Injuries to peripheral nerves are common in all forms of upper extremity trauma but management of them remains a challenge. The use of the operative microscope has facilitated repair of nerve injuries, however, complete restoration of function is often difficult, if not impossible, to obtain. Factors to consider when evaluating a potential nerve injury are: type and severity of the nerve injury, experience of the surgeon and ancillary staff (i.e., operative staff, occupational therapists, and electrodiagnostic technicians), available equipment, and patient variables.

Galen was the first to distinguish nerves from tendon. In the 7th century CE, Aegineta reported on the repair of a nerve injury and Ferrara would later document a successful nerve repair in 1608. In the last 150 years, a more comprehensive understanding of nerve physiology has unfolded. During the 19th century, Waller elucidated the process of axonal degeneration following nerve transection. In the early 20th century, Ramon y Cajal further explained the process of nerve regeneration after injury. Experiences from the Civil War (Mitchell), World War I (Tinel), and World War II (Seddon and Woodhall) provided thousands of cases that served as a foundation for our current understanding of nerve injuries and their repair.

Epidemiology and Anatomy

The typical patient who sustains a nerve laceration is a male in his late teens or early twenties. Injuries are most often caused by domestic or industrial accidents. The mechanism of injury is a cut by glass over half the time, followed by sharp metal objects and machinery. The most frequently injured nerves are the radial nerves of the index finger, the ulnar digital nerves of the small finger, and the median and ulnar nerves at the wrist level.

The smallest functional unit of a peripheral nerve is a nerve fiber. These can be either myelinated (single axon) or unmyelinated (several axons). Each fiber or group of fibers is enveloped by endoneurium, a loose collagenous matrix that protects and nourishes each axon. Groups of nerve fibers form fascicles, which are then surrounded by a perineurial sheath. This layer is the strongest component of the nerve trunk and serves to regulate the local environment by acting as a diffusion barrier and maintaining intrafascicular pressure. It is also a major contributor to nerve tensile strength.

Lying on top of each individual perineurial-surrounded fascicle is a connective tissue matrix called the inner-epineurium that facilitates motion between fascicles. This, in turn, is surrounded by a sheath called the outer-epineurium that maintains the nerve’s structural continuity. The mesoneurial matrix is a collection of loose areolar tissue that surrounds the epineurium and contributes to the longitudinal excursion of peripheral nerves.

The blood supply of peripheral nerves is a network of intrinsic and external branches. The intrinsic (internal) longitudinal system is located within the perineurium and endoneurium. It is an extensive system that is fed by regional nutrient vessels that run transversely and link the two systems. The external segmental blood supply lies within and on top of the epineurial layers. This “arteriae nervosa” enters from the mesoneurium and provides the segmental
blood supply to the nerve. Capillaries are only found in the endoneurium and function as an extension of the blood-brain barrier. Impermeable tight junctions can be damaged by trauma, ischemia, toxins, or mast cell secretions. Injection studies by Sunderland revealed the relative tortuosity of these vessels. This tortuosity facilitates the strain and glide of the nerve.

**Pathophysiology**

Understanding the series of events in the repair process is essential to comprehending the timing and technique of repair. After a peripheral nerve is injured, morphologic and metabolic changes occur. Within the first few hours to days, morphologic changes occur in the cell body with the advent of chromatolysis. There is cell body and nuclear swelling as well as nuclear eccentricity. Within 2 to 3 days of injury, edema forms in the axonal stumps and they undergo Wallerian degeneration. The hallmarks of Wallerian degeneration are axoplasmic condensation and myelin and axonal disintegration. Schwann cells and macrophages are recruited to the zone of injury to remove cellular debris. These events last 3 to 6 weeks and, ultimately, endoneurial tubes are left behind that consist of basement membranes lined with Schwann cells. These Schwann cells then proliferate and organize into columns, guiding the regenerating axonal sprouts between the basement membranes to their targets.

Metabolic changes within the neuronal cell body involve switching the machinery normally set up to transmit nerve impulses to manufacturing structural components needed for reconstruction and repair of the damaged nerve. This includes increasing RNA synthesis to stimulate the production of proteins, lipid building blocks, and hydrolytic enzymes.

End organs also undergo change after nerve injury. Muscle and spindle cells begin to atrophy and the perimysium and endomysium thicken. Complete atrophy occurs within 2 to 6 weeks of denervation. Fibrosis occurs between motor fibers at 1 to 2 years and fragmentation and disintegration occur by 2 years. It is generally agreed that functional recovery is diminished if the nerve does not reach the motor end-plate by 12 months.

