Principles of Peripheral Nerve Repair

Chapter 65

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Biology of Nerve Repair and Regeneration

Surgical Repair of Peripheral Nerves

References

Surgical repair of peripheral nerve injuries is not a new concept. Reports of successful peripheral nerve repair appeared in the literature as early as 1836. Additional reports of successful case management punctuated the 19th century. The first controlled study of experimental injury and subsequent repair was performed in dogs by Howell and Huber in 1893. This was followed by a similar study performed by Sherren in 1908.(159)

Interest in advancement of knowledge in the area of peripheral nerve injury was fostered by World War I. Management of extremity wounds included recognition of the importance of restoration of nerve function as part of the process of reconstructive surgery.(124) Numerous reports of peripheral nerve repair resulted from the experiences of this war. Very few of the techniques described were compatible with our present understanding of nerve biology and regeneration after injury.

Working independently, Babcock and Bunnell proposed standardized surgical techniques for peripheral repair. These principles encompassed management of injured nerve tissue, surgical techniques for repair of the injury, and postoperative management. Much of the information presented in these reports forms the basis for operative management today.(5,25)

It was recognized that not all nerve injuries were amenable to direct end-to-end repair. Many injuries resulted in loss of nerve tissue and thus the formation of nerve gaps. To restore function after injury, the possibility of nerve tissue grafting was explored. Nerve grafting was first reported by Philipeaux and Vulpian in 1870. The first human allograft was reported in 1878 by Albert. Sherren wrote of his experiences with nerve grafting in 1906.(89) Huber described autologous nerve grafting in the dog with good results as early as 1920.(70) Grafting gained popularity in 1932 with the work of Ballance and Duel.(35,89) Bunnell and Boyes reported on the use of digital nerve autografts in 1937.(26) No uniform success was reported by these authors. Alternate experimental methods for lengthening nerve stumps centered around mobilization and transposition of existing nerve tissue.(10) It was recognized that regardless of technique used, excessive tension at the suture line would increase the probability of clinical failure.

It was observed at this time that further advancement in the management of peripheral nerve injuries could be a product only of greater understanding in basic biology of peripheral nerves. Research in this area intensified during the 1930s and was stimulated by the anticipation of an upcoming global conflict. Much research performed during this time provided a basis for our current understanding of nerve degeneration, regeneration, and healing of surgical repair.(1,15,38,57,112,118,148,157)

The last several decades have evidenced refinement in basic principles of nerve injury and repair. Based on an improved understanding of basic nerve biology, advances have been made in surgical repair and management. Continuous research in the area of suture material and biologic implants has contributed to increased clinical success in the management of peripheral nerve injuries. Use of the operating microscope has contributed to the advancement in reconstructive techniques.(72) Suturing of individual nerve bundles and alternate techniques for macroscopic nerve repair are an outgrowth of this technology.

An investigation into technology and basic biologic principles has accompanied the study of nerve grafting techniques. Research in autografting, allografting, and heterografting techniques has helped to provide answers that add to our knowledge of the factors that Contribute to the success or failure of grafting techniques. Ongoing research will provide answers to questions concerning the relationship of immunologic response to allografting techniques.

Finally, the application of alternate reconstructive techniques is under study. Transposition of nerve trunks may help to restore activity to denervated musculoskeletal areas.(31,49,79,98) Direct implantation of nerve stumps into muscle tissue resulted in return of motor function.(109,111) Both of these topics are current areas of research in the quest for answers to questions related to basic biology and clinical restoration of peripheral nerve function.

