



Peripheral Nerve Injuries

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There are different types of peripheral nerve problems that include nerve trauma, compression, tumors, and so on, and repair of peripheral nerve injuries continues to be a major challenge in reconstructive surgery. Satisfactory functional recovery after a peripheral nerve injury is dependent on accurate regeneration of axons to the original end organs. Reconstruction of peripheral nerve injuries has improved particularly over the last two decades with the experience in traumatic nerve injuries gained particularly during wartimes. In this chapter, we review different types of peripheral nerve injury problems including neuropathies, nerve repair techniques, clinical outcomes, and future strategies.

the nerve, associated injuries, age, and general health of the patient.³⁸

After peripheral nerve injury, a complicated sequence of events commences to begin the reparative process, but this process is unique because it does not involve mitosis and cellular proliferation.¹⁸ Although some of the peripheral nerve injuries recover spontaneously, most of them require surgical intervention. Despite over 150 years of experience in modern surgical management of the peripheral nerves, even meticulous surgical repair cannot guarantee full functional recovery, since the surgeon has no control over the “biological battlefield” occurring inside damaged nerves.⁷⁸

History

The first report of acute nerve injury can be traced to 3,500 years ago. Jacob experienced a sciatic nerve injury with a traumatic hip dislocation during his battle with the angel in the well-known biblical story (Genesis 32:25–33).²⁴ Hemophilus differentiated peripheral nerves from tendons in 300 BC. He traced nerves to the spinal cord to demonstrate the continuity of the nervous system.⁸⁷ The first reference to nerve repair was by Rhazes in AD 900, but peripheral nerve regeneration after nerve repair was demonstrated by Cruikshank in 1795. Nelaton described the secondary nerve repair in 1864, and primary epineural nerve suture concept was introduced by Hueter²⁵ in 1871. Mikulicz described the sutures that reduced tension on the nerve suture

Abbreviations

CTS	Carpal tunnel syndrome
NSAIDs	Nonsteroidal anti-inflammatory drugs
NGF	Nerve growth factor

Introduction

Peripheral nerve injuries may result in devastating outcome, which is determined by the extent of cellular damage, site of lesion, degree of disruption of connective tissue sheaths that surround

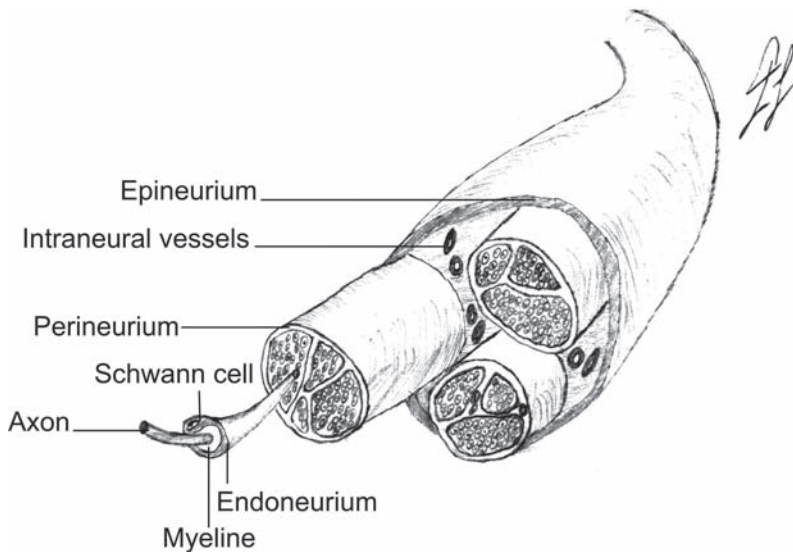


Figure 37.1. A myelinated peripheral nerve branch with associated structures, including epineurium, perineurium, endoneurium, intraneural vessels, Schwann cell, axon, and myelin.

in 1882, and Loebke described bone shortening to decrease the tension on the suture line in 1884. Albert described grafting nerve gaps in 1876. Cajal pioneered the concept of axonal regeneration from neurons and their guidance by chemotropic substances. Plenty of experience in evaluation and treatment of traumatic nerve injuries was gained in wartimes. During World War I, nerve injuries were repaired under tension and risked disruption after repair because of extensive soft tissue injuries and significant infections. After World War II, in 1945 Sir Sunderland demonstrated the detailed internal anatomy of the major peripheral nerves and developed microsurgical techniques to improve nerve repair outcomes.⁸⁷

Peripheral Nerve Anatomy

All members of the mammalian system have the same peripheral nervous system anatomy. In the peripheral nervous system, nerve fibers are ensheathed by Schwann cells, either individually in case of myelinated fibers or in groups in the case of unmyelinated fibers. They form the sheath covering the axons in myelinated peripheral nerves, and they form basal membrane in unmyelinated nerves. The basal lamina layer envelops Schwann cells and supports axonal regeneration. Myelinated and unmyelinated nerve fibers are embedded

within a connective tissue compartment called endoneurium. Endoneurium is the layer that covers and nourishes the axons. The endoneurium is encircled by a compact layer called the perineurium, which is a key component in nerve strength. The perineurium partitions nerve fibers into fascicles. These nerve fascicles are embedded within a connective tissue compartment called the internal epineurium. Epineurium is the connective tissue layer of the peripheral nerve, which both encircles and runs between fascicles. Its main function is to nourish and protect the fascicles. The outer layers of the epineurium are condensed to form a sheath-like structure that forms the external epineurium.⁵⁸ The perineurium and the nonfenestrated endothelium in the endoneural vessels form the blood nerve barrier, which blocks the infiltration of cells into the endoneural environment of the peripheral nerve (Figure. 37.1).

Nerve Injury Classification

Nerve injuries were classified by Seddon⁸⁰ in 1947, and Sunderland⁸⁷ further refined this classification in 1951.

Seddon classified nerve injuries into three major groups: neuropraxia, axonotmesis, and neurotmesis. Neuropraxia is characterized by a localized conduction deficiency and local myelin damage, usually secondary to compression.