Sensory end-organs are less sensitive to denervation than motor end-organs. It has been shown that recovery of protective sensibility is possible many years after nerve injury but that the degree of functional sensation preserved (i.e., two-point discrimination) decreases with a delay in nerve repair longer than 6 months.

Nerve regeneration follows Wallerian degeneration. The Schwann cell basal lamina persists and more Schwann cells are recruited to this site and align themselves longitudinally, creating columns of cells called Bünger bands. This serves as the scaffold for the regenerating axon. The tip of the intact proximal axon sprouts a growth cone, which is the motile exploring apparatus. It is composed of lamellipodia and filopodia, delicate cytoplasmic extensions that permit exploration of the microenvironment. Actin within the filopodia allows contraction and elongation along the tube. The growth cone releases proteases, which dissolve the matrix in its path. Growth is centrifugal at 1 mm to 2 mm/day, but scar tissue can impede the organized advancement of the regenerating axon and cause nerve fibers to run in a criss-cross fashion to avoid the obstruction.

**Classification of Injuries**

Nerve injuries were classified by Seddon and colleagues into neuropraxia, axonotmesis, and neurotmesis. Their classification scheme was a result of extensive World War II experiences with injured soldiers. Sunderland later expanded on this classification according to the structures damaged, usually discernible by histological exam only. He described five types of pathophysiologic changes. Neuropraxia (Sunderland Type 1) is described as an injury to the myelin sheath only. This is the least severe type of injury, because axonal continuity remains preserved. Local conduction is blocked at the site of injury, but is normal proximally and distally. The usual mechanism for this type of injury is a stretch or compression. No Wallerian degeneration occurs and recovery is expected within days to weeks.

An axonotmetic injury is when the axon is disrupted and Wallerian degeneration occurs distal to the injury. Sunderland Type 2 injuries occur only to the axon, whereas Type 3 and 4 damage the endoneurium and perineurium, respectively. A three-month observation for clinical improvement is generally recommended for these types of injuries. Type 2 injuries are expected to show a full recovery because the tubes are intact and the axons are guided along their original course. Type 3 injuries recover incompletely for several reasons:

1. There is a more severe retrograde injury;
2. Intrafascicular fibrosis leads to mismatching of fibers; and
3. With longer recovery delays, end organs undergo irreversible changes.

Type 4 lesions are essentially a “neuroma-in-continuity” and generally require surgical repair or reconstruction. Minimal useful recovery is expected when these injuries are treated without operative intervention.

Neurotmesis is a lesion that completely disrupts the nerve and is defined as a Sunderland Type 5 injury. The epineurium is transected and spontaneous recovery is negligible, therefore, surgical intervention is indicated.

After a nerve injury, function fails in a predictable order. Motor function fails first, followed by proprioception, touch, temperature, pain, and sympathetic regulation. Recovery of nerve function generally occurs in the reverse sequence.

**Diagnosis**

To make the diagnosis of a peripheral nerve injury, one must first take a detailed history. The timing of the injury will help
guide treatment recommendations. The mechanism of the injury aids the examiner in determining the type of the nerve injury and what recovery can be anticipated. Other important questions are: Was the joint extended or flexed? What happened at the time of injury (i.e., a sudden or progressive numbness or was there profuse bleeding or associated injuries)? How old is the patient, what is his occupation and what is his hand dominance? One must also perform a thorough physical exam. Special studies such as electrodiagnostics or vascular tests may be necessary to confirm a suspected nerve lesion. During the physical exam, sensibility and motor function are tested and the results recorded. This is important for not only the initial injury, but also to document and follow clinical recovery after repair.

Sensation is the subjective appreciation of a physical stimulus. Sensibility is the capacity for sensation (i.e., the responsiveness to sensory stimuli). Various methods have been described to test sensibility. A tuning fork is used to test vibratory perceptions at various frequencies. Vibration is detected by quickly adapting fibers of group A axons. Vibration testing is useful for detecting deficits before subjective complaints, and to follow early recovery or test for a neuroma-in-continuity.

Two-point discrimination using a paper clip or other standard measuring device measures the sensitivity of group A axons’ slowly adapting fibers. It is useful only when light constant touch is perceptible. Moberg described a successful exam as when the subject correctly discerns 7 out of 10 trials. Moving two-point discrimination returns earlier than static, because both slow and rapid fibers are stimulated.10

The von Frey pressure test used horse hairs of varying thickness and stiffness to stimulate group C axons and delta fibers and was later modified to the Semmes-Weinstein monofilament test. The examiner sequentially places standard sized filaments on the subject with a constant downward pressure. The smallest one detected is recorded and compared to a standard chart.