Biology of Nerve Repair and Regeneration

MORPHOLOGY

The basic subunit of any peripheral nerve is the axon.(115) The axon is an extension of the nerve cell body. Histologically, the axon may be seen as several distinct components.(46,128,129) The center of each axon is composed of axoplasm, which is the cytoplasmic extension of the nerve cell body. As will be described below, axoplasm comprises several physiologically distinct zones that aid in transport of nutrients and essential biochemical components from the nerve cell body to the terminal axon and neuromuscular terminals. The cell membrane surrounds the axoplasm and is referred to as the axolemma. Surrounding this axoplasmic unit is the Schwann cell. The Schwann cell may invest one or more axoplasmic units. A myelinated nerve has a Schwann cell and associated structures surrounding one axoplasmic unit (1 u - 15 u diameter). The plasma membrane of the Schwann cell forms a lamellar spiral around the axoplasm. The myelin sheath is a double spiral of lipoprotein that is contiguous to the plasma membrane of the body of the Schwann cell. The formation of myelin sheath occurs during development of the Schwann cell and is a product of cytoplasmic extrusion from the lamellae (Fig. 65-1).(47)

Each Schwann cell and its associated myelin encase a histologically distinct zone. This area is referred to as an internode zone. Gaps appear between two internodes and are referred to as nodes of Ranvier. Branching of axons always occurs at this junction (Fig. 65-1).(42,47,104)

Unmyelinated nerves are not as well organized histologically. Multiple small-diameter nerve fibers (0.2u-2.0u) are invested by invaginations or pseudopodia of a Schwann cell. Evidence for a feedback mechanism from the axon to regulate the production of myelin by the Schwann cells has been documented experimentally. In regeneration after injury, the axon determines the degree and amount of myelin that the Schwann cell will produce.(47,104)

Enveloping the Schwann cell-axon unit is the basement membrane. This structure serves as a histologic demarcation between the neural and connective tissue elements of the peripheral nerve. Immediately adjacent to the basement membrane is the endoneurium. The endoneurium is composed of a fibrocytic stroma of a double layer of collagen, fibroblasts, and vascular components. It forms a tubular structure that surrounds the axon unit. In instances of injury, it does not degenerate as will axon components.(104) Axons and associated endoneurium form aggregates that are referred to as nerve bundles, fascicles, or funiculi. A funiculus is enclosed by a collagenous envelope of larger diameter termed the perineurium. The perineurium consists of 7 to 15 lamellae of fibrous connective tissue compressed into a tubular arrangement. The inner surface of the perineurium is lined with mesothelial cells. Within the funiculus, intrafunicular septae separate individual axon units. The function of these septae is not fully understood. The perineurium acts both as a diffusion barrier and as a lattice-work for vascular beds. Enclosing the bundles of funiculi is the outer covering of the nerve, the epineurium, which is a loose network of collagen, elastin, and fibrocytes. Much of the ability of the peripheral nerve to undergo elastic deformation without rupture can be attributed to the tensile strength and elastic properties of the epineurium.(42,47, 104)

Funiculi are not arranged in simple uninterrupted strands along the course of a peripheral nerve. Frequent divisions and fusion with other funiculi form numerous plexuses along the course of the nerve tank (Fig. 65-2). Redistribution is active along the entire length of the nerve but is particularly prominent in the proximal portion of the nerve trunk. Two types of funiculi are incorporated into every peripheral nerve. Simple funiculi are those that are composed of fibers that serve solely a particular muscle or cutaneous area. Compound funiculi are composed of axons from several sources in varying combinations and proportions. This feature allows for the integration of various funicular components that distribute to innervate specific anatomical regions. Several important considerations arise from this plexus formation. Unless complete transection of a nerve trunk occurs, partial function of the nerve may remain in cases of injury. Cross-sectional morphometric studies have indicated that funicular anatomy changes every 0.5 mm to 15 mm. If neural tissue is lost in the course of traumatic wounds, funicular continuity and alignment may not be possible at the time of surgical repair. (128-130)

FIG. 65-1 A myelinated motor nerve branch with associated anatomical features The motor nerve is a sum of individual funiculi, which in turn are aggregates of axon subunits. Each axon is enclosed in a lamellar whorl of condensed lipoprotein classified as the Schwann cell. The intercellular zone is referred to as the node of Ranvier. Note the anatomy of regional vascularization entering through the mesoneurium The neuromuscular junction is directly confluent with the sarcolemmal membrane. The postsynaptic invaginations (clefts) are the site of action for the biochemical transmitter acetylcholine.

