Introduction

Peripheral nerve entrapment is often associated with neuropathic pain symptoms. These recommendations – an update of the recommendations first published in 20051—describe the management of some of the more common causes of neuropathic pain due to peripheral nerve entrapment. The recommendations are structured by nerve level as follows:

- Root level
  - Cervical radiculopathy
  - Lumbar radiculopathy
  - Less common causes
  - Brachial plexus injury
  - Thoracic outlet syndrome
- Peripheral nerve level
  - Carpal tunnel syndrome
  - Cubital tunnel syndrome
  - Other sites
  - Less common cause
  - Radial tunnel syndrome

Treatment of neuropathic pain associated with peripheral nerve entrapment differs from other neuropathic pain conditions, such as post-herpetic neuralgia, painful diabetic neuropathy and trigeminal neuralgia, in that surgical decompression is often a first-line treatment option, rather than pharmacological treatment. Nerve repair may be required in cases of nerve injury; these procedures are beyond the scope of this paper. In the presence of a definite mechanical compression, the primary...
goal is surgical decompression of the nerve. However, conservative treatment and pharmacotherapy tend to be more effective when neuroimaging shows no significant compression on the affected nerve root. Neuropathic pain sometimes persists following surgical decompression or repair of compressed or damaged nerves. In these cases, pharmacotherapy is an appropriate treatment option.

Neuropathic Pain Associated With Nerve Entrapment at the Root Level

Cervical Radiculopathy
Cervical radiculopathy is a common symptom in patients with cervical spondylosis. Cervical spondylosis is a degenerative condition of the cervical vertebrae, intervertebral discs and surrounding ligaments. While cervical spondylosis may occur in people with a previous neck injury, the main risk factor is ageing.

Symptoms typically include neck pain, pain and paraesthesia radiating down the arms; dizziness; headache; progressive neck stiffness; and progressive weakness of the upper limbs. Cervical spondylosis is characteristic of radiculopathy. Cervical radiculopathy is commonly the result of nerve compression at the root, caused by a bulging intervertebral disc, osteophytes or a hypertrophic facet joint. Recommendations for diagnosis and management of cervical radiculopathy associated with spondylosis are summarized in Table 1.

Diagnosis
Patients with cervical radiculopathy may have weak muscles in the affected myotome, sensory deficit in the affected dermatome, and abnormal reflexes. Pinprick and light touch sensation may be reduced on the affected side. Helpful investigations in the diagnosis of cervical spondylosis include:3

- History and physical examination (e.g., muscle weakness, reduced reflexes, reduced sensation)
- Cervical spine or neck X-ray
- CT or MRI scan of the spine
- Electrophysiological studies*
- Myelogram (largely replaced by MRI)

Treatment

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Surgical interventions

| Anterior discectomy with spinal fusion | Discetomy |
| Microforaminotomy                  | Microdiscectomy |
| Cervical arthroplasty               | Percutanous discectomy |
| Lumbar foraminotomy                | Lumbar spinal fusion |

* Electrophysiological studies are recommended in cases where clinical diagnosis is not certain.

CT = computed tomography; MRI = magnetic resonance imaging; NSAID = nonsteroidal anti-inflammatory drug; PENS = percutaneous electrical nerve stimulation; TENS = transcutaneous electrical nerve stimulation.

Table 1. Diagnosis, management and treatment of neuropathic pain associated with nerve injury/entrapment at the root level

- **Cervical spine or neck X-ray:** Degenerative changes consistent with cervical spondylosis should be present, including narrowing of the intervertebral foramina by osteophytes.
- **Computer tomography (CT) or magnetic resonance imaging (MRI) scan of the spine:** To confirm that the nerve root or spinal cord are compressed.
- **Neurophysiological studies:** Nerve conduction testing and electromyography (EMG) to measure the impact on nerve conduction and skeletal muscle activity.
- **Myelogram:** This invasive technique can confirm the extent of thecal sac narrowing. It is not commonly used with the advent of MRI.

Treatment

**Conservative treatment:** This may include short-term use of a cervical collar during the acute phase (a soft collar will in most cases be sufficient for conservative treatment), oral nonsteroidal anti-inflammatory drugs (NSAIDs), neck care exercises, postural training and activity modification, and intermittent cervical traction. While many cases of cervical spondylosis respond to conservative treatment, patients with cervical radiculopathy
may require surgical decompression of the nerve root.

