Neuropathies

Michael Lunn
Hadi Manji

Abstract
Peripheral neuropathies are common neurological disorders. A diagnosis can be reached in 75% of cases with a detailed history and examination, neurophysiological assessment and now standard laboratory investigations, which include antibody and DNA studies. The necessity for nerve biopsies is now limited to a number of specific indications only. Inflammatory neuropathic disorders such as chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and vasculitic neuropathies, though relatively rare, are treatable with intravenous immunoglobulin (IVIG) and/or corticosteroids.

Keywords chronic inflammatory demyelinating polyradiculoneuropathy; entrapment; Guillain–Barré syndrome; inherited; multifocal motor; neuropathy; nerve biopsy; small fibre; vasculitis

Peripheral neuropathic disorders, resulting mainly from diabetes mellitus, HIV infection or leprosy, are a significant cause of morbidity worldwide. The population prevalence is 2.4–8% depending on location and age. Early diagnosis is important because disease modification (e.g. strict glycaemic control in diabetic neuropathy or treatment of infective causes) can prevent progression. Inflammatory neuropathic disorders such as chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) are treatable with intravenous immunoglobulin (IVIG) and corticosteroids.

Clinical aspects

The various peripheral neuropathic disorders are detailed in Figure 1. The history and examination should address the following questions.

Over what period of time has the condition evolved?

- acute (days up to 4 weeks, e.g. Guillain–Barré syndrome (GBS), vasculitis)
- subacute (4–8 weeks)
- chronic (>8 weeks, e.g. CIDP).

Michael Lunn *MBBS MRCP PhD is Consultant Neurologist and Clinical Lead in Neuroimmunology at the National Hospital for Neurology, London, UK. His research interest is inflammatory mechanisms in peripheral nerve disorders.*

Hadi Manji *MA MD FRCP is Consultant Neurologist and Honorary Senior Lecturer at the National Hospital for Neurology, London, and Ipswich Hospital, UK. His research interests are inflammatory neuropathies and neuro-infections, particularly HIV/AIDS.*

What's new?

- Chronic inflammatory demyelinating neuropathy is a treatable inflammatory neuropathy that can be diagnosed by detailed neurophysiology and CSF protein elevation on lumbar puncture
- Multifocal motor neuropathy with conduction block is a treatable mimic of motor neurone disease
- Genetic neuropathies can be diagnosed using appropriate DNA tests, making invasive investigations such as nerve biopsy unnecessary
- Small-fibre neuropathies can be diagnosed using thermal threshold measurements and skin biopsies; standard nerve conduction tests may be normal

Which parts of the peripheral nervous system are involved?

- motor (distal or proximal; focal, symmetrical or asymmetrical distribution)
- sensory (small fibres transmitting pain and temperature, and/or large fibres transmitting vibration and position sense).
- Is the autonomic nervous system involved? (This is seen in diabetes, familial and acquired amyloid neuropathy, GBS and porphyria.)
- Is there cranial nerve involvement? (Involvement of the cranial nerves, particularly the facial nerve, may indicate sarcoidosis, Lyme disease, HIV, CIDP, malignant infiltration or familial amyloid neuropathy.)

  Are there clues in the family history, in symptoms since childhood or on examination for hereditary neuropathy?

