FOCAL PERIPHERAL NEUROPATHIES

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J Neurol Neurosurg Psychiatry 2003;74(Suppl II):ii20–ii24

The management of focal peripheral neuropathies is based on certain general principles with a relatively limited backing from clinical trials. These principles relate to understanding the:

- types of peripheral nerve injury
- mechanisms of injury
- ability and limitations of neurophysiology to aid diagnosis
- peripheral nerve anatomy.

Types of peripheral nerve injury
Regardless of the cause, nerve injury can be classified according to severity. This directs management and acts as guide to rate of recovery. The types of injury are:

- a neuropraxia, where there is focal or segmental demyelination with preservation of the axon and recovery in 2–12 weeks
- an axonotmesis, where the axon is divided but the epineurium remains intact and regrows at 1 mm per day from the site of injury
- a neurotmesis, where the nerve is divided and no longer in continuity with no recovery.

At the site of focal nerve injury there may be a combination of these types of injury, most commonly a mixture of neuropraxia and axonotmesis. This can be observed clinically by the relatively rapid early recovery followed by a more protracted improvement thereafter.

Mechanisms of peripheral nerve injury
A focal neuropathy results from injury to a peripheral nerve at one site. For every nerve there are anatomical weaknesses making injury more likely at a particular location, typically where a nerve runs beside bone or across a joint. Nerve injury can occur:

- from external insult, such as direct trauma, including prolonged external compression as occurs in prolonged unconsciousness, repeated minor trauma, traction, injection, cold, burns, radiation
- from internal entrapment or compression; examples would include entrapment of the median in the carpal tunnel or the ulnar nerve in the cubital tunnel and compression by tumours/deposits or vascular malformations
- an intrinsic lesion to the nerve—for example, an infarct. This usually arises as a focal manifestation of a more generalised process—for example, a nerve infarct caused by vasculitis, an area of conduction block in multifocal motor neuropathy
- as a result of increased susceptibility to nerve injury—for example, in diabetes—combined with minor entrapment or compression.

Neurophysiology in the diagnosis of focal peripheral neuropathies
Investigation of a focal neuropathy aims to determine the site of focal involvement and its cause. The site of involvement may be determined neurophysiologically (this also screens for evidence of abnormalities in other nerves or a generalised neuropathy). However neurophysiology has limitations; indeed, one of the main reasons trainees in neurology can benefit from practical knowledge of neurophysiology is to appreciate these (table 3).
Nerve conduction studies can identify a focal neuropathy in several ways, depending on the nerve studied and the manner in which it is affected. The significance of different findings vary and provide more or less clear cut evidence of a focal neuropathy.

- Demonstrating a focal delay (slowing over a short segment of nerve) and conduction block (a reduction in the amplitude and dispersal of the response) in one segment of the nerve, with associated denervation changes in the muscles supplied by the nerve, would be the clearest indication of a focal neuropathy.
- Demonstrating a focal delay without either conduction block or denervation changes would also show the existence of a focal neuropathy and determine the level directly, though less clearly. Unfortunately this depends on having the segment of peripheral nerve involved accessible for the application of superficial electrodes, as with the median nerve at the wrist or the ulnar nerve at the elbow.
- Demonstrating denervation changes limited to muscles innervated by a specific nerve or a reduction in motor or sensory responses from the affected nerve not found in other nerves. These findings determine the lowest site a lesion could be to produce the clinical problem; the exact site of nerve dysfunction to be inferred from the clinical presentation and other studies.
- Finding a reduction in size of motor or sensory responses also indicate a lesion proximal to the site of recording, though do not determine its level.

The use of neurophysiological studies to explore prognosis will be discussed below.

Peripheral nerve anatomy
A knowledge of peripheral nerve anatomy allows clinical localisation. Making the diagnosis of a focal peripheral neuropathy depends on recognising that a patient's symptoms and any physical signs fall within the distribution of a single peripheral nerve. For the more commonly affected nerves—the median, ulnar, and lateral cutaneous nerve of the thigh—this can often be considered on the basis of symptoms alone. For less commonly affected nerves the diagnosis is usually based on signs. Diagnosis is going to depend on an appropriate knowledge of anatomy to allow these rarer entities to be diagnosed. Tables 1 and 2 provide a brief summary of most focal peripheral neuropathies likely to be encountered.

