Peripheral neuropathies in diabetes are a diverse group of syndromes, not all of which are the common distal symmetric polyneuropathy. The focal and multifocal neuropathies are confined to the distribution of single or multiple peripheral nerves and their involvement is referred to as mononeuropathy or mononeuropathies multiplex.

Mononeuropathies are due to vasculitis and subsequent ischemia or infarction of nerves (1). Common mononeuropathies involve cranial nerves III, IV, VI, and VII and thoracic and peripheral nerves, including peroneal, sural, sciatic, femoral, ulnar, and median. Their onset is acute, associated with pain, and their course is self-limiting, resolving over a period of 6 weeks. They must be distinguished from entrapment syndromes that start slowly, progress, and persist without intervention (Fig. 1). Common entrapments involve the median, ulnar, and peroneal nerves, the lateral cutaneous of the thigh, and the tibial nerve in the tarsal canal. The entrapment neuropathies are highly prevalent in the diabetic population, one in every three patients has one, and it should be actively sought in every patient with the signs and symptoms of neuropathy because the treatment may be surgical (2) (Table 1).

**Carpal Tunnel Syndrome** — Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy encountered in diabetic patients and occurs as a result of median nerve compression under the transverse carpal ligament. It occurs thrice as frequently in a diabetic population compared with a normal healthy population (3,4). The increased prevalence in diabetes may be related to repeated undetected trauma, metabolic changes, accumulation of fluid or edema within the confined space of the carpal tunnel, and diabetic chorioarthritis (5), rheumatoid arthritis, and hypothyroidism (1,3). CTS is found in up to one-third of patients with diabetes, when demonstrated electrophysiologically, but may only be symptomatic in ~5.8% (6). It is more common in females and in obese individuals (BMI >30 kg/m²) and affects the dominant hand (7). It occurs in 2% of the general population, 14% of diabetic subjects without diabetic polyneuropathy, and 30% of diabetic subjects with diabetic polyneuropathy. It peaks at around 40–60 years of age and an increased “wrist index” (wrist depth/wrist width [in millimeters]) is a risk factor (8,9). It used to be associated with work-related injury, but now seems to be common in people in sedentary positions and is probably related to the use of keyboards and typewriters (dentists are particularly prone) (10). As a corollary, recent data (3) in 514 patients with CTS suggest that there is a threefold risk of having diabetes compared with a normal control group. If recognized, the diagnosis can be confirmed by electrophysiological studies. Therapy is simple, with diuretics, splints, local steroids, and rest or ultimately surgical release (11). The unaware physician seldom realizes that symptoms may spread to the whole hand or arm in CTS, and the signs may extend beyond those subserved by the nerve entrapped. Motor weakness is uncommon, but thenar muscle wasting particularly occurs in the elderly. Tinel sign for median nerve percussion at the wrist is positive in 61%, and Phalen’s test wrist flexion is only 46% positive, with a high false-positive rate. Quantitative sensory tests for the different sensory modalities, including pain, temperature, and spatial orientation, are notoriously unreliable (4). Thus, the very nature of the trouble goes unrecognized, and an opportunity for successful therapeutic intervention is often missed. Electrophysiological studies measure the speed of conduction across the carpal tunnel, and median sensory nerve conduction studies are compared with radial and/or ulnar sensory latencies. Their interpretation is made difficult if there is a coexisting peripheral neuropathy affecting the upper limbs or if there are no symptoms of CTS. Demyelination is thought to be the primary pathological abnormality. Electromyography activity can be particularly useful in distinguishing this from distal symmetric polyneuropathy (DSPN) and the double-crush syndrome of C7–8 radiculopathy (12). The high sensitivity and specificity of nerve conduction studies make them the most valuable diagnostic method for CTS (80% sensitive). Wrist-palm stimulation is the most sensitive technique (61% sensitivity in diagnosis of CTS). Moreover, it is the only technique to diagnose subclinical cases and differentiate...
entrapment from DSPN. Combined entrapment of median and ulnar nerves can mimic DSPN and can only be distinguished by nerve conduction velocity (NCV) with median nerve stimulation in the palm.