Axon continuity is preserved and the nerve does not undergo distal degeneration. Axonotemesis is defined as loss of continuity of axons, with preservation of the connective tissue elements of the nerve. Wallerian degeneration is seen distal to the trauma zone. Neurotemesis is the most severe injury, equivalent to physiologic disruption of the entire nerve; it may or may not include actual nerve transactions.⁸⁰

The Sunderland classification is based on the widely variable prognoses of axonotemetic injuries. Axonotemesis grade is divided into three types in this classification depending on the fascicular structure coverage. Neuropraxia is equivalent to Sunderland type 1 injury. In Sunderland type 2 injury, the endoneurium and the epineurium are still intact. Complete functional recovery can be expected, because the regenerating axons from the proximal segment are directed along their original course. The time for recovery is directly related to the level of injury because of the need for axon regeneration distally to the end organ. In a Sunderland type 3 injury, the endoneurium is disrupted, but the perineurium and endoneurium are intact. Endoneurium fibrosis, which hinders axonal regeneration, occurs because of this disruption, and recovery is incomplete unless the intrafascicular fibrosis is excised. If there is severe retrograde injury to cell bodies, which either destroys neurons or slows their recovery with longer delays, end organ changes may develop and the recovery will be incomplete. In a Sunderland type 4 injury, there is full-thickness fibrosis formation, and only the epithelium is intact. Retrograde neuronal damage is intensified. This type of injury requires excision of the damaged segment and surgical repair or reconstruction of the nerve. Sunderland type 5 injury is equivalent to Neurotemesis, and it is characterized by complete nerve disruption. Recovery is impossible without surgical intervention.⁸⁷ In 1988, Mackinnon and Dellon presented a “type 6” injury that represented a complex peripheral nerve injury. This grade involved combinations of Sunderland’s grades of injuries.⁵⁷

Nerve Degeneration

Waller described the degenerative changes developing in the distal nerve after nerve transection in 1850, which was later called “Wallerian degeneration.” Just after nerve injury, myelin starts to break down. Axonal and myelin debris are removed by the phagocytic action of macrophages and

Schwann cells, a process that can take from 1 week to several months. Schwann cells become active within 24h after injury, exhibiting nuclear and cytoplasmic enlargement as well as an increased mitotic rate. Schwann cells appear to ingest axonal and myelin debris, and then pass this on to macrophages. Same changes also occur in the proximal end of the injury for a varying distance, depending on the severity of the injury. Endoneurial sheath of the nerve fibers form the tubes called “Bands of Bungner,” which are organized by the proliferating Schwann cells, and they are the potential tubes into which the nerve sprouts will grow.⁵⁷

Nerve Regeneration

Within the first 24h following nerve injury, while Wallerian degeneration continues distally, axons from the proximal segment start to sprout at the same time. Multiple axons are produced from each axon. These axons are unmyelinated at the beginning even when the axon from which they have originated is myelinated. As the regenerating units mature, they become myelinated fibers, and functional recovery can be seen. If these regenerating fibers cannot reach appropriate distal routes and are lost in the extraperineurial environment, then a neuroma will form, which represents a potential loss of functional recovery and may be a source of neurogenic pain. There is a growth cone that consists of filopodia rich in actin in the distal part of regenerating axons. The tips of the filopodia will explore the distal environment, and if they are in contact with the basal lamina of the Schwann cell, they draw the entire growth cone distally. The axonal sprout regenerating rate toward the distal segment ranges between 1 and 4 mm/day.^{57,58}

Nerve Repair

Peripheral nerves that are interrupted by trauma or surgical resection of a mass require reapproximation of their ends. Nerve repairs may be primary or secondary depending on the time of repair after injury.

Primary repair is a direct reconnection of the nerve after disruption of its continuity. Historically it was thought that the best approach is to wait 3 weeks before repair to allow for completion of the Wallerian degeneration process, but Mackinnon et al. have shown that immediate repair is associated with better results.⁵⁸



Prerequisites for early repair are a clean wound, good vascular supply, no crush component to the injury, and adequate soft tissue coverage.

Secondary repairs are delayed repairs that may contain different strategies when the prerequisites of primary repair cannot be met. However, within 3 weeks after injury, a nerve may lose as much as 8% of its length.⁹⁴

An end-to-end repair is preferred if the gap is small, and the two ends can be approximated with minimal tension. Best results occur when the nerves are either purely sensory or purely motor and when the intraneural connective tissue component is small, which can vary from 22% to 80%.^{93,94} End-to-end nerve repair techniques are "Epineural repair," "Group-fascicular repair," and "Fascicular repair." Sharp lacerations without loss of nerve substance or partial lacerations with proper alignment are good examples of injuries that benefit from epineural repair. In a crushing or delayed repair requiring trimming of nerve ends, group-fascicular repair improves fascicular alignment without an excessive number of sutures. Excessive sutures add to scar tissue production. Fascicular repair is not practiced widely, because it requires numerous sutures, and it is technically difficult.⁹⁴ Proponents argue that group-fascicular repair is better, because axonal alignment is more accurate with this technique. However, others have shown that there is no functional difference in outcome between epineural and group-fascicular repair. Furthermore, group-fascicular repair has the potential disadvantage of increased scarring and damage to the blood supply as a result of the additional dissection. Lundborg et al.⁵⁵ showed that although this technique ensures correct regeneration of regenerating axons, there is little evidence that it is superior to the less exact but simpler epineural repair.

"Epineural sleeve neurorrhaphy" is another nerve coaptation technique introduced by Siemionow et al.⁸² It is a modification of the "epineural cuff" technique described by Snyder et al.⁸³ before. In epineural sleeve technique, the free edge of the epineurium at the distal stump is rolled back and a 2-mm nerve segment of the distal nerve stump is resected. The epineural sleeve created is then pulled over the proximal nerve end to cover the coaptation site and is anchored to the epineurium 2 mm proximal to the coaptation site with two sutures placed 180° apart. In this study, it was proven that epineural sleeve neurorrhaphy technique revealed faster

functional recovery when compared with conventional end-to-end nerve coaptation. This finding was attributed to the fact that in this technique no tension or compression was created at the repair site. Instead, the tension was applied to the epineural sleeve, which is proximal to the coaptation site. In addition, the epineural sleeve provides a biologic chamber at the coaptation site, where axoplasmic fluid is collected, leaving a perfect milieu for regeneration of the nerve. Finally, perfect fascicular matching without bulging was possible using this technique, because the nerve's own epineurium guided the alignment of regenerating fascicles. Faster functional recovery has been shown in the experimental model with this technique, but it has to be verified clinically.⁸⁹

Although the classic technique of neurorrhaphy is devoid of tension, Hentz et al.⁴⁰ studied a primate model and showed that direct nerve repair under modest tension actually does better than a tension-free nerve graft over the same regenerating distance.

