

Neuropathic pain: recognition and diagnosis

GUY BASHFORD MB BS, Dip MSM, FAFRM, FFPMANZCA

Despite the complex pathophysiology of neuropathic pain, diagnosis is usually straightforward, relying on negative and positive symptoms and signs in the presence of a condition that can damage the somatosensory system.

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Neuropathic pain is a common cause of persistent pain in the general practice population. It is defined as 'pain arising as a direct consequence of a lesion or disease affecting the somatosensory system'.¹ This replaces the less strict definition used in the past – pain initiated or caused by a primary lesion or dysfunction in the nervous system.

In a significant proportion of patients, neuropathic pain arises when disease or trauma affects the sensory peripheral nerves or somatosensory regions of the spinal cord or brain. The most common causes of neuropathic pain and their prevalence are shown in the Table.

Most neuropathic pain is due to ectopic nerve activity in damaged peripheral nerves and complex neuroplastic changes occurring in the spinal cord and brain in response to the damaged somatosensory nervous system – termed central sensitisation. Similar central sensitisation is seen in conditions such as complex regional pain syndrome type I and fibromyalgia, but without evidence for an underlying nerve lesion.

Nociceptive pain, in contrast, is caused by tissue damage or potentially tissue-damaging stimuli. However, even in seemingly straightforward cases of nociceptive pain, such as in osteoarthritis of the knee, persistent pain often leads to central nervous system changes that blur the correlation between the severity of tissue damage and the pain perceived by the individual. In addition, neuropathic pain is not a diagnosis of exclusion and often coexists with nociceptive pain.

Associate Professor Bashford is a Staff Specialist in Pain and Rehabilitation Medicine at the Illawarra Pain Management Service, Port Kembla Hospital, Port Kembla; and Clinical Associate Professor at the Graduate School of Medicine, University of Wollongong, NSW.

TABLE. COMMON CAUSES AND PREVALENCE OF NEUROPATHIC PAIN

Cause of pain	Prevalence (per 100,000)
Sciatica (a mixed pain)	2100
Diabetic peripheral neuropathic pain	600
Postherpetic neuralgia	500
Cancer-related neuropathic pain	200
Spinal cord impairment	120
Multiple sclerosis	51
Phantom limb pain	50
Central poststroke pain	30
Trigeminal neuralgia	15

Patients with neuropathic pain have, on average, greater distress and psychosocial comorbidities than those with nociceptive pain.² This is likely to be due in part to delayed diagnosis and to inaccurate psychiatric or nociceptive labels used to explain the patient's symptoms.

It is important to identify neuropathic pain for the following reasons:

- to avoid frustrating and potentially dangerous diagnostic efforts seeking a nonexistent source of nociceptive pain
- to help the patient and their family understand the basis of their pain as a first step to managing it
- to provide appropriate treatment, as neuropathic pain responds to pharmacological and nonpharmacological therapies largely different from those used for nociceptive pain; for example, neuropathic pain is usually refractory to simple analgesics but may respond to tricyclic antidepressants such as amitriptyline, serotonin and noradrenaline reuptake inhibitors (e.g. venlafaxine, duloxetine) and certain antiepileptic drugs (e.g. gabapentin, pregabalin).

Management of neuropathic pain will be discussed in a future issue of *Medicine Today*.

RECOGNITION OF NEUROPATHIC PAIN IN GENERAL PRACTICE

The prevalence of neuropathic pain is around 7 to 8% in the general population but is higher among people with conditions that damage the peripheral or central somatosensory nervous system.^{3,4} In diabetes and stroke, a minority of patients develop neuropathic pain (around 11% and 8%, respectively), but in other, less common, conditions such as multiple sclerosis and spinal cord injury, the prevalence of neuropathic pain may be much higher (over 50%). Postherpetic neuralgia is another well-recognised cause of neuropathic pain.

Postsurgical neuropathic pain is potentially the most common form of neuropathic pain, although its prevalence in the general population is unclear. Some types of surgery result in neuropathic pain in almost 50% of patients (e.g. breast, hernia and thoracotomy procedures). Other common procedures such as total knee arthroplasty can lead to persistent neuropathic pain in 10 to 15% of cases. The understandable desire of GPs and surgeons to identify complications of surgery can enormously delay diagnosis of neuropathic pain and lead to inappropriate treatments.

In some disease states, such as stroke,

the onset of neuropathic pain can be delayed and sensory deficits can be subtle, making diagnosis difficult. In people with diabetes, neuropathic pain due to polyneuropathy must be distinguished from vascular, musculoskeletal and infective causes of pain.

HISTORY AND PHYSICAL EXAMINATION

The complicated pathophysiology of neuropathic pain can lead doctors to believe diagnosis is more difficult than it is in reality. The first step is recognising the presence of a condition in which the peripheral or central nervous system may have been damaged and where underlying tissue damage is unlikely to be causing the pain. Relatively straightforward history taking and physical examination are then likely to provide the diagnosis.