Various pick-up tests have been described11,12 to test for general sensibility and tactile gnosis. These tests combine sensibility and sensory input with motion. Multiple objects are placed in a container or on a table, and the blindfolded subject is instructed to find certain objects with the affected hand. The patient’s ability to perform this task is timed and compared to the contralateral side. This test and the two-point discrimination exam are two tests that are used to monitor end-stage recovery.

Sudomotor activity13 is assessed via the water immersion test in children whereby the hand is held in water until the fingers wrinkle. The absence of wrinkling indicates a nerve injury. In adults, the ninhydrin (sweat) test is used to indicate a nerve lesion by whether or not sweat is detected by a starch and salt solvent. The absence of perspiration indicates a nerve injury to that distribution.

Motor function is tested during the physical exam and is graded from 0 to 5. Completely paralyzed muscle groups are scored zero; a flicker of contraction is given a score of one; two represents contraction with gravity eliminated; and three is a contraction against gravity. Contraction against some resistance is given a score of four, and a contraction against powerful resistance is given the maximum score of five. One must be cautious of anomalous innervations and supplementary actions when performing this part of the physical exam. When the median nerve is interrupted, the ulna-innervated flexor pollicis brevis can mask the absent opposition function of the thumb. A Martin-Gruber anastomosis consists of a cross over of motor median fibers to the ulnar nerve in the proximal forearm and can confuse a neurological exam.

Special diagnostic studies are sometimes necessary to confirm or support a diagnosis of a nerve injury. Electromyography (EMG), nerve conduction studies, and electrical muscle stimulation have all been used. It is important to maintain the extremity temperature greater than 30 degrees centigrade to avoid false slowing of conduction. The EMG records electrical potentials produced by muscle fibers. A needle is inserted directly into a muscle belly and records motor-unit action potentials a fixed distance away from the transducer. Decreased duration, amplitude, or firing frequency indicates a lesion. The resting muscle should be electrically silent, but if it is denervated, it will show fibrillation potentials and sharp waves 2 to 3 weeks after an injury.

Nerve conduction studies measure conduction velocities and response amplitudes of a nerve fiber. A percutaneous depolarizing current is introduced and the motor or sensory nerve action potential is measured a certain distance from the stimulus. The conduction velocity measures the integrity of the myelin sheath and the amplitude of response indicates the quantity of functionally conducting axons in a nerve. This test is especially useful in compressive lesions and partial lesions, however, only after Wallerian degeneration has ceased (5 to 7 days post-injury).

Muscle stimulation tests the continuity of a muscle-tendon unit. It allows the examiner to differentiate between a laceration to a muscle belly or tendon versus a nerve transection. If the desired response occurs when the muscle belly is directly stimulated, a nerve injury is likely.

Nerves respond quickly to ischemia, their function being directly related to the quality of circulation. Vascular changes secondary to local compression (i.e., hematomas) or interruption in blood flow cause a local ischemic neuritis often affects motor and sensory end organs. Other systemic diseases such as diabetes or peripheral vascular disease can affect the local circulation. Doppler flow studies or plethysmography may be necessary to assess blood flow to the peripheral nerve.

**Timing of Intervention**

A primary nerve repair is defined as an end-to-end anastomosis. Secondary repair is conventionally defined as occurring one week or more after injury. Several investiga-
tors have reported that nerve repair is better when performed within 6 months of injury and several studies have shown primary repair to be superior to secondary repair as long as the tissue bed is adequate.14-17

Once the diagnosis of peripheral nerve lesion is established, one must determine whether the injury is partial or complete. Fifteen percent of injuries are partial lesions; local contusion or stretch being responsible for the deficit. In these cases, most authors18-20 agree that secondary repair should be advocated to give the injured nerve time to recover on its own. Eighty-five percent of lesions are complete transections and primary or secondary repair depends on the circumstances of the injury. If a complete lesion is suspected, exploration is advocated. If the epineurium and fascicles are neatly divided and have minimal contusion, primary repair without tension can be performed. If, on the other hand, one finds ragged epineurium or severe contusion or if a tension-free repair cannot be performed, tagging of the ends for later repair or grafting should be done.21

Intraoperative monitoring can be useful to facilitate the decision to repair, graft, or resect nerve tissue. However, while it does not substitute for preoperative electrodiagnostics, it is helpful to monitor nerve function, guide dissection, and identify neural elements from scar tissue.22-24 If a nerve action potential can be recorded across a damaged segment, then intact fascicles can be dissected free. If no nerve potential is recordable beyond a zone of injury, repair or graft may be necessary.