Neuroma in Continuity

A neuroma in continuity may arise like a bulbous swelling as a sequel to peripheral nerve injury. This lesion may be composed of some functional and nonfunctional fascicular components, which have to be determined by a careful preoperative assessment. Effective treatment of a painful neuroma remains as a challenging problem, because it is possible that the surgeon may sacrifice the functional fascicles while trying to repair the nonfunctional fascicles of the nerve.⁶³

A sharp pain associated with a scar and functional loss in the distribution of the involved nerve is typical for neuroma in continuity. The character of pain and its psychological implications are important in the selection of patients for surgery.

In the surgical treatment of the neuroma in continuity, fascicles may be separated by micro-neurolysis and regenerating axons are directed appropriately to distal ones when the nerve stumps and surgical bed are suitable for this. The functional fascicles can be identified proximal and distal to the injury site via electrodiagnostic testing. These fascicles are preserved, and potentially damaging dissection within the neuroma incontinuity should be avoided.⁶⁰

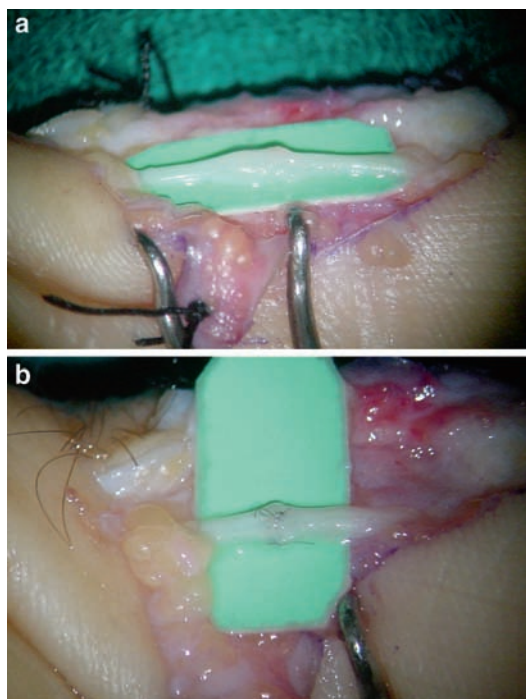


Figure 37.2. (a) A neuroma in the continuity of the digital nerve. (b) Epineurial end-to-end repair of the digital nerve after excision of the neuroma.

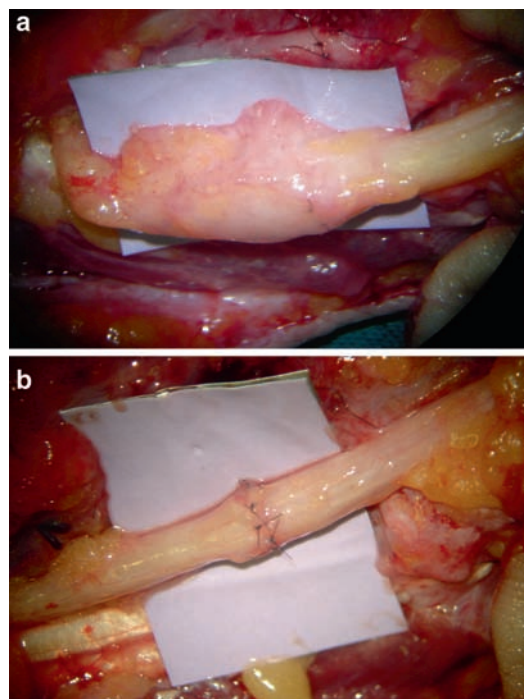


Figure 37.3. (a) A neuroma in the continuity of the ulnar nerve. (b) Epineurial end-to-end repair of the ulnar nerve after excision of the neuroma

When there is insufficient length for tension-free end-to-end repair, a nerve graft can be used. The second alternative for painful neuroma treatment is resection of neuroma and transposition of the proximal stump into muscle (or bone, e.g., in digits) for noncritical or function distal nerves, in cases of previous treatment failure, or if the wound bed is not suitable for neural repair^{72,74,97} (Figures 37.2 and 37.3).

Nerve Sheath Tumors

Neurofibroma (from Schwann cells and fibroblasts), neurilemmoma (from Schwann cells), and neurofibrosarcoma (from Schwann cells and fibroblasts) are the three types of tumors originating from intrinsic cells of the nerve.

Neurofibroma

Neurofibromas are usually seen with neurofibromatosis. They rarely cause some symptoms like pain or paresthesia, and their usual location is

along peripheral nerves. They are nonencapsulated fusiform tumors, composed of excess of cells within nerve fascicles.^{65,92}

If the tumor size is small without causing major neurological deficit, simple enucleation is recommended. If the tumor size is large, with major neurological symptoms, en bloc resection of the tumor with the peripheral nerve is the treatment of choice.^{43,92} (Figure. 37.4).

Neurilemmoma

Neurilemmomas (also called “schwannoma” and “neurinoma”) mostly arise from major mixed (motor and sensory) nerves and are solitary unless the patient has neurofibromatosis (von Recklinghausen’s disease). They are well-encapsulated tumors, composed of differentiated Schwann cells. Large neurilemmomas may cause some neurological symptoms such as paresthesia and pain, but the small ones are usually asymptomatic. Surgical dissection of the tumor from the nerve is the treatment of choice, and recurrence is rare after excision of neurilemmomas^{65,92} (Figure. 37.5).