Patients with painful cervical radiculopathy and neuropathic pain symptoms may improve with pharmacotherapy, such as antidepressant or anticonvulsant agents. A recently published observational, prospective study in the treatment of painful cervical or lumbosacral radiculopathy in a primary care setting revealed that pregabalin monotherapy or add-on therapy, versus non-pregabalin pharmacotherapy, for 12 weeks resulted in improvements in pain, anxiety symptoms, depression, sleep disturbance, general health and level of disability; improvements were significantly greater in the pregabalin groups.4

There is some evidence for a role for epidural corticosteroids in the management of cervical radiculopathy.5,6 One systematic review concluded that there is moderate evidence for cervical interlaminar and transforaminal epidural steroid injections in providing long-term relief.6 However, care must be taken with these procedures, with some evidence for rare, but severe, neurologic complications reported for transforaminal cervical epidural steroid injection.7 A review of complications of interlaminar cervical epidural steroid injections revealed that it is a relatively safe procedure, with most adverse reactions being minor and transient, but serious complications may also result.8 Hence, patients should be referred to experienced physicians for epidural corticosteroid injection.

Surgical interventions: Surgery is indicated when other treatments have failed. The main aim of surgery in patients with cervical myelopathy and radiculopathy is decompression of the spinal cord or nerve root. However, surgical interventions are associated with complications (1% to 8% of patients), including death (0% to 1.8%).9 Complications resulting from damage to the spinal cord include tetraplegia, and those resulting from damage to the nerve root include muscle weakness. Patients with pain only are the most difficult group to treat; surgery tends to be more beneficial in patients with severe neurologic deficits.

Surgical decompression of the nerve root is often achieved via an anterior approach (with removal of the intervertebral disc and osteophyte), or a posterior approach (with laminectomy). A 2002 Cochrane review on the role of surgery in cervical spondylotic radiculomyelopathy identified two controlled trials involving 130 patients.9 The most common surgical interventions were via an anterior cervical approach with spinal fusion. Patients receiving surgery via a posterior approach underwent laminectomy. Control interventions included physiotherapy, hard or soft cervical collar, anti-inflammatory drugs, intermittent bed rest and prevention of vigorous activities. Surgery patients had greater improvements in pain, weakness and sensory loss in the short term than control patients. However, after 1 to 2 years’ follow-up, there were no significant differences observed between groups. The authors concluded that there was inadequate data with which to determine whether surgical interventions were superior to more conservative therapy.

Recent years have seen new modalities put into practice, including microsurgical cervical foraminotomy, either via an anterior or a posterior approach, and spinal arthroplasty. Posterior or anterior cervical microforaminotomy, designed to enlarge the space through which the nerve root exits the spinal cord, is associated with good clinical outcomes even without a discectomy being performed.10–12 Two prospective, randomized, multicentre trials in 2007 reported significantly greater neurological and clinical improvement in patients treated by cervical arthroplasty compared with those treated by anterior cervical disectomy and fusion.13,14 Appropriate patient selection is crucial to achieving good outcomes with these procedures.

Lumbar Radiculopathy
Lumbar radiculopathy is a common cause of low back and lower limb pain, occurring when the lumbar root nerves are compressed. Lumbar spondylosis is a degenerative condition of the lumbar vertebrae, intervertebral discs and surrounding ligaments. While lumbar spondylosis may occur in people with a previous back injury, the main risk factor is ageing. Pain can radiate from the back into the buttock and, sometimes, down the entire lower limb.

Symptoms of lumbar radiculopathy include changes in sensation in the calf muscle and feet, numbness, pain (which may be severe) and paraesthesia. Patients with lumbar radiculopathy may also have weakness in the knee or foot, and difficulty walking. Recommendations for diagnosis and management of lumbar radiculopathy are summarized in Table 1.

Diagnosis
Patients with lumbar radiculopathy may have weak muscles in the affected myotome, sensory deficit in the affected dermatome, a positive straight-leg-raising test, and abnormal reflexes. Pinprick and light touch sensation may be reduced on the affected side. Some of the more common tests to diagnose
Lumbar radiculopathy include:

- **Lumbar spine X-ray:** Degenerative changes consistent with lumbar spondylosis should be present, including narrowing of the intervertebral foramina by osteophytes.
- **CT or MRI scan** to determine the location of disc herniation or nerve root compression.
- **Neurophysiological studies:** Nerve conduction testing and electromyography (EMG) to measure the impact on nerve conduction and skeletal muscle activity.
- **Myelogram,** which is invasive and has been largely replaced by MRI.