The management of a neuroma-in-continuity remains a clinical challenge. Some improve spontaneously and require no intervention. Current recommendations for this suspected lesion is to wait 8 to 10 weeks for neuropraxia to resolve.25 Of prime importance is whether or not the neuroma-in-continuity is complete or incompletable by clinical and electrical criteria. If it is incomplete (especially if distal function is spared), further improvement of function typically follows. If the lesion is complete, and no improvement is observed after several months of observation, exploration is necessary.

Situations that generally require immediate intervention are aneurysms or A-V fistulas, a blood clot in a closed space (i.e., compartment syndrome), a missile or foreign body lodged in or on a nerve and causing symptoms, and injection injuries.

Types of Intervention
In general, nerve exploration and repair should be performed with operative magnification. After the zone of injury is defined, the nerve endings are cut back to healthy fascicles. The nerve ends must be cut cleanly using a sharp instrument; a number 11 blade over a tongue depressor typically works well. If additional nerve length is required, releasing constricting fascia, dividing mesoneurial attachments, and dissecting any tethering bands will mobilize the nerve further. Flexing joints above and below the nerve injury and performing transpositions can gain several centimeters of length. Bone shortening (especially of the humerus) can be done to maximize length. Tensionless repairs have demonstrated superior results. Exceeding 10 percent of the resting length of the peripheral nerve has been shown to decrease blood flow to the nerve by 50 percent.26 Depending on the caliber of the nerve, sizes 8-0, 9-0, or 10-0 nonabsorbable suture is used for the repair.

Primary End-to-End Repair
Favorable conditions to undertake a primary end-to-end repair include wound characteristics, patient factors, and the appropriate setting. A sharp transection with a clean wound and adequate soft tissue coverage in a patient who is metabolically and emotionally stable, as well as free of associated injuries is preferred. An experienced surgeon with the proper equipment performing a tension-free repair is mandatory. If the above are not possible, tagging the nerve ends for secondary repair or grafting is recommended.

The technique for primary repair includes resecting the damaged nerve to normal appearing ends, mobilization for maximal length, aligning the longitudinal blood vessels and assuring proper rotational alignment. Epineural repair has been shown to have similar functional results to group fascicular repair27 with less scarring in smaller, more distal nerves. Grouped fascicular repair is preferred in larger nerves where motor and sensory fibers can be accurately matched. One must be careful to analyze the cross-sectional appearance of the proximal and distal stumps to be repaired. Topographic sketches can be helpful and staining techniques have been described to isolate motor from sensory fibers,28 but these staining techniques can be time-consuming and impractical. Awake patient electrical stimulation for proximal sensory fascicles can be done after Wallerian degeneration is complete, but motor stimulation is possible only in fresh injuries before Wallerian degeneration has commenced.

Nerve grafting
Nerve grafting was first performed by Albert,29 in 1876. Historically, the nerve graft was considered to be an inferior technique30,31 due largely to misconceptions regarding multiple coaptation sites and the lack of awareness regarding the importance of living Schwann Cells. Success with nerve grafting has increased due to recognition of the efficacy and success of tensionless repairs, Schwann cell contribution to regeneration, and the inconvenience of the length of grafts.32

Although allografts and xenografts have been used experimentally and in some restricted clinical settings, autograft is the preferred source of nerve graft.33 The most common site for harvesting peripheral nerve graft material is the sural nerve. Up to 40 centimeters can be obtained, but one can resect the entire length to avoid painful neuromas, even if only a few centimeters are needed. Other sites of donor nerves include the medial and lateral antebraclial
The advantages are:

Peripheral nerves can be harvested as a free nerve with mixed motor and sensory fibers that need to be revascularized by the third day to avoid fibrosis. Multiple small caliber nerve grafts can be arranged in parallel between fascicular groups to make a cable graft. Fibrin glue can be used as a supplement to promote adherence of these small grafts. Vascularized nerve grafts have been described, but their results are no better than a well-performed free graft.

Whatever the source or type of graft used, general surgical techniques need to be followed to optimize results. Nerves should be grafted within 6 months of injury in order to ensure maximal motor recovery. Protective sensibility is possible many years after injury but functional sensation is lost when the repair is delayed. Even if the transection is sharp and clean, any significant delay will allow the nerve to retract up to 28% from elastic recoil. There is no absolute length limit for grafts; it will vary from patient-to-patient. What is vitally important, however, is to harvest a nerve to regain its native tensile strength.