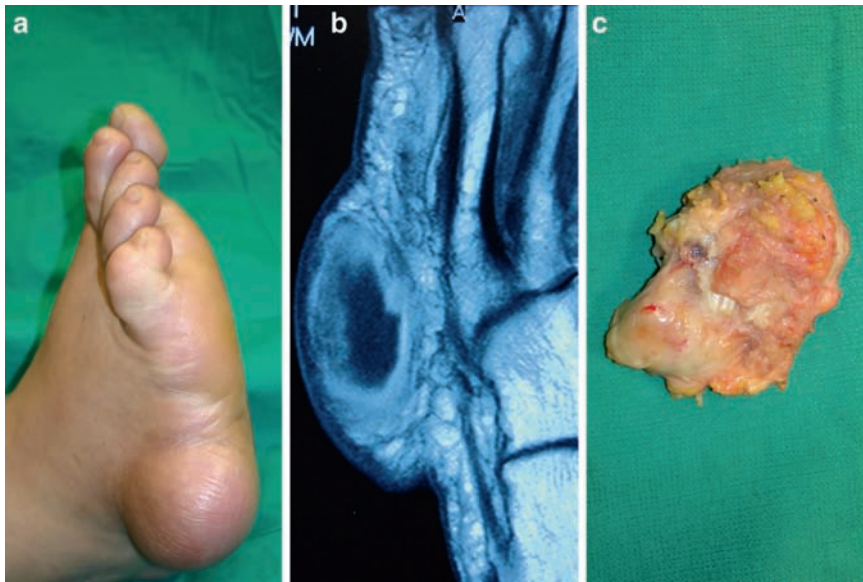


Figure 37.4. (a) A case of neurofibroma of the lateral aspect of the foot. (b) Magnetic resonance imaging confirming neurofibroma lesion. (c) Neurofibroma measuring 5 cm \times 2 cm after excision.

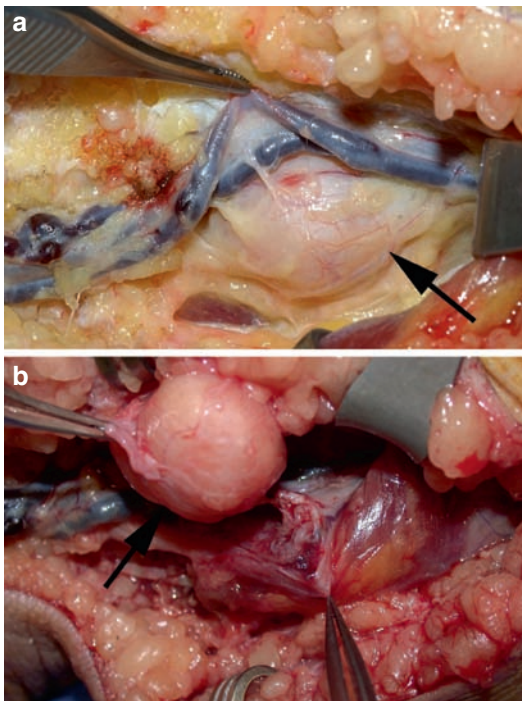


Figure 37.5. (a) Neurilemmoma (*arrow*) of the posterior tibial nerve above the medial malleolus of the foot. (b) Posterior tibial nerve after resection of the tumor (*arrow*).

Neurofibrosarcoma

This is a highly malignant tumor, which is found either in a patient with neurofibromatosis or in patients who have undergone radiotherapy. Neurofibrosarcoma may be termed a malignant schwannoma, since the tumors arise from the sheath of Schwann cells covering neural tissues. Radical excision followed by chemotherapy and radiotherapy is the treatment of choice in this aggressive tumor, and patients with neurofibrosarcomas have recurrence rates of more than 10%.^{21,31,33,50,62}

Compressive Neuropathies

Although any nerve in the body can be compressed, certain nerves are more vulnerable because of their anatomic locations. The common symptoms include pain, sensorial deficit, and motor loss. Diagnosis is based on physical examination, whereas electrodiagnostic and imaging studies help to confirm the diagnosis and provide information regarding the recovery potential.⁸⁵



Upper-Extremity Compressive Neuropathies

Carpal Tunnel Syndrome

Carpal tunnel syndrome (CTS) is the most frequent nerve compression syndrome. The median nerve is compressed inside the carpal canal by the transverse carpal ligament at the wrist. This compression may be caused by intrinsic (inside the carpal canal) or extrinsic factors (outside the carpal canal). CTS may be related to congenital, traumatic, metabolic/endocrine, inflammatory, infectious, or idiopathic causes. In addition, repetitive use is thought to increase the incidence of CTS.³⁵

Physical examination may reveal percussion tenderness of the median nerve at wrist region (Tinnel's sign). Sensory deficits such as decreased sensation to light touch or pain may be present in the radial three digits.¹² Weakness of the abductor pollicis brevis and atrophy of the thenar muscles are common in the late phases of the disease. Many tests have been described for CTS such as Phalen's test, reverse Phalen's test, compression test, tourniquet test, closed fist test, "flick sign," and hand elevation test. Electrodiagnostic tests are helpful in the conformation of the diagnosis and to show the severity of the condition and also in differential diagnosis.

Treatment options for CTS can be categorized as operative and nonoperative. Nonoperative options include activity modifications to avoid exacerbating positions, nonsteroidal anti-inflammatory drugs (NSAIDs), splinting the wrist at neutral position, steroid injections to carpal tunnel, pyridoxine, and diuretics. In cases of nonoperative treatment failure or in advanced cases, operative treatment is indicated.³⁶ Surgical treatment may be classified as open and closed techniques. In the classic open technique, transverse carpal ligament is released under direct visualization via a mid-palmar incision.² In the closed technique (endoscopic), mid-palmar incision is avoided. Earlier recovery and return to work than the open release has been shown in some studies. Neurovascular complication incidence is not increased in the closed technique.^{8,95} Incomplete release and longer operation time are among the disadvantages of closed technique, particularly at the beginning of the learning curve^{1,16} (Figure 37.6).

Anterior Interosseous Nerve Syndrome (Kiloh–Nevin Syndrome)

Anterior interosseous nerve is compressed in the forearm region by various anatomic structures. It may be compressed by the deep head of pronator teres and other fibrous bands or vessels in the forearm region.

Patients present with weakness of flexor pollicis longus, flexor digitorum profundus (of second and sometimes third digit), and pronator quadratus muscles of the affected hand. These patients are unable to make the shape of letter "O" between first and second digits. Electrodiagnostic tests are particularly helpful for its differentiation from the "pronator syndrome."