The fascicular arrangement of peripheral nerves can lead to difficulties in localisation, as a proximal nerve lesion may mistakenly be thought to be peripheral. For example, a partial sciatic nerve lesion at the level of the hip can be mistaken clinically for a common peroneal nerve lesion at the fibular head.

**PRESENTATIONS OF FOCAL NEUROPATHIES**
These can be broadly divided into acute lesions and those of more insidious onset. The clinical approach to each differs.

**Acute deficit**
The cause of an acute lesion is often straightforward and identifiable from the history—for example trauma, laceration, surgery or injections. Sometimes it can be easily deduced—for example, a period of unconsciousness (anaesthetic or otherwise), a post-ictal state, and coma from drugs or alcohol intoxication. These raise the possibility of prolonged external nerve compression, the ulnar, sciatic, common peroneal, and gluteal nerves being especially vulnerable. In patients with acute focal neuropathies the clinical focus is on optimising recovery and assessing prognosis.

An acute spontaneous deficit that develops at a site that is not a common site of external compression strongly suggests an intrinsic nerve lesion—for example, infarction. Investigation for evidence of a multifocal, particularly vasculitic, neuropathy needs to be undertaken (see Willison and Winer*).
If the lesion is traumatic, regardless of cause, anything that could continue or worsen nerve injury must be identified and removed. Examples would include local factors such as continued compression from local haematoma or compartment syndromes (this may require imaging of the site of compression with timely decompression) as well as systemic factors such as hypoxia and hyperglycaemia.

Subsequent management depends on the type of nerve injury. If the lesion is a neuropraxia or axonotmesis and the cause of nerve damage is removed there will be spontaneous recovery. Sometimes this pattern can be recognised clinically, when a nerve lesion is incomplete and there is some power, no matter how little, to indicate the nerve is in continuity. The same phenomenon can be found neurophysiologically by demonstrating single units under voluntary control on electromyelogram (EMG).

However, a nerve that has no clinical or neurophysiological evidence of active motor function can still have suffered a severe neuropraxia or axonotmesis and acutely this is indistinguishable from a neurotmesis. This is a very important distinction, as a neurotmesis will not recover unless the nerves are sutured or grafted. The only way these can be reliably identified is by surgical exploration. The nature of injury and the likelihood of a neurotmesis need to be considered when contemplating exploration.

Physiotherapy to maintain joint mobility and occupational therapy to improve function and to direct the use of splints are both important during the recovery phase. Neuralgic pain is common and pain modulating drugs such as amitriptyline, carbamazepine or gabapentin are helpful.

**Insidious onset**

Here you need to understand fully the aetiology before contemplating treatment. Insidious lesions tend to arise from internal entrapment or compression, sometimes combined with factors that increase nerve susceptibility or from repeated external

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**Table 2 Outline of focal neuropathies in the lower limb**

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Site of lesion</th>
<th>Common causes</th>
<th>Motor deficit</th>
<th>Sensory deficit</th>
<th>Differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common lateral cutaneous nerve of the thigh</td>
<td>Inguinal ligament</td>
<td>Obesity, pregnancy, surgery</td>
<td>None</td>
<td>Lateral thigh</td>
<td>L2 radiculopathy</td>
</tr>
<tr>
<td>Common peroneal</td>
<td>Fibular head</td>
<td>External compression (femoral, iatrogenic), trauma</td>
<td>Foot dorsiflexion and eversion, toe extension</td>
<td>Lateral calf and dorsum of foot</td>
<td>L5 radiculopathies, proximal sciatic lesions. Also upper motor neurone weakness and motor neurone disease</td>
</tr>
<tr>
<td>Interdigital</td>
<td>Between heads of metatarsals</td>
<td>Entrapment</td>
<td>None</td>
<td>Web spaces between affected toes</td>
<td></td>
</tr>
<tr>
<td>Femoral</td>
<td>Sciatic</td>
<td>Hip flexion, knee extension, Hamstrings plus common peroneal and tibial nerve deficits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tibial, at ankle</td>
<td>Tarsal tunnel</td>
<td>Entrapment</td>
<td>Adbuctor hallucis (not reliably tested clinically)</td>
<td>Distal sole, sparing heel</td>
<td>Partial sciatic, S1 radiculopathy</td>
</tr>
<tr>
<td>Perineal</td>
<td>Alcock’s canal</td>
<td>Cycling</td>
<td>None</td>
<td>Penis or labia majora</td>
<td>Corus lesions</td>
</tr>
<tr>
<td>Saphenous</td>
<td>Thigh or knee</td>
<td>Knee surgery or arthroscopy</td>
<td>None</td>
<td>Medial calf</td>
<td></td>
</tr>
<tr>
<td>Rare</td>
<td>Tibial, at knee</td>
<td>Trauma</td>
<td>Plantar flexion, inversion heel</td>
<td>Sole of foot, including heel</td>
<td>Partial sciatic, S1 radiculopathy</td>
</tr>
<tr>
<td>Uncommon</td>
<td>Posterior cutaneous nerve of the thigh</td>
<td>Compression, trauma</td>
<td>None</td>
<td>Posterior thigh</td>
<td>S3, 4 radiculopathy</td>
</tr>
<tr>
<td>Obturator</td>
<td>Obturator foramen</td>
<td>Obturator hernia, pelvic tumours, surgery</td>
<td>Adductors of the hip</td>
<td>Medial thigh</td>
<td>Lumbosacral plexopathy</td>
</tr>
<tr>
<td>Gluteal</td>
<td>Trauma</td>
<td>Hip extensors, abductors</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sural</td>
<td>(especially biopsy!)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Table 3 Some difficulties in neurophysiological diagnosis of focal neuropathies**