FIG. 65-2 An individual funiculus demonstrates repetitive morphometnc fusion

and division of axon units through the entire course of the nerve trunk. This redistribution allows for organization of regional innervation components.

The vascular supply to peripheral nerves is by small segmental nutrient arterioles that arborize into an extensive capillary network. The nutrient arterioles arise at irregular intervals and, as they course toward the peripheral nerve, are enclosed by a delicate connective tissue referred to as mesoneurium. Mesoneurium is analogous in function and certain anatomical features to the mesentery of the small intestine. All vessels entering the nerve do so at the mesoneurial border (Fig. 65-1). After entry through the epineurium, vascular arborization and alignment parallel to the funiculi are noted. The second generation vessel aligns with the funiculus and courses parallel to the epineurial vessels. Tertiary arborization proceeds to supply individual axon units by means of an axon-capillary plexus. Multiple anastomoses between branches of perineurial and axon vessels ensure adequate collateral vascular supply in instances of segmental interruption. (30,48,121,123,129)

Peripheral nerve blood flow appears to be unaffected by autoregulation. Experimental measurements of blood flow in normal cats and in cats immediately after severance of the nerve trunk conclude that injury to peripheral nerves causes only transient effects in blood flow. This is in contrast to evidence gathered in the central nervous system, where autoregulation plays an important role in maintenance of tissue nutrition.(122)

The origin of the axon is the nerve cell body. The histologic components of the nerve cell body are the same as those of other cell types, including a centrally placed nucleus and surrounding substructures. The Golgi apparatus and mitochondria are histologically prominent within the cell. Other characteristic cell inclusions are classified as Nissl bodies or chromophil substance. Nissl bodies represent endoplasmic reticulum and associated polyribosomes. As will be discussed below, the role of these cellular components was misunderstood and improperly interpreted in much of the early work on the response of the cell body to injury.(21,104)

Nerve cells may be classified as unipolar, bipolar, or multipolar. The configuration of the nerve cell can be associated with the function within the body. Sensory nerve cells of the dorsal root ganglion have a unipolar configuration in which one process exits from the nerve cell body and then divides into the dorsal root and afferent sensory branches, which course to their respective functional zones. Bipolar nerve cells have one axon and one dendrite. They are located in retinal tissue. Motor cells of the ventral horn of the spinal cord are of the multipolar variety. One axon and multiple dendrites characterize this configuration. This cell type predominates in peripheral motor nerves.(59,104)

There is a histologically distinct zone in which peripheral nerve tissue separates from the central nervous system. In this transitional area, the axons abruptly change envelope cell types from the central zone oligodendrocyte to the peripheral zone Schwann cell. The axons are enclosed by pia mater at this point, then subsequently pass through a dura mater tunnel and become enclosed in perineurium. This transition occurs in both dorsal and ventral roots. Microscopic evaluation of this pia mater-perineurial junction shows contiguous extension of the pia with the perineurium in a smooth layer transition.(47,135) Efferent terminal motor units are of two types. Large diameter nerve fibers (alpha motor neurons) innervate the extrafusal muscle fibers. Alpha motor neurons subdivide at this juncture to supply innervation to multiple muscle fibers. These muscle fibers together with the terminal nerve branches are referred to as a motor unit. Gamma motor units supply intrafusal muscle fibers of the muscle spindle. Their activity is influenced by basal muscle tone and control of sensory activity by the muscle spindle. Fine motor control is influenced by the number of motor unit components. The higher the ratio of motor units to muscle fibers, the finer control can be effected. This ratio is highest in extraocular muscles and lowest in skeletal musculature.(47,50,59)

The neuromuscular junction is the transition zone from peripheral nerve to musculoskeletal systems. As the nerve approaches a neuromuscular junction, the sheath composed of myelin and the Schwann cell terminates. The cell membrane of the axon expands to form the terminal neural junction in association with the sarcolemmal membrane. A gap of 200 nm to 300 nm is noted on histologic evaluation and is referred to as the synaptic cleft. At the terminal border of the nerve, synaptic vesicles filled with acetylcholine are opposed by invaginations of the sarcolemmal membrane classified as secondary synaptic clefts. From this area, release of acetylcholine and receptors for this chemical combine to transmit neural impulses to the musculoskeletal system.(50,59)

