Criteria for the diagnosis of peripheral neuropathies

S H Horowitz

Is there a "gold standard"?

The diagnosis of a peripheral neuropathy is one of topographic localisation within the nervous system; not of aetiology. It is not a diagnosis in isolation as peripheral nerves are damaged consequent to some other condition, such as systemic exposure to exogenous agents in the environment and workplace. In subjects at risk, it is important to determine if and when peripheral nerves become affected, hopefully before clinical dysfunction and permanent damage occur. Many studies have employed clinical, electrophysiological, quantitative psychological sensory, and pathological procedures in the investigation of peripheral nerve disease. Their success has been less than optimal, mostly because of complexities in the peripheral nervous system and inherent procedural limitations.

Peripheral neuropathies can be divided into:

- Those which are bilaterally symmetrical—polyneuropathies (for example, most neurotoxins, diabetes mellitus)
- Those which are focal—mononeuropathies (nerve entrapment)
- Multiple mononeuropathies (vasculitides, leprosy, multifocal motor)

Other subdivisions are based on the predominant site of dysfunction:

- Axons—axonopathies (diabetes, organophosphates)
- Nerve cell bodies—neuropathies (poliomyelitis, pyridoxine)
- Schwann cells and/or their myelin sheaths—demyelinating neuropathies (Guillain-Barré syndrome, acute arsenic poisoning).

There are also different types of peripheral nerve fibres: motor, sensory, and autonomic. Sensory fibres are divided into at least three groups anatomically, physiologically, and functionally:

- Aα (or Aβ)—large diameter, myelinated, fast conducting; mediating vibration, position, and touch sensations
- A8—small diameter, myelinated, slow conducting; mediating cold sensation
- C fibres—very small diameter, unmyelinated, very slow conducting; mediating hot and pain sensations.

Not all fibre types are affected in all peripheral nerve disorders; neuropathies can preferentially affect motor fibres (Guillain-Barré syndrome), sensory fibres (diabetes), or both (hereditary motor and sensory neuropathies—Charcot-Marie-Tooth disease, most neurotoxins). Most polyneuropathies affect all sensory fibres, but others mainly involve small fibres (amyloidosis, metronidazole toxicity).

The peripheral nervous system is thus more complicated than might appear at first glance; hence not all peripheral nerve functions or fibre types can be evaluated with a single test. This dilemma has been recognised for years, and with modern predilections for quantitation and state of the art technology, multifaceted approaches to evaluate peripheral nerves have been devised, perhaps the most complete to date being that of Peter Dyck’s group at the Mayo Clinic (reviewed in Dyck’s, 3).

This methodology includes symptoms questionnaires, a neurological examination with special attention to peripheral nerve activities, quantitative sensory (QST) and autonomic testing, and nerve conduction studies. The QST findings characterised the neuropathy as predominantly sensory of the small fibre type. It is somewhat problematic that one study found the screening procedure to be of limited reproducibility (Jamal et al., whereas the second study (Buchanan et al.) used that screening procedure to characterise the presence and severity of neuropathy. Further, the diagnostic value of QST appears to be limited by technical factors in the field (Jamal et al.) and by the findings that, although 52% of subjects (12/23) with probable/definite neuropathy had clinical and electrophysiological evidence for neuropathic dysfunction, 91% of them (21/23) had abnormalities on small fibre QST (Buchanan et al.). What should be made of the nine (39%) in this group who had abnormal QST but no other evidence of neuropathic dysfunction?

This review suggests that confirmation of polyneuropathy is still imprecise. The most tried and true tests are the clinical examination and nerve conduction studies. However, even nerve conduction studies are problematic. The usual studies employ surface electrodes which only measure the velocities of the fastest conducting (Aα) fibres. Patients with “small fibre” neuropathies, therefore, can have normal velocities. The near
nerve technique, employing fine needle electrodes guided to peripheral nerves, can measure Aδ fibre activity, but this is a more difficult, time consuming, and invasive procedure. C fibre activity cannot be measured in nerve conduction studies. When QST of large (Aβ) and small (Aδ) myelinated fibres was compared with near nerve conduction studies in mild symptomatic diabetic neuropathy, Aδ conduction abnormalities were closely related to cooling detection threshold abnormalities (also mediated by Aδ fibres). Thus it could be argued that, in “small fibre” neuropathy, neuropathic dysfunction when measured by nerve conduction, would be found more frequently if the more sensitive technique had been employed. However, the conclusion of that same study was that in a mixed fibre neuropathy, such as that associated with diabetes, either conduction technique is more sensitive than QST. Finally, in a small study of farmers chronically exposed to organophosphates without neuropathic complaints, but with high vibration thresholds at screening, the neurological examination was found to be the most sensitive test; subclinical polyneuropathy was not present or could not be diagnosed with either near nerve or QST studies.7

The problems seen in the current reports of potential neuropathic dysfunction in workers exposed to organophosphates underscore the difficulties of evaluating the peripheral nervous system clinically. Not only is there no “gold standard” for determining clinical neuropathic dysfunction, there is no single standard at all. For the present, the approach taken by these investigators seems reasonable, with the caveat that a good clinical neurological examination in the field would be a valuable addition to their protocol and attention to QST technical factors is requisite.

REFERENCES