<table>
<thead>
<tr>
<th>Anatomy, limitation of access. Nerve conduction studies can only routinely study nerves that run subcutaneously. Segments available for study may be long, limiting the precision in localising a focal neuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short segments. Focal slowing is most useful if demonstrated over a short segment as it most precisely localises the lesion. However, measuring distances of short segments is prone to large errors, increasing the risk of error</td>
</tr>
<tr>
<td>Subclinical involvement. Population studies have found high levels (up to 18% have median dysfunction at the wrist in one study) of abnormalities in asymptomatic patients</td>
</tr>
<tr>
<td>Multiple pathologies. Denervation changes from coexistent cervical or lumbosacral radiculopathies limit EMG localisation</td>
</tr>
<tr>
<td>Absent or limited denervation changes: A demyelinating lesion does not lead to the development of fibrillations or fasciculations; the changes in motor units and interference pattern are more subtle and thus less reliable</td>
</tr>
<tr>
<td>Timing of denervation changes: Denervation changes take 2 weeks to develop, early studies may be misleading</td>
</tr>
</tbody>
</table>

EMG, electromyelogram.
compression. The history needs to be reviewed for clues, asking directly about previous trauma, postures, habits, and hobbies. Are there any symptoms outside the distribution of this nerve, suggesting a multifocal or generalised process? Are there any factors in the history that might make the nerves more vulnerable to injury—for example, excess alcohol intake, diabetes? Have there been any previous focal neuropathies suggesting a liability to pressure palsies?

A careful neurological examination should look particularly for evidence of other focal neuropathies or a more generalised neuropathy. Neurophysiology may confirm the site or simply support the diagnosis of focal neuropathy and may provide evidence of multifocal involvement.

Further investigation
If the history provides an appropriate explanation (for example, trauma, repeated external compression) or if the nerve is involved at a common site of entrapment then no further investigations may be needed. If no explanation is found, particularly if the nerve is involved at an unusual site, then further investigation is indicated. These aim to identify unusual causes of internal entrapment or compression such as nerve tumours, or vascular malformations. Magnetic resonance imaging of the site of involvement should be considered initially. At the same time evidence of any factors that could make the nerves more vulnerable should be addressed, including the investigation of multifocal neuropathies as described elsewhere in this supplement. If all this proves unhelpful, exploration of the nerve could be considered, depending on the site and the severity of the focal neuropathy. Some internal entrapments—for example, fibrous bands—will only be found on exploration.

If neurophysiological studies have not identified direct evidence of a focal neuropathy you should consider other sites/conditions, such as radiculopathies, within the differential diagnosis. These will then require their own appropriate investigations. It is always worth considering whether the focal neuropathy demonstrated neurophysiologically is an adequate explanation of the clinical picture.