The mainstays of nonsurgical treatment are resting the wrist, aided by the placement of a wrist splint in a neutral position for day and night use, and the addition of anti-inflammatory drug medications. Injections of cortisone into the carpal tunnel may provide short-lived relief and, in the majority of cases, repeat injections are required. Surgical sectioning of the transverse carpal ligament provides variable degrees of pain relief but does not particularly benefit muscle wasting or sensory loss (2). The decision to proceed with surgery should be based on several considerations, including severity of symptoms, appearance of motor weakness, and failure of nonsurgical treatment. Of particular note is the very elegant study by Ozkul et al. (13). They compared the outcome of carpal tunnel release in 22 diabetic patients with that of 25 nondiabetic patients. Global symptom scores as well as electrophysiological evidence of recovery of nerve function were evaluated at 1 month and again at 1 year after decompression. They observed im-

<table>
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<td>Femoral neuropathy, radiculopathy L2–3, and lumbar plexopathy</td>
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*Radial nerve entrapment requires conduction velocity done over muscles of forearm because, unlike the ulnar median nerves, the radial nerve does not innervate muscles in the hand.

Table 1—Clinical features of entrapment syndromes: location, impairments, and diagnosis

![Figure 1](image_url)

Mononeuritis vs. Entrapment

- **Mononeuritis**
  - onset sudden
  - usually single nerve but may be multiple
  - common nerves: CN III, VI, VII, ulnar, median, radial, peroneal, femoral
  - not progressive and resolves spontaneously
  - treatment symptomatic

- **Entrapment**
  - onset gradual
  - single nerves exposed to trauma
  - common nerves: median, ulnar, peroneal, radial, and lateral plantar, lateral femoral cutaneous nerve, femoral
  - progressive
  - treatment, rest, splints, diuretics, steroid injections and surgery for paralysis
Improvement in median nerve latencies and sensory conduction velocity in both groups, but the degree of recovery was less and slower in the diabetic population. Specifically, they excluded insulin-treated diabetic subjects because of the neurotrophic effects of insulin and of conditions such as peripheral neuropathy, cervical radiculopathy, brachial plexopathy, pronator teres syndrome, and lesions of the 6th cervical root, as well as previous medical treatments with steroids, diuretics, or splints and surgery. They concluded that factors other than compression are important in entrapment syndromes in diabetes and suggest that sorbitol accumulation, myoinositol deficiency, and accumulation of advanced glycation end products may be relevant to the slowing of recovery in diabetes. It may also of course also relate to the impairment in nerve regeneration in diabetes (14). Whatever the case, it is abundantly clear that one must not neglect the burden of dysmetabolism on diabetic nerves that are entrapped, and attention to metabolic control may be essential to permitting adequate recovery of the nonentrapped nerve. Aszmann, Kress, and Dellon (15) carried out decompression of the median nerve at the wrist, the ulnar nerve in the ulnar canal at the elbow, and the posterior tibial nerve in 20 diabetic patients who had had diabetes for 14.8 years and compared the responses in operated and unoperated limbs (a total of 31 nerves) in patients who had a positive Tinel sign, ostensibly indicative of surviving neurons. They also excluded patients with absent electrical impulses in whom dead nerves were unlikely to respond. Overall, there was a 79% improvement of loss of two-point discrimination in the operated side compared with a 32% progression of neuropathy in the unoperated nerves. Upper limbs fared better than lower limbs (88 vs. 69% improvement). Unfortunately, these results must be interpreted with caution. The test is not a good measure of sensory function (4); no measure of conduction across the entrapment site was shown to confirm entrapment, no Tinel-negative patients were included, and no sham operative procedure was carried out. The analysis of a responder rate as opposed to the degree of the response, which might have depended on the severity of the lesion, is also not addressed. Indeed, the same group of investigators (16) have proposed use of a pressure-sensing device for the detection of entrapment and reported in 72 clinical entrapment syndromes that the pressure-specified sensory device (PSSD) was 100% sensitive compared with electrodiagnostic testing. They conclude that the PSSD has a high sensitivity but low specificity because it detected abnormalities in sensory function in 25% of patients who had negative electrodiagnostic tests. An alternative explanation is that the subjective PSSD gives 25% more false-positives than electrodiagnostic testing and thus would not be reflecting changes in entrapment. This would be more in keeping with the lack of specificity of quantitative sensory tests shown by Perkins, Olaleye, and Bril (4) and further emphasizes the need to use a “gold standard” for the diagnosis and quantitation of response to therapy.