Its treatment is usually surgical release of the structures compressing the median nerve in the forearm region such as lacertus fibrosus, deep head of pronator teres, and other structures such as muscles or vessels overlying the interosseous branch of the median nerve, via an S-shaped incision extending from distal arm to proximal forearm.^{29,85}

Pronator Syndrome

The pronator syndrome is described as compression of the sensory branch of the median nerve in the elbow region by the anatomic structures such as pronator teres, the superficial arch of flexor digitorum superficialis, and the bicipital aponeurosis.⁶ Patients suffer from pain in the volar proximal portion of the forearm, which may also extend to the distal arm. Electrodiagnostic motor tests are typically normal. Increased pain with resisted pronation of the forearm and elbow extension (compression of pronator teres), pain with resistance to flexion of the middle finger proximal interphalangeal joint (compression of flexor digitorum superficialis arch), and pain with resisted elbow flexion and forearm supination (compression of bicipital aponeurosis) are the provocative maneuvers in this syndrome.⁸⁵

Conservative treatment is the first choice in these patients. Physical therapy, NSAIDs, and local steroid injections are usually effective in most of the patients. In the resistant cases, the median nerve may be decompressed in the forearm region.^{69,85}

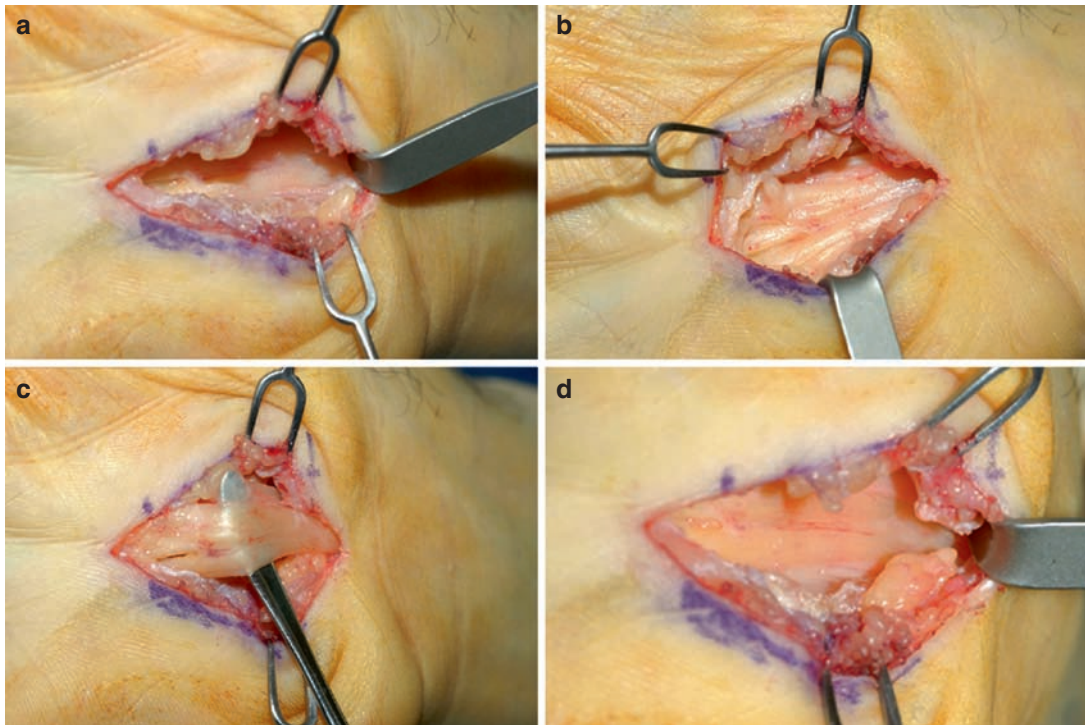


Figure 37.6. Classic open technique of transverse carpal ligament release. (a) Mid-palmar incision. (b) Exposure of the median nerve after transverse carpal ligament release. (c) Presence of engorged vasonervorum after median nerve decompression. (d) Median nerve within carpal tunnel following release.

Ulnar Tunnel Syndrome

In this syndrome, ulnar nerve is compressed within Guyon's canal. Trauma, soft tissue masses, and variant muscular and vascular anomalies may cause this compression.³⁷

Patients may present with intrinsic muscle weakness of the affected hand, wrist pain, and diminished sensation in the cutaneous dermatome of the ulnar nerve of the affected hand. Motor weakness of the adductor pollicis, hypothenar, and interosseous muscles with positive Wartenberg's sign may be seen. Diminished sensation on the ulnar site of the palm, with normal sensation on the dorsum of the hand, differentiates the distal ulnar nerve compression from a more proximal site than the wrist region. Froment's sign and Phalen test may be positive in this syndrome.^{85,98}

Surgical decompression is required in most of the patients, while conservative treatment can be tried in patients with mild symptoms. Ulnar nerve can be decompressed via a curvilinear incision that is centered on the hook of hamate in this region. It

is important to decompress both superficial and deep branches of the ulnar nerve.³⁰

Cubital Tunnel Syndrome

It is the second most common entrapment syndrome after CTS. In this syndrome, the ulnar nerve is typically compressed beneath the cubital tunnel retinaculum at the elbow. This compression may be spontaneous due to repetitive and sustained elbow flexion, presence of mass, arthritic spur, synovitis, and anatomic variations (e.g., anconeus epitrochlearis).⁸⁵

Medial elbow pain with dorsoulnar-sided palm and digit paresthesias or dysesthesias may be the symptoms of these patients. Intrinsic muscle weakness and hand clumsiness are late symptoms.¹⁹ Tenderness over the elbow at the level of the medial epicondyle may be revealed by examination of the patient. Electrodiagnostic testing reveals motor weakness of the flexor digitorum profundus, flexor carpi ulnaris, and interosseous muscles and slowing at the elbow level.¹⁴