Management of focal neuropathies at common sites of entrapment
Despite these problems being very common—for example, carpal tunnel syndrome has a prevalence of 3–5%—there is still limited evidence as to the best approach to diagnosis and management. The difficulties arise, at least in part, because of case definition. These focal neuropathies are not present or absent but constitute a spectrum. This can be recognised clinically and neurophysiologically. A patient with minor intermittent ulnar sensory symptoms with minor reduction in ulnar sensory action potential (SAP), and a patient with a wasting claw hand and severe ulnar motor loss and no sensory responses from the ulnar nerve with denervation, both have focal ulnar neuropathies but can scarcely be considered as having the same extent of problem. In addition, the natural history of the common focal neuropathies is poorly understood. Such factors lead to difficulties in studies considering both diagnosis and treatment.

Carpal tunnel syndrome
Identifying a patient with a severe carpal tunnel syndrome is relatively straightforward, recognising lesser degrees is less so. There are a wide range of clinical signs taken to support the diagnosis. The specificity and sensitivity of the clinical signs have recently been reviewed, as have the specificity and sensitivity for different neurophysiological methods of assessment. This approach is inherently difficult when there is no “gold standard” method of diagnosis. Interestingly, clinical tests such as Tinel’s and Phalen’s signs were not found to be helpful predictors of neurophysiological abnormality; however, hand diagrams, where the patient draws and marks the location of their symptoms of numbness and tingling (likelihood ratio of positive (LR+) = 2.4, 95% confidence interval (CI) 1.6 to 3.5; LR of negative (LR−) = 0.5, 95% CI 0.3 to 0.7), square wrist sign* (LR+ 2.7, 95% CI 2.2 to 3.4; LR− 0.5, 95% CI 0.4 to 0.8), and weak thumb abduction (LR+ 1.8, 95% CI 1.4 to 2.3; LR− 0.5, 95% CI 0.4 to 0.7) all achieved statistical significance. The flick sign, where the patient flicks their hand to improve symptoms, is promising but has only been the subject of a single study (LR+ 21.4, 95% CI 10.8 to 42.1; LR− 0.1, 95% CI 0 to 0.1).

The Cochrane reviews of carpal tunnel support the use of oral steroids, splinting, ultrasound, yoga, and carpal bone mobilisation to provide short term benefit in mild cases. Local corticosteroid injections improve outcome at one month compared to placebo, and at three months when compared to oral steroids, but no benefit was demonstrated over non-steroidal anti-inflammatory and splinting at two months. Surgery improved outcome compared to splinting, a finding supported by a recent randomised study. No one technique is clearly superior to another.

Thus, patients with mild carpal tunnel should try non-invasive treatment initially, particularly if there is another factor such as pregnancy or hypothyroidism, and then proceed to decompression if symptoms persist. Patients with moderate carpal tunnel syndrome should probably proceed directly to decompression, though a trial of splinting while awaiting surgery might spare some surgery. It is not clear whether patients with severe compression, atrophy, and dense sensory loss benefit from surgical interventions. A large pragmatic trial is therefore strongly needed.

Other nerves
While ulnar nerve lesions at the elbow are the second most common focal neuropathy, advice on treatment is not currently based on the results of trials. Conservative management to avoid repeated trauma may lead to resolution, particularly if a history of recent trauma or external compression has been established. More distant trauma, leading to the “tardy” ulnar palsy, tends not to improve with conservative management. If conservative management fails then surgical decompression could be considered. Two procedures are commonly used: simple decompression within the cubital tunnel or alternatively combining this with anterior transposition. There are no randomised studies comparing these procedures. Occasionally an unusual cause of internal entrapment, such as a ganglia or cyst, is found at operation. Again a large pragmatic trial is needed.

The lateral cutaneous nerve of the thigh is commonly entrapped in the inguinal ligament. As the symptoms are sensory and usually tolerable no specific treatment is needed. Identification and reversal of any potential cause, particularly recent weight gain, seems prudent.

*Square wrist sign present when anteroposterior dimension of wrist divided by mediolateral dimension, measured at the distal wrist crease, is greater than 0.7.
Management of focal neuropathies at uncommon sites of entrapment

Once again this advice reflects the experience derived from case reports and clinical series. If no repeated external compression is identified these are patients in whom unusual causes of internal entrapment need to be considered and investigated as outlined above. In the absence of a systemic cause, where there is no improvement or progression, exploration should be considered.

REFERENCES


7 None of the tests are perfect; this brings together what is known.


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*J Neurol Neurosurg Psychiatry* 2003 74: ii20-ii24
doi: 10.1136/jnnp.74.suppl_2.ii20

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