Sensory receptors are the peripheral component of myelinated and unmyelinated afferent nerve fibers. These fibers, in turn, terminate in the dorsal spinal roots. The sensory receptors arise from skin, muscle spindles, joints, and other areas in which neural input is important for maintenance of homeostasis. They transduce various forms of energy into nerve impulses. These afferent impulses are integrated at the level of the spinal segment or at higher levels and evoke a response to compensate for the change in homeostasis. Of clinical importance in diagnosis of peripheral nerve disorders is the class of sensory receptors turned nociceptors. This class provides sensory input for recognition of noxious stimuli. In carnivores, a subcategory referred to as mechanonociceptors predominates. These receptors are influenced more strongly by mechanical damage than by thermal changes. When clinically evaluating peripheral nerve disease or injury, evaluation of nerve deficits by application of a noxious stimulus to nociceptors can aid in diagnosis of specific nerve injury.(47,50,59) The topography of cutaneous innervation is well documented for the hindlimb; however, some disagreement of zone boundaries for the forelimb still exists. This can be related to overlap of cutaneous nerve function in certain superficial regions. Cutaneous regions supplied by only one cutaneous nerve are referred to as autonomous zones. Some areas have a dual innervation from two or more peripheral nerve branches and are called intermediate zones. Knowledge of regional distribution is essential for correct diagnosis.(47,73)

Mechanoreceptors predominate in joints and muscle spindle regions. Joint receptors detect acceleration in any direction of that joint and thereby provide input to compensate for gravitational influences. Muscle mechanoreceptors from the muscle spindle fibers and Golgi tendon organ at musculotendinous insertions represent sites of adherent input. These receptors, along with alpha and gamma motor neurons and the spinal cord segment, form the arcade for segmental reflex evaluation. Absence of or deviation from standard response to clinical testing may aid in localizing peripheral nerve or spinal cord lesions.(50)

PHYSIOLOGY

The axon consists of subunits that provide the vital functions of intracellular nutrition and transport of biochemical substances involved in the regeneration process following nerve injury. The proteins that make up this cytoskeleton are classified as microtubules, neurofilaments, and microfilaments. Microtubules are protein structures that possess an axial alignment with direction of the axion. Neurofilaments are of similar morphology; however, the internal diameter of the tube is narrower. Microfilaments have an actin component chemically related to contractile actin of skeletal muscle. Their orientation is both transverse and longitudinal with the long axis of the peripheral nerve. (47,114,153)

These internal elements are important for the two types of substance transport within the nerve cell. By far the majority of proteosynthesis and nutritive substances are produced in the nerve cell body. Early experimental work in nerve injury and regeneration indicated that the average growth of the nerve was I mm to 3 mm per day. From this work, it was inferred that axoplasmic migration occurred in the direction from the nerve cell body to the periphery; this migration was classified as axoplasmic flow. (114,153)

This concept was accepted until certain observed phenomena could not be explained by the prevailing theory. Following experimental constriction of peripheral nerves, swelling proximal to the constriction site occurred earlier than anticipated by calculated axoplasmic flow. Radioactive labeling of protein components using amino acids and tritium revealed migration as rapid as 410 mm per day in feline sciatic nerves. The rapidity of transport and organization provided the basis for recognition of a second type of

motion, axonal transport. (41,114,153)

The function of axonal transport is movement of neurotransmitter substances and axolemmal replacement material from the nerve cell body to the periphery of the nerve. However, it has been deduced that axonal transport is not unidirectional. Retrograde as well as antegrade flow of materials can occur in the microtubular network. This observation may aid in the explanation of retrograde migration from the periphery of central nervous system agents such as rabies, herpes viruses, and tetanus toxin. The normal function of retrograde transport is the return of cell membranes to the cell body for degradation or resynthesis and return of a portion of synaptic vesicles to the nerve cell body for recycling. The rate of retrograde transport is one half to two thirds that of antegrade conduction. (114,153)