**Treatment**

**Conservative treatment:** Conservative treatment for lumbar radiculopathy is often appropriate as the condition can resolve with time; most patients with lumbar disc herniations improve over 6 weeks. Compared with conservative care, early surgery results in more rapid relief of sciatica, but both treatments show similar outcomes in the long term. Maintaining mobility is important; bed rest has minimal effectiveness in reducing pain and symptoms associated with lumbar radiculopathy. Physiotherapy, including hot packs, manipulation and intermittent pelvic traction, may be beneficial. Oral NSAIDs may help improve pain and reduce symptoms.

A 2003 study demonstrated that gabapentin was effective in patients with chronic radiculopathy (L4-5 and L5-S1 bulging and/or protrusion). This study randomized 50 patients to gabapentin (up to 3,600 mg daily in three divided doses) or placebo for an 8-week trial period, with gabapentin-treated patients achieving significant improvements in pain at rest and other clinical parameters. More recently, a published case report described two patients with sciatica who were successfully treated with gabapentin. In addition, as mentioned in the section on cervical radiculopathy, pregabalin as monotherapy or add-on therapy improved patient-reported clinical outcomes in patients with painful lumbar or cervical radiculopathy. Epidural corticosteroid injections provide short-term symptom relief; however, it is less clear whether these benefits are maintained in the long term. Recently published systematic reviews evaluating the evidence for different corticosteroid injection techniques—interlaminar, caudal and transforaminal—concluded that each is effective for the short-term relief of pain of disc herniation or radiculitis, but that evidence of long-term relief is lacking. Few side effects have been reported with epidural corticosteroid injections. Since epidural injections confer only transient benefit for symptoms and self-reported function in a select group of patients, their cost-effectiveness has been questioned.

Other treatments for lumbar radiculopathy include chemonucleolysis, which can provide long-term relief. Although there are few adverse effects (<0.1%) associated with this technique, those that do occur may be serious (e.g., anaphylaxis, infection and neurological deficit). Percutaneous and transcutaneous electrical nerve stimulation (PENS/TENS) have also been shown to provide short-term relief and improve function in lumbar radiculopathy patients. Longer-term use of such nerve stimulation tends not to provide additional benefits.

**Surgical interventions:** The standard surgical intervention for lumbar radiculopathy is discectomy, which has a high success rate (80%–96%), but is only slightly better in the long term than non-surgical management for selected patients. Microdiscectomy gives broadly comparable results to standard lumbar discectomy. Moreover, a recent retrospective study of 172 patients concluded that those who underwent minimally invasive discectomy, a refinement of the open microsurgical discectomy technique, had similar perioperative results to those who underwent microdiscectomy. Percutaneous discectomy is likewise utilized for the treatment of disc herniation-associated radiculopathy. Various techniques are available, such as laser radiofrequency ablation and mechanical aspiration. Although percutaneous laser disc decompression is used to treat lumbar radiculopathy, no consensus exists on methodology (i.e., type of laser, wavelength, duration of application, energy applied) or surgical and clinical outcomes. If the cause of radiculopathy is related to facet joint hypertrophy or lumbar spondylolisthesis, lumbar foraminotomy or lumbar spinal fusion may be needed.

**Neuropathic Pain Associated With Nerve Entrapment at the Peripheral Level**

**Median Nerve: Carpal Tunnel Syndrome**

Entrapment or compression of the median nerve can cause carpal tunnel syndrome, anterior interosseous syndrome and pronator teres syndrome. The focus in these recommendations will be on carpal tunnel syndrome, as it is the most common of these conditions.

Carpal tunnel syndrome results from compression of the median nerve in the carpal tunnel. Symptoms mostly affect the hand, but can also radiate to the elbow. They include paraesthesia, tingling especially in the lateral three fingers, numbness (particularly at nighttime), clumsiness and weakness.
The most common cause of carpal tunnel syndrome is repetitive stress injury or overuse syndrome. It is the most common nerve entrapment neuropathy, usually affecting women. Carpal tunnel syndrome may be bilateral, but often affects the dominant hand first. Repetitive finger or wrist movements, such as typing or household chores, and a congenitally narrow carpal tunnel, are predisposing factors.

Other than repetitive injury, carpal tunnel syndrome can also be caused by local and systemic conditions. Local causes include trauma, synovitis, arthritis, vascular injury and local tumor. Systemic causes include endocrine or metabolic disorders, infection, collagen disease and chronic renal failure. Recommendations for diagnosis and management of carpal tunnel syndrome are summarized in Table 2.