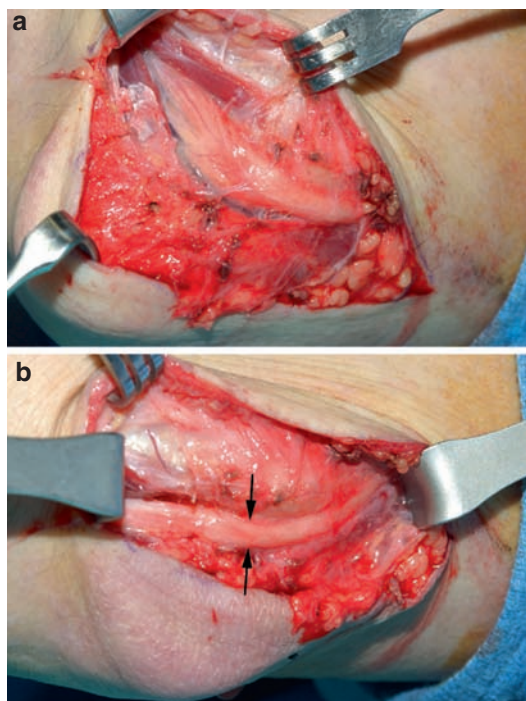


Figure 37.7. Cubital tunnel release. (a) Exposure of the ulnar nerve within the ulnar nerve groove. (b) Ulnar nerve after decompression showing narrowing at the compression site (arrows).

Conservative treatments such as an activity modification, NSAIDs, and nighttime elbow splint are beneficial in some patients.²⁸ Operative treatment is indicated if the nonoperative treatment fails. Decompression of the ulnar nerve with or without medial epicondylectomy and ulnar nerve transposition are performed as a surgical treatment⁷⁵ (Figure. 37.7).

Posterior Interosseous Nerve Compression

Posterior interosseous branch of the radial nerve is compressed in the proximal forearm region in this disease. The most common site of compression is the Arcade of Frosche (proximal edge of supinator muscle), followed by fibrous bands in the vicinity of the radiohumeral joint, vascular malformations (leash of Henry), tendinous edge of the extensor carpi radialis brevis, and substance or distal edge of the supinator muscle.⁴

Forearm pain with extensor weakness is the typical symptom of these patients. Physical examination reveals varying degrees of finger or thumb drop without sensory deficit. Surgery is

the treatment of choice via anterior (Henry) or posterior (Thompson) approach.⁵³

Radial Tunnel Syndrome

Radial tunnel syndrome is attributed to the cases of proximal forearm pain caused by compression of the posterior interosseous nerve without motor paralysis. Electrodiagnostic studies are usually normal. Local nerve blockade may be useful in differential diagnosis of this syndrome.³² Long-term conservative treatment with physical therapy is recommended. Surgery is indicated in resistant cases via the Thompson approach.⁸⁵

Posterior Interosseous Nerve Syndrome

“Arcade of Frohse” (proximal edge of the supinator muscle) is the most common site where the posterior interosseous nerve is compressed in this syndrome. These patients present with weakness or paralysis of the extensors of the wrist and digits. Vague forearm pain may accompany the symptoms, without any sensory deficit. Conservative treatment with physical therapy is recommended for 6–12 weeks, and surgery is indicated if no improvement occurs.⁵³

Wartenberg Syndrome

Patients with Wartenberg syndrome present with pain over the distal radial forearm along with paresthesia on the dorsal radial hand, which is associated with the compression of the superficial radial nerve at the wrist near the radial styloid. This nerve is susceptible to compression in this region due to extrinsic compression, trauma, surgery, or repetitive movement. Most of the patients are treated nonoperatively, including rest, splinting, and removal of the compression sources. Surgery is indicated in resistant cases^{53,84} (Figure. 37.8).

Lower-Extremity Compressive Neuropathies

Lateral Femoral Cutaneous Nerve Compression (Meralgia Paresthetica)

The lateral femoral cutaneous nerve (LFCN) may be compressed by the inguinal ligament. Dysesthesia and hypesthesia of the lateral thigh region are common in these patients. Tinnel’s sign may be present on the tract of LFCN under the inguinal ligament.^{61,91}

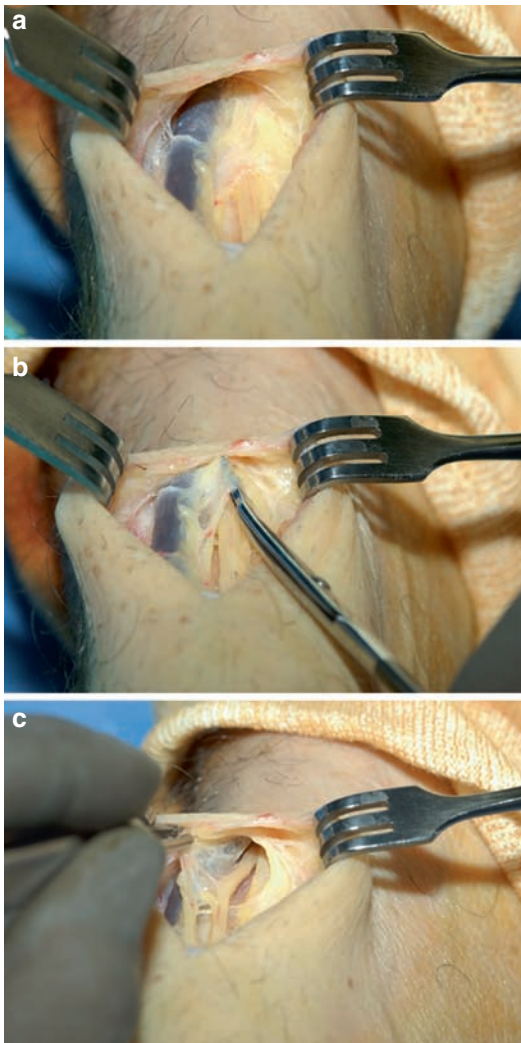


Figure 37.8. Surgical decompression of the superficial radial nerve at the wrist region. (a) Exposure of the superficial radial nerve. (b) Decompression of the superficial radial nerve. (c) Superficial radial nerve after decompression.

Electrodiagnostic tests are not used in this nerve entrapment. Adjustment in the posture may be the first treatment of choice, but if this fails, surgical decompression with transaction of the inguinal ligament is indicated.^{46,61}

Common Peroneal Nerve Compression

It is the most common nerve entrapment of the lower extremity. The common peroneal nerve is compressed at the region of the neck of fibula. Patients present with sensorial deficit in

the anterolateral aspect of the leg and dorsum of the foot. Foot drop is accompanied in more advanced cases.^{42,91}

Although most of the cases were caused by traumas, bony tumors, and ganglia, it has also been reported in athletes due to repetitive trauma or nerve traction injury.⁶⁸ Surgical decompression is the treatment of choice in most of the cases via curvilinear incision over the neck of fibula⁹⁰ (Figure. 37.9).