**Ulnar Entrapment** — The second most common entrapment neuropathy (2.1%) occurs as a result of ulnar nerve compression immediately distal to the ulnar groove beneath the edge of the flexor carpi ulnaris aponeurosis in the cubital tunnel. It may develop as a result of deforming at the elbow joint secondary to fracture or as a consequence of prolonged pressure during surgery and has been most commonly associated with alcoholism. Typical symptoms include painful paresthesiae in the fourth and fifth digits associated with hypothenar and interosseous muscle wasting and weakness. Froment’s sign (weakness of adduction and opposition of thumb) and impaired flexion of the fourth and fifth fingers are classic signs. The etiology of ulnar nerve entrapment includes trauma, arthritis, and systemic diseases (less often than in CTS). As in CTS, conduction through the elbow is decreased. A C8-T1 radiculopathy, thoracic outlet syndrome, and entrapment at the wrist must be excluded.

The pathology is a combination of de-myelination and axonal degeneration. The key electrophysiological findings include low-amplitude ulnar sensory nerve action potentials, reduced sensory NCV, and fibrillation potentials in the interossei (17). Management of patients is primarily conservative, with advice to avoid pressure to this area because the results of surgery are very poor. However, if symptoms and signs progress, then a number of approaches may be used. They include medial epicondylectomy, transaction of the flexor carpi ulnaris aponeurosis, and ulnar nerve transposition (18).

**Radial Nerve Entrapment** — This is rare (0.6%), occurring as a consequence of radial nerve compression in the spiral groove. It presents with the characteristic motor deficits of wrist drop and sensory impairment over the dorsum of the hand, intact elbow extension, and sensation in posterior arm and forearm distribution. The causes of radial neuropathy that mostly lead to weakness of muscles innervated by motor branches include humeral fracture, blunt trauma over the posterolateral aspect of the arm and forearm, and external compression of radial nerve in the spiral groove and posterior interosseous nerve (the distal motor branch) in the forearm. Isolated neuropathy of the superficial radial nerve can be caused by entrapment and is known as Wartenberg’s syndrome, whereas external compression of the same sensory branch is known as wristwatch or bracelet neuropathy. Electrophysiologically, the amplitude is reduced compared with the same response from the contralateral radial as well as the ipsilateral median sensory nerve. Decreased conduction velocity through the compressed segment in the forearm and arm is still the hallmark of diagnosis (19). Management is conservative, with pressure relief in sensory neuropathy.

**Common Peroneal Entrapment** — Peroneal nerve entrapment at the level of the fibula head is the most common entrapment syndrome in the lower limbs. It is due to the ease of external compression of the peroneal nerve, while under general anesthesia, while crossing legs, while sleeping in older people especially, and during weight loss. It needs to be distinguished from an L5 radiculopathy (foot drop) when tripping and fractures occur, especially in older people. Involvement of the motor fibers in the common peroneal nerve results in weakness of the dorsiflexors and foot drop, but the loss of the motor supply to the tibialis anterior muscle also leads to weakness in inversion. A simple bedside test entails asking the patient to stand on his or her heels and see whether he or she is unable to raise the forefoot off of the ground. This is accompanied by a sensory deficit in the lateral anterior tibial compartment, but charac-
teristically no pain or paresthesiae. Tinel sign may be positive and is elicited by striking the peroneal nerve at the neck of the fibula, which produces pain and tingling in the distribution of the peroneal nerve supply. Diabetes was thought to be a relatively uncommon cause of peroneal nerve palsy (5–12%) (20); however, in the Women’s Health and Aging Study (21), weakness of dorsiflexion occurred in two-thirds of women >65 years of age and more so if diabetes was superimposed on aging. Conduction blocks were found across the fibular head and suggested external compression at the fibular head during sleep with the legs crossed or in bedridden patients. Other causes are anesthesia, being placed in the stirrups for obstetrical and gynecological procedures, and are a result of inappropriately placed plaster casts following lower-limb fractures. An important differential is a radiculopathy involving the L5 root. Features that define L5 involvement include pain in the lower back and additional loss of inversion. Another critical differential is spinal stenosis with claudication of the cord. These people have pain in the buttocks radiating down the leg made worse when walking downhill and relieved by bending forward. It is due to constriction of the anterior spinal artery, and emphasis at the watershed sites, such as T12-L1. MRI of the spine, can be very useful. Electrophysiological studies help to distinguish these syndromes from peroneal entrapment. In such cases, there is demyelination with conduction block in mild lesions, with a marked loss of amplitude that is presumably secondary to axonal degeneration in more severe lesions (22). Because the majority of these lesions are caused by external pressure that, if relieved, will result in the resolution of the motor deficit within 3–6 months, a conservative approach is advocated, with removal of pressure and a foot brace in the interim.