Axonal transport occurs by means of the cytoskeleton network described above. Although no definitive work has been done, it is postulated that motion imparted by one of several mechanisms provides the basis of propulsion down one microtubular or neurofilamentous track. Tracks probably have polarity so that only unidirectional flow can occur. The basis for propulsion is probably actin filaments arranged around the tubulofilamentous network that provide peristaltic waves or plasma flow changes to propel units up or down this network. Further work is needed to elucidate the exact transport mechanism and the relationship, if any, to maintenance or activity of the excitable neural membrane.(114,153)

Nerve tissue has dynamic properties similar to any excitable membrane. A peripheral nerve may be thought of as an electrical conduit in which impulses are conducted from a central terminal (light switch) to an effector organ (light). The event that is produced by conduction of this impulse is referred to as an action potential. An action potential can be conducted only when the cell membrane is in an excitable state. This is achieved by development of concentration differences for sodium and potassium ions across the cell membranes. Maintenance of this differential by the sodium-potassium pump within the cell membrane imparts an electrical differential across the cell membrane of - 85 mV. The value, referred to as a resting potential, remains in a stable state until a stimulus sufficient to create threshold occurs. When the threshold value is reached, activation of the cell membrane occurs. Configurational changes in the membrane pore rearrange "gates" to allow for sodium ion influx. The membrane then depolarizes and transmits the length of the axon in either direction. This phenomenon is referred to as the "all-or-nothing" principle and states that once depolarization begins at any point on the nerve, the entire membrane is obligated to depolarize. The rate of this propagation is referred to as nerve conduction velocity. Factors commonly involved in the speed of conduction include fiber diameter, degree of myelination, and membrane temperature. The effect of these factors on peripheral nerve conduction will be discussed below.(47,50,59)

Repolarization always begins at the same point at which depolarization occurred. Efflux of potassium ions from cytoplasm to cell membrane surface allows for re-establishment of appropriate ionic barrier charge. Potassium ion is then exchanged for sodium ion by the sodium-potassium pump to reestablish baseline continuity of ion balance.(50,59)

The velocity of depolarization depends upon the presence of organized myelin structure in the nerve fiber. Myelinated nerves have concentric layers of Schwann cell membranes interspersed by sphingomyelin. As noted above, histologic gaps occur at intervals between the Schwann cell units. These gaps are classified as nodes of Ranvier and constitute an important element in nerve impulse conduction. Schwann cell units with associated myelin are analogous to electrical insulation. Owing to its increased transmembrane potential, impulse conduction does not occur along the entire length of the nerve but only at the nodes of Ranvier. The cell membrane in this area is especially permeable to ion exchange and can aid in rapid impulse conduction. As an impulse travels along the surface of the cell membrane, its transmission occurs at the nodal junction and jumps from node to node in a manner classified as saltatory conduction. Because of the jumps in impulse transmission, velocity of conduction in a myelinated axon is greater than in its unmyelinated counterpart. An additional benefit of saltatory conduction is the conservation of energy for the axon, accomplishing conduction with less of fewer ions than standard excitable tissue. This allows for more rapid repolarization with minimal energy expenditure (Fig. 65-3).(47,59)

Unmyelinated nerves have no organized mechanism of saltatory conduction. Impulse propagation occurs in an organized sequential manner involving the entire membrane of the axon. Membrane depolarization is accompanied by an ion-exchange current across the cell membrane surface. This flow of ion exchange is described as an eddy current. Speed of depolarization of the cell membrane by eddy currents is influenced by axon diameter. A larger cross-sectional diameter of an unmyelinated nerve allows for a larger current flow and faster local excitation and results in a higher conduction velocity (Fig. 65-4). (50,59)

FIG. 65-3 Gap depolarization of a myelinated nerve fiber. As shown, electrical depolarization travels along the cell membrane, but depolarization occurs at the internodal zone. Impulse conduction then jumps in an antegrade and retrograde (shown) direction to ensure total membrane depolarization.