**Nerve Transfers**

Although nerve transfers are usually reserved for patients with brachial plexus avulsions, they have had superior outcomes to long nerve grafts. The objective of nerve transfer is to convert a high level injury to a low level injury. The advantages are:

1. Muscle structure is preserved, as reinnervation must be made prior to 18 months to avoid irreversible fibrosis and long nerve grafts may not reach the target muscle in time;
2. Nerve grafting is avoided which eliminates a second interface and potentially an avascular donor nerve; and finally,
3. Potential mismatching is avoided, as nerves with dedicated function are selected as transfer donors.

Examples of nerve transfers are:

1. The thoracodorsal nerve to the deltoid muscle for axillary nerve lesions;
2. The pronator quadratus branch of the anterior interosseus nerve (AIN) to the motor branch of the ulnar nerve at Guyon’s canal; and
3. The common digital nerve from the fourth webspace to provide sensation to the thumb and index finger.

**Conduits**

“Entubulation” repair was first described by Gluck, in 1880, using decalcified bone; and Buengner, in 1891, was the first to use a segment of the brachial artery as a bridge for an injured sciatic nerve. Chiu reported successful repairs using vein sleeves in the 1980s. Recently, animal studies and clinical trials have shown good results using biologic and biodegradable substances such as mesothelium, omentum, vein, artery, and polyglycolic acid (PGA) as conduits that allow regenerating nerve fibers to course their way to the end organs or nerve stump. Conduits enable neurotrophic factors to be introduced as a medium to facilitate the quality of nerve repair and growth within the tube and to prevent peripheral disorganized sprouting. Synthetic conduits such as silicone and Maxon tubes have had poorer results due to chronic inflammatory changes and compression.

**Results of Repair**

The British Medical Research Council promoted and standardized a grading scale for motor and sensory outcome after World War II (Tables 1 and 2). Development of the scale was a response to the awareness that objective results were confounded by interobserver variability. Using various methods for assessment, including two-point discrimination tests, monofilaments, vibratory stimuli, Tinel’s sign, and electrodiagnostic tests, nerve recovery occurs in a predictable, orderly fashion. Pain and temperature sensibility return first, as these pathways are conducted via smaller caliber, unmyelinated axons. Low-frequency (30 Hz) vibration, moving touch, and static touch follow next. Last to recover is high-frequency (256 Hz) vibration perception via myelinated, larger caliber axons.

Motor function can be evaluated with force plates, pinch, and grip tension devices. The grading system for the recovery of motor function is similar to that for post-injury evaluation.

Any associated injuries such as fractures or arterial damage contribute to poorer outcomes. Early reports from a 5-year follow-up of war wounds were poor initially, probably owing to associated injuries and an incomplete understanding of the current repair principles.

In general, patients who have less severe or incomplete injuries do well with neurolysis. Over 90% of these patients have good recovery if they show electrophysiologic evidence of regeneration intraoperatively. Younger patients and patients with more distal lesions fare better given similar mechanisms and tissue damage.

For repairs that require nerve grafts, four factors affect outcome the most:

1. Age of the patient,
2. Length of the gap to be spanned,
3. Time delay from injury to surgery, and
4. Level of the injury.
Gaps greater than 5 cm, delays longer than 3 months, an age over 20, and blunt injuries adversely affect the desired outcome. Good to excellent results (M3/S3 or higher) have been obtained 42% to 100% of the time.46-51 Primary, tensionless repair of digital nerves have shown good to excellent results 36% to 68% of the time.49,52-54

Summary
Peripheral nerve injuries are commonly seen as a result of domestic, industrial, or military trauma. Sharp objects usually cause these nerve injuries. When assessing these injuries, it is important to evaluate each nerve's motor and sensory function. One must be cognizant of associated injuries such as fractures, vascular damage, and musculotendinous lacerations. The time since the injury, level of injury, and age of the patient are important prognosticators impacting the return of function. Intraoperatively, one must assess the vascularity of the soft tissue bed and the nerve itself, the nerve gap, conduction, and the topography of the fascicles to insure proper orientation. Application of the principles of nerve repair (magnification, minimal tension, meticulous soft tissue handling, experienced surgeon and staff) can enhance the chances for a successful result. Additionally, to maximize functional recovery following peripheral nerve repair, a carefully planned program of postoperative occupational therapy and rehabilitation must be instituted.

References