**Tarsal Tunnel Syndrome** — The tarsal tunnel is homologous to the carpal tunnel in the upper extremity. Through this space, which lies between the medial malleolus and the calcaneus, passes the tibial nerve and its branches as well as the extrinsic flexor tendons of the foot and ankle. The boundaries of the tunnel are fairly rigid; therefore, any swelling within the tunnel will compress the tibial nerve. Tarsal tunnel syndrome (TTS) (23) is a painful lower-limb entrapment. Passing through the tarsal tunnel, the tibial nerve innervates only muscles of the sole, and clinical signs are mostly sensory. Foot pain may be severe, burning, and worse on standing and walking. Tinel sign on the underside of the medial malleolus with atrophy of the sole muscles is typical. Weakness is rare because most of the small foot muscles (flexor hallucis longus) are not damaged in TTS. Pain on the inside of the foot must be distinguished from other causes of pain, for example, a Morton’s neuroma, plantar fasciitis, heel spurs, arthritis or bone spurs, and early Charcot’s neuropathic foot. Magnetic resonance imaging of the foot can be very helpful to identify neuromas and shows edema of the bone in the midfoot with Charcot’s, which presents as a hot foot with increased blood flow (24). It may also be a manifestation of systemic disease (25). Once these are excluded, NCV can be informative in the case of a normal plantar response from one leg and an abnormal one from the symptomatic leg in unilateral TTS. TTS is not difficult to diagnose clinically when DSPN is not severe and NCV is moderately abnormal. Mild symmetric peroneal and tibial NCV abnormality, with intact ankle jerks and sensation of the dorsal aspect of the foot, together with the above-mentioned clinical signs, are the most important diagnostic features of TTS. When the neuropathy is severe, then diagnosis may be impossible. A positive Tinel sign, tapping just below the medial malleolus, may be helpful, but unfortunately may also simply reflect nerve damage in peripheral neuropathy, which is a negative sign, suggesting that nerve damage predicts a poor outcome of surgery.

Controversy exists as to the role tarsal tunnel release has in the management of the diabetic patient with poor plantar foot sensibility. Due to the intrinsic swelling of peripheral nerves in diabetes (endoneurial edema secondary to increased sorbitol levels within the peripheral nerve), an increased incidence of compression neuropathy has been well documented. The double-crush syndrome as described by Upton and McComas (26) may be applied to the diabetic patient. This hypothesis states that when multiple “subclinical” nerve compressions exist in series, they may be “additive” and give rise to symptoms, even though each compression, by itself, would not. The “first crush” would be the peripheral neuropathy of diabetes and the “second crush” compression of the tibial nerve at the tarsal tunnel. If patients are carefully selected, release of the tibial nerve through the tarsal tunnel in the diabetic patient may improve plantar sensibility and help prevent plantar ulceration and ultimate lower-extremity amputation. Several recent studies lend credence to this notion, though study design flaws need to be rectified before universal acceptance of this principle is achieved. Caffee et al. (27) presented data on 36 patients collected over a 9-year period from 1989 to 1997 reviewed retrospectively. The mean follow-up was 32 months, and these were patients who had severe disease, with foot ulcers in 11 patients and painful paresthesiae in 28. Fifty-eight decompressions were done in 36 patients followed for 7–84 months. In these studies, the Semmes–Weinstein monofilaments were used to monitor responses. Twenty-four of 28 patients had complete relief of pain, some while on the operating table and still under anesthetic, and 13 of 24 had improved subjective sensation. They concluded that there is some room for optimism but had no objective data of recovery, the only record of change being that reported on by the patients. The failure in 50% of patients is attributed to the advanced status of their disease and that objective testing of sensibility is an oxymoron despite the reports by Wieman and Patel (28) and Dellon (29) of improved two-point discrimination after surgical decompression.