Tarsal Tunnel Syndrome

Tarsal tunnel syndrome is the compression of the tibial nerve in the tarsal tunnel in the ankle region. Systemic illnesses such as diabetes mellitus, alcoholism, and hypothyroidism were reported to accompany this syndrome.^{10,34}

Sensorial deficit and pain in the plantar region are the symptoms associated with this syndrome. Intrinsic muscle atrophy with clawing of the toes is seen in advanced cases. Electrodiagnostic tests are usually diagnostic. Operative treatment is the treatment of choice via longitudinal incision between the medial malleolus and calcaneus⁹¹ (Figure. 37.10).

Nerve Repair Using Autograft

Although direct nerve repairs demonstrated better results than nerve grafts, nerve grafts revealed superior results when compared with direct repairs performed under undue tension, which produced nerve ischemia.^{7,49,56,67} In a study that evaluated nerve tension as a determinant of nerve ischemia in a rat sciatic nerve model, blood flow was inversely proportional to nerve tension. Chronic nerve injuries required nearly three times more of the baseline blood flow when compared with acute nerve injuries. Although an 8% elongation was tolerated for both acute and chronic nerve injuries, a 15% elongation produced a profound decrease in blood flow, which never recovered. When primary repair cannot be performed without undue tension, nerve grafting is required. Acute injuries retract only 4%, making primary end-to-end repairs possible, whereas the 28% retraction in delayed repairs cannot be overcome by nerve elongation, and nerve grafts are usually necessary.⁹⁶

Nerve autografts remain the gold standard for nerve grafting. Three major types are cable, trunk, and vascularized nerve grafts. Cable grafts

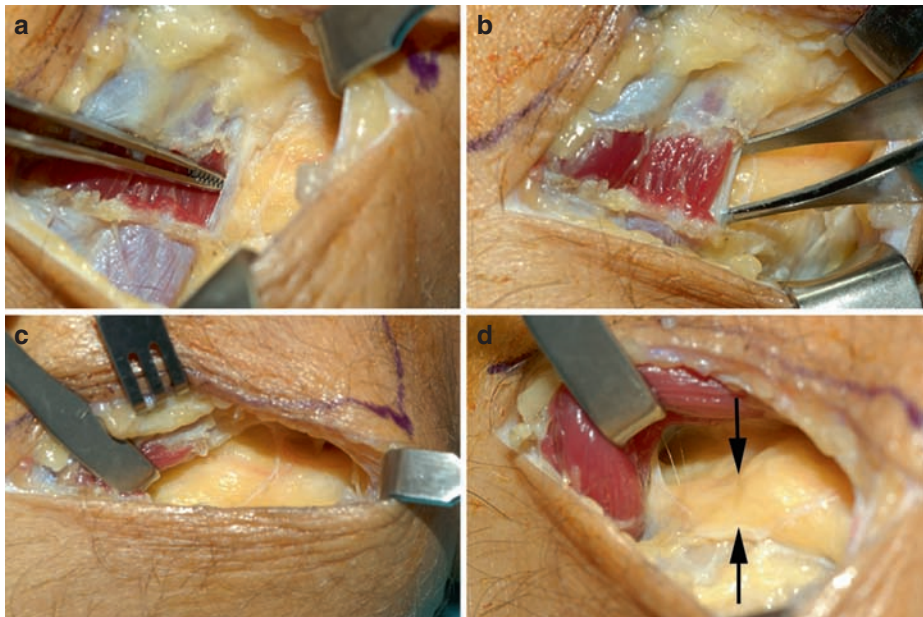


Figure 37.9. Surgical decompression of the common peroneal nerve. (a) Forceps are pointing toward the fascia of the peroneus longus muscle 3 cm below the fibular neck. (b) Entrance of the common peroneal nerve into peroneus longus muscle after release of the peroneus longus fascia. (c) Common peroneal nerve after decompression and resection of the peroneus longus fascia. (d) The site of common peroneal nerve compression (*arrows*) on the entrance to the anterior compartment underneath the peroneus longus muscle, which is elevated by the retractor.

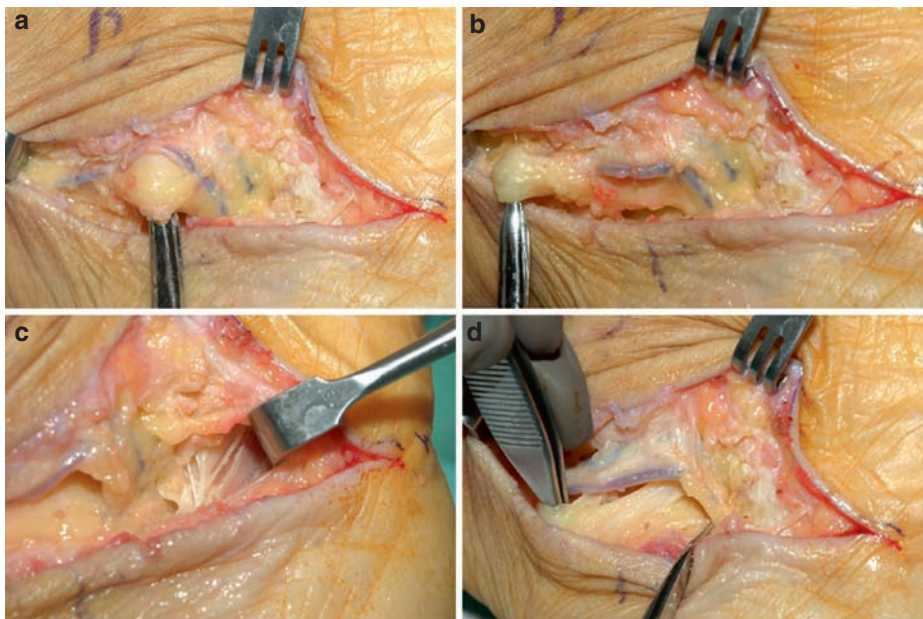


Figure 37.10. Surgical decompression of the posterior tibial nerve in the tarsal tunnel. (a) Decompression of the posterior tibial nerve after release of flexor retinaculum. (b) Decompressed posterior tibial nerve. (c) Decompression of the medial plantar nerve; retractor is holding abductor hallucis muscle. (d) Medial plantar nerve entering medial plantar tunnel after decompression.



may be single or multiple small-caliber nerve grafts aligned parallel to span a gap between fascicular groups. The senior author, Siemionow, evaluated the single-fascicle technique for neural deficit repair and proved that a single-fascicle graft resulted in faster functional recovery and better morphologic outcome compared with conventional nerve repair.⁸⁹

Trunk grafts are mixed motor-sensory whole nerve grafts. They have been associated with poor functional results in large part due to the thickness of the graft and the consequent diminished ability to revascularize after implantation.