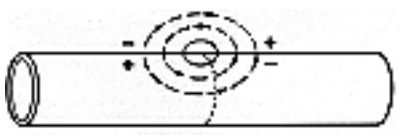

FIG. 65-4 Drawing represents an eddy current depolarization of an unmyelinated fiber. Impulse propagation is ensured by total membrane depolarization.

If an electrical impulse is applied to a nerve trunk and an oscilloscopic recording of this event is made, a characteristic wave form will be seen. This wave form is a summary of individual nerve fiber types and is termed a compound action potential. An analysis of this compound potential shows several distinct subunit waveforms. The earliest wave deflection reflects conduction of the largest-diameter myelinated nerve fibers. These fibers are classified as type A fibers and include three subcategories. Alpha waves represent the largest-diameter myelinated motor fibers and sensory fibers from muscle spindles. Beta waves represent sensory fibers from skin sensory receptors. Gamma waves are produced by gamma motor fibers arising from intrafusal muscle fibers of the muscle spindles.(33,47,50,59)

Type B nerve potential is produced by smaller myelinated fibers such as pain receptors. Type C nerve potential is a result of conduction in unmyelinated fibers such as autonomic fibers. Thus it can be inferred that the majority of peripheral nerve composition is a heterogeneous group of fiber types performing different yet integrated functions to maintain homeostasis.(33,47,50)

As the impulse reaches the synaptic junctions, acetylcholine is liberated from storage vesicles, transverses the synaptic cleft, attaches to receptor sites on the secondary folds of the synaptic clefts, and initiates endplate potential formation. This potential, in turn, initiates sarcolemmal depolarization and muscle contraction. After diffusion from the receptor site, acetylcholine is degraded by the enzyme acetylcholinesterase. The component substances are then metabolized or recycled to form new acetylcholine.(47,50,59)

Sensory conduction is initiated by peripheral receptors and is conducted centrally to the dorsal spinal root. The impulse then initiates reflex arcs in the segmental gray matter and may be transmitted for further integration to the higher centers by internuncial neurons.(50,59)

CLASSIFICATION OF NERVE INJURY

As interest in diagnosis and therapy of peripheral nerve injuries increased, a need arose to standardize the description of types of injury evaluated in clinical practice. The classification presented below is based on indirect diagnostic methods that include history, physical examination, including neurologic examination, and ancillary diagnostic techniques as represented by electrodiagnostics. The classification acts as a guideline for clinical assessment and prognostic evaluation related to medical or surgical management of the injury. The use of this classification can correlate, in addition, changes in neural tissue related to the injury process.

The mildest form of nerve injury is classified as neuropraxia. An acute insult to the peripheral nerve

results in interruption of impulse transmission (Fig. 65-5). Clinical evaluation will show sensory and motor deficits in the region that is innervated by the injured nerve. Partial function may be noted, with an imbalance between degree of sensory and motor deficits noted on examination. Evidence of neurogenic atrophy of muscle fibers is usually not present. Histologic evaluation of tissue shows only minor morphologic alterations that are of a reversible nature. It has been proposed that microvascular alteration resulting in transient ischemia produces this class of injury. Recovery is accomplished with conservative therapy and occurs over a variable time period but is usually complete within 21 days of injury. This time is faster than that expected by regeneration following wallerian degeneration, as will be noted below. (115,117,128)

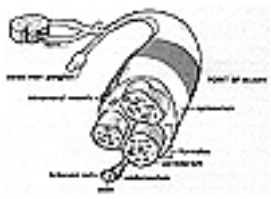

FIG. 65-5 Representation of neuropraxia. A functional conduction disturbance is noted. No histologic injury is present. (Raise MR Peripheral nerve injuries in the dog, Part II Compendium on Continuing Education for the Small Animal Practitioner 1 269 276, 1979)

If there is physical disruption of one or more axons without injury to stromal tissue, the injury is described as axonotmesis (Fig.65-6). This type of injury is generally noted in conjunction with closed long-bone fractures in humans. In this type of injury, the axoplasm and cell membranes are damaged; however, the Schwann cell and connective tissue elements remain intact. Clinical evaluation will reveal deficits related to the zones innervated by the damaged axons. Loss of sensory and motor function will be dependent upon the number and type of injured axons. After the 90th hour post injury, no conduction of electrical potentials past the site of injury will be seen in the dog. Neurogenic atrophy of skeletal muscle will be evident in the injured autonomous branch. (115,117,119,128)