In the report by Wieman and Patel (28) on 33 limbs in 26 patients, 32 had a positive Tinel sign, yet 19 of 26 responded and 7 with positive Tinel signs did not. Thus, as Dellon (29) showed, there may be an 80% response in Tinel-positive people but failure in 20% would be in agreement with the study by Wieman and Patel (28), suggesting that the sign is not a good predictor of response. Unfortunately, in the Wieman and Patel study (28), neither foot pressures nor electrodiagnostics showed any changes in the operated patients, and only symptoms of pain improved. The objective measures of two-point discrimination fell equivalently from 15.1 ± 4 to 11.1 ± 3.5 arbitrary units in responders and from 13.7 ± 3 to 11.1 ± 2.5 arbitrary units in nonresponders, pointing out the lack of validity of this as a test of response to decompression. Thus, these studies have not clearly
established the role of decompression in entrapment syndromes, left us floundering with regard to the value of a positive Tinel sign over the ankle, and created some consternation among those people who are concerned that this is being advocated as a procedure for common or garden diabetic neuropathy in the absence of entrapment, even when there is no evidence of recoverable nerve function. Indeed, as Carneiro (30) pointed out, there is a need to grade the severity of the entrapments using measures of sensory deficits with validated tests, the presence of a Tinel sign, the time taken for Phalen’s test to become positive, and the presence of motor features and atrophy to identify the best candidates for surgery. We would go further than that and add that a conduction block must be present at the site, that there should not be such severe diabetic neuropathy to preclude distinction of this from entrapment, and that controlled sham operations have to be compared with unentrapment for relief of symptoms, if this is the only measurement.

The mainstays of nonsurgical treatment are avoidance of the use of the joint, placement of a splint in a neutral position for day and night use, anti-inflammatory medications, and targeted injections of local anesthetics and steroids. Surgical treatment consists of sectioning the offending ligament. The decision to proceed with surgery should be based on several considerations, including severity of symptoms, appearance of motor weakness, and failure of nonsurgical treatment.

LATERAL FEMORAL CUTANEOUS NERVE ENTRAPMENT — Compression of the lateral femoral cutaneous nerve (meralgia paresthetica) is uncommon. It results in pain, paresthesiae, and sensory loss in the lateral aspect of the thigh (31) and can lead to significant disability when the diagnosis is missed. Obesity and diabetes are the most common causes, followed by trauma due to external injury of the nerve as it runs down the lateral aspect of the thigh. Most will resolve spontaneously and are therefore conservatively managed, using focal nerve block at the inguinal ligament, with a combination of lidocaine and corticosteroids as well as rest, and reduction or elimination of aggravating factors. However, in severe cases, when medical management fails, surgical decompression is a viable option (32).

Other nerves that may be involved include the sciatic and obturator nerves. They can be a cause of significant motor deficit; however, they are extremely rare and their management is conservative.

In conclusion, up to one-third of patients with diabetes are found to have some form of entrapment syndrome. The diagnosis rests on an index of suspicion and electrophysiological tests demonstrating for the most part a block in nerve conduction across the site of the lesion. The value of the Tinel sign in predicting outcome needs validation, and quantitative sensory tests are notoriously unreliable. There are clear indications for surgery when conservative medical therapy fails, and it is not yet clear that decompression should be considered in the treatment of diabetic neuropathy in the absence of compression. Prospective studies on the role for decompression using accepted measures are clearly needed.

References

24. Shapiro SA, Stansberry KB, Hill MA, Meyer MD, McNitt PM, Bhatt BA, Vinik AI: Normal blood flow and vasomotion in...
Focal entrapment neuropathies in diabetes