Vascularized nerve grafts have been used in the past but with conflicting results. They may be considered if a long graft is needed in a poorly vascularized bed. Because of donor-site morbidity, vascularized grafts have been used mainly in brachial plexus injuries.⁵¹

The most common source of autografts is the sural nerve, which is easily obtainable and relatively dispensable. Other autograft sources include the anterior branch of the medial antibrachial cutaneous nerve and the superficial radial sensory nerve.⁸⁷ After end-to-end nerve repair using a nerve autograft, Wallerian degeneration will be seen distal to the coaptation site.

Conduits

Neural conduits are biological (veins) or synthetic structures that guide the regenerating axons to the distal nerve stump. Many researchers have studied different types of conduits that can be used as alternatives to nerve autografts. Both biodegradable and synthetic nonbiodegradable materials, with or without impregnation of growth factors and Schwann cells, have been investigated.

Lotheissen⁵² was the first to use gelatin conduits in 1901. In the 1940s, Weiss and Taylor¹⁰⁰ and in the 1960s, Braun¹¹ and Leeger studied the effects of gelatin on nerve generation. In 1984, Colin and Donoff²² reported good results by using collagen conduits, which were comparable to nerve autografts. Navaro et al.⁷³ used laminin-filled collagen tubes in 3–5 mm of nerve defects with successful results. Takashi et al.⁸⁸ reported successful results using collagen conduits filled with a collagen matrix in nerve defects of 3 mm. Silicone: poly(dimethylsiloxane),⁵⁴ poly(glycolide),⁹⁹ poly(3-hydroxybutyrate),¹⁰³

poly(L-lactide),¹⁰¹ Chitosan,⁴⁵ D-glucosamine,¹⁰² Polyester urethane,⁹ poly 2-hydroxyethylmethacrylate-co-methylmethacrylate²⁷ are the other materials used as conduits so far.

The materials investigated to date are not without disadvantages, such as the induction of scarring, foreign body reactions, conduit collapse, and invasion by scar tissue. Other drawbacks include the technical difficulty of performing the procedure and often the need for a second procedure to remove nonbiodegradable components. None of the conduits has been proven to be as effective as nerve autografts so far.^{17,86}

Synthetic nerve conduits can be used for the reconstruction of small-diameter nerves with a defect of not exceeding 3 cm or with large-diameter nerves with a defect of less than 0.5 cm. The use of vein graft as a conduit is recommended only for nerve gaps less than 3 cm in noncritical areas.^{70,104}

Nerve Repair Using Allograft

Nerve repair with autograft is inadequate when there is an insufficient amount of autologous nerves available for repair of large defects. This prompted the search for alternative means of reconstruction in extensive nerve injuries. Over the past decades some authors,^{5,15,41,44,48,79} particularly Mackinnon et al.,⁵⁹ explored the use of host immunosuppression and cadaveric nerve allografts to restore nerve continuity in clinical cases. The cadaveric nerve allograft provides an unlimited graft source without the morbidities associated with autograft reconstruction. Nerve allografts act as viable conduits. Host motor and sensory axons grow to reach host targets via these conduits. Function is provided by the regenerating autologous nerves, and this regeneration is supported by allogenic cells. In order to ensure Schwann cell viability and minimal fibrosis, allograft must be revascularized in an early post-transplant period.⁶⁶

These grafts are rapidly rejected unless appropriate recipient immunosuppression is achieved. The toxicity associated with immunosuppression required to promote graft acceptance must be compared with the relative benefits of reinnervation before nerve allotransplantation can be safely applied in routine clinical practice.⁶⁶



Nerve Graft Alternatives

Another reinnervation technique of a denervated muscle is the “split nerve transfer method.” This technique was first described by Conley and Baker²³ in 1979. Although they reported that this technique was not clinically very effective, there are reports in favor of this technique in the literature.^{3,26,76}

Neurotization is another technique used for reinnervation of a denervated muscle, described by Gersuny in 1906. In this technique, the motor nerve is directly implanted into the muscle. Zhasng et al.¹⁰⁵ reported the formation of motor end plates by this technique in 1986.

An alternative technique to nerve autograft is “intact nerve bridge” described by McCallister et al.⁶⁴ in 2001. In that study, the authors observed the histological evidence that the intact nerve functioned as a bridge for regenerating axons, which traveled in the outer epineurium of the tibial nerve before entering the distal end-to-side coaptated nerve.

Future Developments

Stem cell supportive therapy and cellular therapeutics such as chimeric cell transplantations are among the current strategies used for tolerance and chimerism induction. Both types of cells may be systemically administered via intravenous or intraosseous routes or may be locally administered. Injections may be also delivered into the synthetic, autologous, or allogenic conduits.^{20,39,71}

The promising results of the stem cell injections in nerve regeneration made us design a study with subepineural injection of the mesenchymal stem cell. The short- and long-term results of this study are currently being reported.

Schwann cell seeding is another method that may be used for creating an adequate environment for nerve regeneration. They help inflammatory cells eliminate debris and upregulate the synthesis of trophic factors such as nerve growth factor (NGF) and laminin.²⁰

Acellular nerve allografts that contain natural extracellular matrix components and structure but not native cells are another valuable alternative to nerve autograft. They are currently used to study the roles of extracellular matrix components and cellular components

on nerve regeneration concomitantly.^{13,47,77,81} All these new technologies will support future studies on nerve regeneration over long nerve gap defects.

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