**Diagnosis**

Clinical signs of carpal tunnel syndrome include:
- Wasting of the thenar muscles
- Weak thumb abduction and opposition
- Decreased pinprick sensation in the radial 3/5 fingers, with sensation intact in the palm
- Positive Tinel sign and Phalen’s test.

Investigations for diagnosis of carpal tunnel syndrome include:
- Tests to determine whether there is a systemic cause, e.g., renal function test, blood sugar levels, thyroid function test
- X-ray of the hand and wrist with a carpal tunnel view
- Ultrasonography of the wrist, which can detect swelling of the median nerve and surrounding structures
- Electrophysiological studies, including sensory nerve conduction velocity, motor nerve conduction velocity, waveform and amplitude, with or without EMG of the thenar muscle.
- Electrophysiological studies, including median nerve conduction velocity and distal motor latency.
- Ultrasonography of the wrist, which can detect swelling of the median nerve.
- X-ray of the hand and wrist with a carpal tunnel view.

**Treatment**

**Conservative treatment**: Conservative treatment of carpal tunnel syndrome includes splinting the wrist in a neutral position, physiotherapy (e.g., ultrasound), oral steroids, local steroid injections and diuretics. Oral steroid use may result in systemic side effects, including fluid retention and hypertension, and weight distribution and menstrual cycle disturbances, which limit use in some patients. While local steroid injections are often effective, complications include injury to the tendon or nerve, and infection. Acupuncture, including laser acupuncture, may also reduce pain.

A 2003 Cochrane review evaluated the effectiveness of nonsurgical treatment (other than steroid injection) for carpal tunnel syndrome versus a placebo or other non-surgical, control interventions in improving clinical outcome. The review concluded that significant short-term benefit may be derived from oral steroids, splinting, ultrasound, yoga and carpal bone mobilization; other non-surgical treatments, like diuretics and NSAIDs, do not produce significant benefit. A more recent systematic review concluded that there is: 1) strong evidence on the efficacy of local and oral steroids; 2) moderate evidence that vitamin B6 is ineffective and splints are effective; and 3) limited or conflicting evidence that NSAIDs, diuretics, yoga, laser and ultrasound are effective.

Patients should also be advised on good ergonomics and the importance of resting at intervals to minimize repetitive injury. Tasks that require hand or wrist movements should be reduced, such as hand-washing clothes or twisting a mop. Surgical treatment is indicated when conservative treatment has failed, or there is motor involvement, or if the patient has severe numbness.

Drug therapy for mild-to-moderate carpal tunnel syndrome includes NSAIDs, diuretics and oral steroids. A randomized placebo-controlled trial of these agents found that 4 weeks' treatment with oral corticosteroids resulted in greater improvements in global symptom score than other medications. Another study found that patients treated with oral prednisolone for 2 weeks or 4 weeks had similar overall responses. The study concluded that short-term, low-dose, oral steroids are effective for carpal tunnel syndrome.

Local steroid injection is an effective therapy for carpal tunnel syndrome. Injection with methylprednisolone proximal to the carpal tunnel improved symptoms of the syndrome at 1 month in 77% of patients in the intervention group (n=30) compared with 20% of patients in the control group (n=30). After 12 months’
follow-up, about half the patients were still receiving benefit from the single injection of methylprednisolone. Comparison of local versus systemic corticosteroids revealed that a single local injection of methylprednisolone was superior to oral prednisolone.38

A Cochrane review evaluated the effectiveness of local steroid injection for carpal tunnel syndrome versus placebo injection or other non-surgical interventions.39 The review concluded that, compared with placebo, local steroid injection provides greater clinical improvement in carpal tunnel symptoms 1 month after injection; however, significant symptom relief beyond 1 month has not been demonstrated. Moreover, local corticosteroid injection provides significantly greater clinical improvement than oral corticosteroids for up to 3 months.

Surgical interventions: Surgical treatment is indicated when conservative treatment has failed, there is motor involvement, or the patient has severe numbness. Some patients may experience recurrence of symptoms following surgery, so in selected cases further surgery is indicated. Until recently, the standard procedure for carpal tunnel syndrome was open carpal tunnel release (OCTR) via a long, palmar, curvilinear incision. The less invasive technique of endoscopic carpal tunnel release (ECTR) has now been developed and is in widespread use. However, a 2007 Cochrane review comparing the efficacy of the open and endoscopic approaches in relieving carpal tunnel symptoms and promoting return to work or activities of daily living concluded that there is no strong evidence supporting the replacement of standard OCTR by existing alternative surgical procedures.40 The review authors observed that the decision to apply ECTR instead of open release seems to be guided by surgeon and patient preferences. Moreover, an earlier systematic review concluded that OCTR, being technically less demanding, is associated with a lower risk of complications.41

Another recent Cochrane review compared the efficacy of surgical treatment of carpal tunnel syndrome with nonsurgical treatment.42 The authors concluded that surgical treatment relieves carpal tunnel symptoms significantly better than splinting, but that further research is necessary to elucidate whether this conclusion applies to patients with mild symptoms, and whether surgical treatment is better than local steroid injection.