History taking should seek negative and positive symptoms:

- negative symptoms reflect reduced sensation and are present in a distribution corresponding to the proposed peripheral or central nervous system lesion; these symptoms may be subtle (e.g. reduced peripheral sensation in people with diabetes, reduced light touch, hot or cold sensation in patients with stroke, and reduced sensation to one side of a surgical scar)
- positive symptoms include:
 - spontaneous pain (pain arising without a stimulus)
 - hyperalgesia (increased pain sensitivity to a nociceptive or painful stimulus)
 - allodynia (pain in response to a non-nociceptive stimulus).

Because of the involvement of the central nervous system in the development of positive symptoms such as allodynia and hyperalgesia, these symptoms are not always confined to the distribution of the damaged peripheral nerve.

A history of pain evoked by light touch such as clothes or bedclothes, an abnormal response to hot or cold sensations or

spontaneous pain in an area of numbness suggest neuropathic pain. Another characteristic clinical feature is summation, where repetitive stimulation evokes progressively worsening pain. Paraesthesias (e.g. tingling or the sensation of ants crawling under the skin) are more common in patients with neuropathic pain than in those with nociceptive pain.

Complex neurological examinations are often undertaken in research settings but are usually not necessary for the diagnosis of neuropathic pain in general practice. The physical examination should include an attempt to identify an area of reduced sensation in an anatomical area consistent with the presumed underlying neurological disease or trauma. Examples include stocking sensory loss in a person with diabetes and numbness to one side of a surgical scar. Allodynia can be elicited by the stroke of a brush. In some circumstances, GPs may wish to test with other stimuli, such as cold or heat, but this is rarely necessary for diagnosis.

The likelihood of neuropathic pain can be graded using an algorithm outlined by Treede and colleagues.¹ In the presence of pain with a distinct neuro-anatomically plausible distribution and a history suggesting a relevant lesion or disease, neuropathic pain is considered:

- definite if both the distribution of the pain and the relevant lesion have been confirmed by at least one test (which may include clinical sensory examination for distribution)

- probable if either the distribution or the lesion has been confirmed by at least one test
- possible if neither the distribution nor the lesion has been confirmed by a test.

SCREENING TOOLS

Several screening tools for neuropathic pain are recommended in recent guidelines and can be of use to GPs.^{5,6} The simplest of these are:

- the DN4 (Douleur Neuropathique-4) questionnaire, which gives a score out of 10 after two simple historical questions have been answered and two simple physical examination techniques performed.⁷ It formalises the recommended history and physical examination for GPs (see the box on this page)
- Pain Detect, which is a self-report questionnaire (available online at http://www.virtualmedicalcentre.com/calc_pfizer_pain_detect.asp).

As with all forms of persistent pain, it is important for GPs to regularly assess the psychosocial aspects of the patient's pain as well as the biological components. The Brief Pain Inventory can assist with this.⁸

OTHER INVESTIGATIONS

Radiological or electrophysiological testing may provide additional evidence for a disease or lesion involving the somatosensory nervous system (e.g. a thalamic stroke). However, it is important to

DN4 SCREENING QUESTIONNAIRE FOR NEUROPATHIC PAIN⁷

Each characteristic or symptom is checked yes or no, and each yes answer is scored one point, giving a score out of 10. A score of 4 or more is diagnostic of neuropathic pain.

Interview of the patient

1. Does the pain have one or more of the following characteristics?

- Burning
- Painful cold
- Electric shocks

2. Is the pain associated with one or more of the following symptoms in the same area?

- Tingling
- Pins and needles
- Numbness
- Itching

Examination of the patient

3. Is the pain located in an area where the physical examination reveals one or more of the following characteristics?

- Reduced touch sensation
- Reduced pinprick sensation

4. In the painful area, can the pain be caused or increased by:

- Brushing?

remember that standard nerve conduction studies are relatively insensitive for detecting A-delta or C-fibre dysfunction. Damage to these small sensory fibres is a frequent cause of neuropathic pain.

At a research level, functional neuroimaging (positron emission tomography and functional MRI) provides enormous insight into the neuroplastic nature of pain and is likely to help accelerate the development of more effective treatments for neuropathic pain.

SUMMARY

- Neuropathic pain is a common cause of persistent pain in the general practice population and results from damage to the peripheral or central parts of the somatosensory nervous system. Some of the central pathophysiology of neuropathic pain is shared with other types of persistent pain.
- Nociceptive causes of pain should also be considered, but neuropathic pain is not a diagnosis of exclusion and often both types of pain are present in the same patient.
- Diagnosis of neuropathic pain is important to help patients understand that they are suffering from real and distressing symptoms in the absence of tissue damage and to allow early treatment with appropriate pharmacological and nonpharmacological therapies.
- It is important to identify individuals with disease processes that are likely to lead to neuropathic pain, including persistent postsurgical pain.
- Screening tools such as DN4 and Pain Detect can be of assistance to GPs.
- History taking and physical examination need not be complicated; they involve seeking negative and positive sensory symptoms and signs consistent with a sensory lesion and the resulting pain.
- Patients with neuropathic pain have, on average, greater distress and

psychosocial comorbidity than those with nociceptive pain. **MT**

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