetric motor, sensory and sphincter dysfunction below the level of the lesion. Incomplete spinal cord syndrome is frequently encountered, particularly in the case of myelitis. Sensory symptoms include neuropathic pain, which may be asymmetric and can be the dominant presenting feature, as illustrated in this case. The level of sensory symptoms is an important clue to determine the location of the underlying spinal cord lesion.

### Management

After the identification of transverse myelitis, adequate work-up to identify any underlying associated disease, such as infection, connective tissue disease and vasculitis, are required to delineate the exact diagnosis. This has important implications for subsequent management. The diagnosis in this case was idiopathic acute transverse myelitis, though transverse myelitis can be caused by multiple sclerosis. The patient was treated with intravenous pulse methylprednisolone (1 g daily for 3 consecutive days). Motor function recovered rapidly, but the patient still had troublesome dysaesthesia on his left side. The neuropathic pain responded well to a combination of amitriptyline and carbamazepine. The patient returned to work soon after discharge and within 2 weeks of the onset of symptoms. A follow-up MRI several months later showed complete resolution of the spinal cord abnormalities.

Figure 4: MRI of the cervical spine shows hyperintense T<sub>2</sub> signal (left); gadolinium enhancement (right) from C<sub>2</sub> to C<sub>4</sub> level demonstrates mild spinal cord expansion



## Q&A

Readers are encouraged to send questions to members of the Multidisciplinary Panel on Neuropathic Pain. Please forward your questions concerning any aspect of neuropathic pain and its management to [mpnp@medimedia.com.hk](mailto:mpnp@medimedia.com.hk) or fax to (+852) 2559 6910.

### Is sciatica a type of neuropathic pain?

Sciatica, a common cause of low back pain, is a type of neuropathic pain that occurs when the sciatic nerve or lumbar root nerves are compressed. It is often accompanied by pain radiating from the back into the buttock and, sometimes, down the entire leg. Common symptoms of sciatica include changes in sensation in the calf muscle or foot, pain, paraesthesia and numbness. Some patients may have difficulty walking. Conservative treatment involves physiotherapy, hot packs and manipulation, and is often an appropriate treatment approach as sciatica can resolve on its own with time. Patients should be instructed to try to maintain mobility. Other treatment options include oral NSAIDs, gabapentin (see Literature Review), epidural corticosteroid injections, percutaneous and transcutaneous electrical nerve stimulation, chemonucleolysis and surgical interventions, such as discectomy.