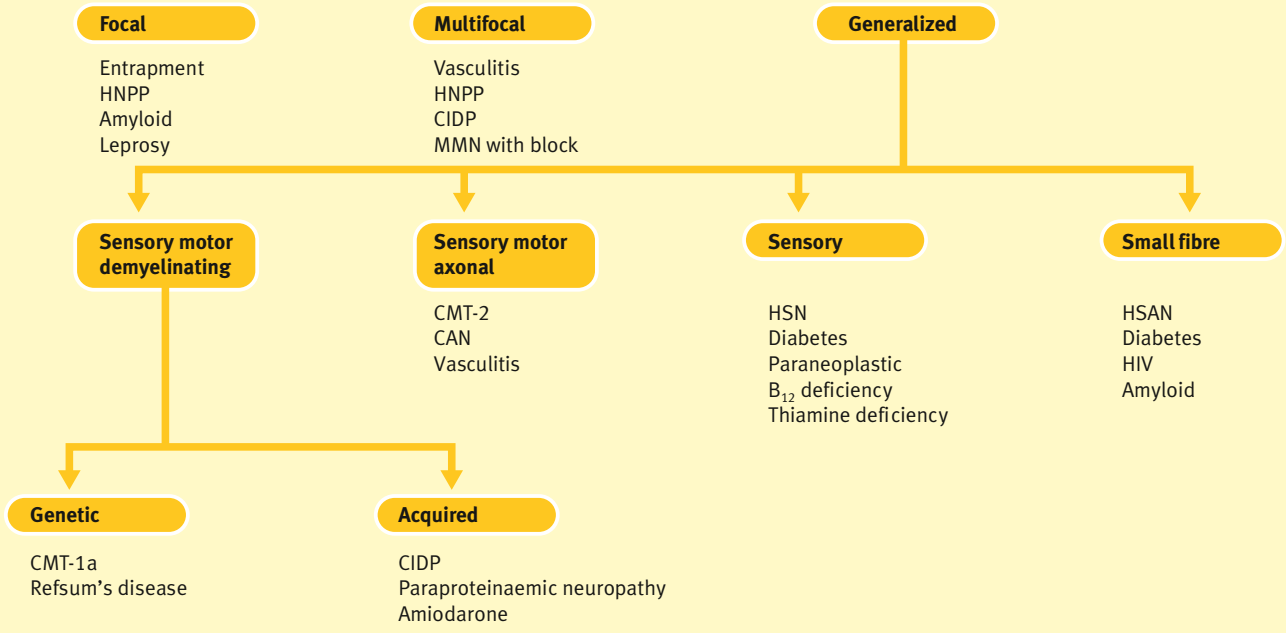
  Could this be a toxic neuropathy? (This requires a detailed account of occupational history, e.g. exposure to heavy metals such as lead, social history including alcohol intake and recreational drug use, e.g. inhalation of N_2O results in a myeloneuropathy due to disruption of vitamin B12 metabolism, and prescribed medication (Table 1)).

History

Motor symptoms include difficulty with tasks requiring manual dexterity (e.g. opening jars, fastening buttons) and tripping as a consequence of foot drop, although the latter may also result from an upper motor neurone lesion in the spinal cord or cerebral cortex. Proximal weakness and/or onset in the upper limbs are seen in radiculopathy, radiculoneuropathy (e.g. CIDP) and vasculitis;myopathic disorders are a differential diagnosis.

Positive sensory symptoms include pins and needles, burning and tight-band sensations (Table 2). These indicate acquired rather than hereditary neuropathy, in which the symptoms tend to be 'negative' (e.g. numbness). A predominant loss of large fibres causes sensory ataxia, which may result from ganglionopathy caused by Sjögren's syndrome, paraneoplastic neuropathy, HIV or an excess of vitamin B_6. Neuropathic pain may be described as burning, gnawing, sharp or jabbing.

Peripheral nerve disorders



HNPP, hereditary neuropathy with liability to pressure palsies; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; MMN, multifocal motor neuropathy; CMT, Charcot–Marie–Tooth disease; CAN, chronic axonal neuropathy; HSN, hereditary sensory neuropathy; HSAN, hereditary sensory and autonomic neuropathy

Figure 1

Drug-induced neuropathies[1]

Drug	Type of neuropathy
Cardiovascular drugs	
Amiodarone	Demyelinating; motor and sensory
Antineoplastic drugs	
Vincristine, vinblastine	Axonal; motor and sensory
Cisplatin	Axonal; sensory (large fibres)
Thalidomide	Axonal; sensory
Antibiotics	
Isoniazid	Axonal; sensory and motor (preventable with pyridoxine)
Chloroquine	Axonal; sensory and motor (also myopathy and myaesthenic syndrome)
Metronidazole	Axonal; sensory
Antivirals	
ddI, ddC and d4T	Axonal; sensory (small fibres)
Miscellaneous	
Phenytoin	Axonal; sensory (usually asymptomatic)
Vitamin B_6 (pyridoxine) >200 mg/day	Axonal; sensory (large fibres)

Table 1

Examination

Foot deformities, such as pes cavus, clawing of the toes and scoliosis may indicate hereditary neuropathy.

Nerves should be palpated for signs of thickening – specifically the ulnar nerve at the elbow, the superficial radial nerve at the wrist, and the common peroneal nerve around the fibular head. Causes of thickened nerves include leprosy, CIDP, Refsum's disease, amyloidosis and some forms of hereditary motor and sensory neuropathy (HMSN types I and III) (see below).

Clinical signs suggesting large-fibre involvement (vibration and joint position) include pseudo-athetosis (involuntary movement of outstretched fingers with the eyes closed) and Romberg's sign.

In small-fibre neuropathies, because damage is restricted to unmyelinated and small myelinated fibres, pain and temperature

Definitions

Paraesthesiae	Abnormal sensations that can be spontaneous or evoked and are not unduly painful or unpleasant
Dysaesthesiae	Unpleasant paraesthesiae
Hyperaesthesia	Increased sensitivity to a stimulus
Allodynia	A painful sensation resulting from a non-painful stimulus such as light stroking

Table 2