Ulnar Nerve: Cubital Tunnel Syndrome

Cubital tunnel syndrome arises from injury or compression of the ulnar nerve at the elbow. This results in pain, paraesthesia and numbness along the ulnar aspect of the hand; however, there is no numbness along the medial forearm. The hand may become progressively clumsy and weak.

The key cause of cubital tunnel syndrome is nerve entrapment; other causes of ulnar nerve neuropathy include tardive ulnar palsy due to an old fracture, deformity of the elbow, rheumatoid arthritis, osteoarthritis, a ganglion or lipoma, a subluxing ulnar nerve and a supracondylar spur. Recommendations for diagnosis and management of cubital tunnel syndrome are summarized in Table 2.

Diagnosis

The clinical signs of cubital tunnel syndrome include:

- Claw hand deformity
- Weak flexor carpi ulnaris and flexor digitorum profundus to the ring finger and little finger
- Atrophy of intrinsic muscles, except for the thenar muscles and two radial lumbrical muscles
- Weak finger abduction
- Positive Froment sign
- Reduced pinprick sensation in the ulnar 1½ fingers and corresponding area of the palm and dorsum
- Positive Tinel sign at the level of the median epicondyle

Tests to confirm the diagnosis of cubital tunnel syndrome include:

- X-ray of the elbow, with a cubital tunnel view
- Electrophysiological studies measuring sensory nerve conduction velocity, motor nerve conduction velocity, waveform and amplitude, with or without EMG of the muscle supplied by the ulnar nerve. Sensory and motor nerve conduction velocity tests show slowing of velocities across the elbow.

Treatment

Conservative treatment: Cubital tunnel syndrome may resolve with rest and activity modification to avoid placing pressure on the nerve. A recent study randomized cubital tunnel syndrome patients with mild or moderate symptoms to three groups: night splinting, nerve gliding exercises or control.43 All patients were informed about the cause of their symptoms. After 6 months’ follow-up, 90% of patients had an improvement in symptoms, and no significant difference was observed between the groups. Patients with mild or moderate symptoms therefore have a good prognosis if they are educated about the cause of cubital tunnel syndrome and are taught the ways to avoid exacerbating symptoms. Other forms of conservative treatment do not have a great role in management of ulnar neuropathy at the elbow; a release operation is frequently required if symptoms persist.
Surgical interventions: The most common surgical interventions for cubital tunnel syndrome are:

- Simple neurolysis
- Anterior transposition of the ulnar nerve
- Medial epicondylectomy of the distal humerus
- Endoscopic cubital tunnel release.

A recent meta-analysis comparing simple decompression to anterior transposition of the ulnar nerve concluded that there was no statistically significant difference between the two procedures, though there was a trend toward improved clinical outcome with nerve transposition.44

As with carpal tunnel syndrome, the endoscopic approach is now being utilized in the treatment of cubital tunnel syndrome; recent articles in the literature report encouraging results with this technique.45,46

Other Sites
Tarsal tunnel syndrome results from compression of the posterior tibial nerve or plantar nerves in the tarsal tunnel. Symptoms include pain, numbness and tingling paresthesia in the sole of the foot. Ill-fitting footwear, post-traumatic fibrosis, tendon sheath cysts or tenosynovitis, ganglia, rheumatoid arthritis, hypothyroidism, acromegaly or a thickening of the flexor retinaculum can cause tarsal tunnel syndrome.

Treatment of tarsal tunnel syndrome where there is no motor deficit includes drug therapy, such as NSAIDs and anticonvulsants. If symptoms persist, surgical intervention to release the nerve is required.

Summary
Peripheral nerve entrapment is often associated with neuropathic pain symptoms. In many cases, the symptoms can resolve with rest and conservative treatment, including patient education of their condition, physiotherapy, splinting, and use of oral NSAIDs. Patients with persistent symptoms or severe pain should be referred to assess whether surgery is required: various surgical interventions are available, depending on the site of nerve entrapment.

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A list of references can be obtained upon request to the editor.