FIG. 65-6 Severance of individual axons resulting in axonotmesis. Note that the nerve remains intact except for injured elements. (Raffe MR: Peripheral nerve injuries in the dog, Part II. Compendium on Continuing Education for the Small Animal Practitioner 1 269 276, 1979)

Examination of histologic sections shows degeneration of the axoplasm and associated structures distal to the site of injury. Proximal to the injury site, degenerative changes in the axoplasm are noted for two to three nodes of Ranvier proximal to the site of injury. If surgical exploration of the lesion is undertaken, examination of the injured area may show several classes of tissue change: (1) slight thickening of the epineurium without additional gross pathology; (2) a spindle-shaped swelling that may be firmer than normal, referred to as a fusiform neuroma; (3) an indurated area of scar tissue that is either swollen or constricted in relation to the remaining nerve tissue; and (4) a lateral neuroma associated with injured axons. Prognosis for recovery varies with the degree of lesion severity and the evaluation of clinical and diagnostic impressions.(115,117,128,135)

Neurotmesis refers to complete severance of the peripheral nerve trunk. Sensory and motor innervation to all autonomous branches of the injured nerve is lost (Fig. 65-7). Clinical and diagnostic evaluation will show complete loss of clinical function of the nerve. Histologically, degeneration of all axons occurs distal to the site of injury. Axons will also manifest degenerative changes for one to two nodes of Ranvier proximal to the site of injury. Except in rare cases, spontaneous recovery from lesions of this class does not occur.(115,117)

As can be noted from the classifications of injuries described above, certain types of injuries border on more than one category. In an attempt to improve and further define types of peripheral nerve injury, an alternate classification by degree of injury was later proposed. The advantage to this classification is that description of injury to individual components of the nerve trunk can be accounted for more accurately. A first-degree injury correlates with neuropraxia. A second-degree injury is one in which only the axon is disrupted. A third-degree injury involves the axon and associated endoneurial tube while the nerve funiculus remains intact. A fourth-degree injury disrupts axons, endoneurium, and funiculi while the

epineurial sheath remains intact. A fifth-degree injury is evidenced by complete severance of the nerve trunk. (128)

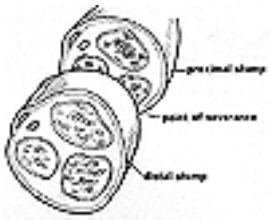

FIG. 65-7 Transection of entire nerve trunk results in neurotmesis. (Raffe MR Peripheral nerve injuries in the dog, Part II. Compendium on Continuing Education for the Small Animal Practitioner 1:269 276, 1979)

Although not all aspects of the classification systems can be appreciated on a clinical basis, certain parallels between clinical presentation of injury and severity of peripheral nerve damage may be drawn. In cases of blunt compression injury to soft tissue, it is likely that neuropraxia results from temporary peripheral nerve compression. This can produce temporary ischemia and loss of neural conduction. A mild form of injury of this class would be loss of sensation after steady pressure has been placed on a nerve trunk for a short period of time. Axonotmesis, or secondand third-degree peripheral nerve injuries, may be the sequel of closed long-bone fracture and traction injury to peripheral nerves from altered orthopaedic biomechanics. Neurotmesis, or fourth- and fifth-degree injury, may be associated with open long-bone fractures, penetrating wounds, and altered biomechanics resulting from trauma. An example of this last category could be avulsion of nerve roots of the brachial plexus at the time of traumatic injury. (115,117,129)

The ability of an injured nerve to regenerate is dependent upon the degree of continuity remaining in the nerve trunk following injury. In general, neuropraxic lesions have a greater probability of regeneration than axonotmesic or neurotmesic lesions. The supporting structures and Schwann cells remain intact in the milder injury; thus a "lesion in continuity" is present. The prognosis is more favorable for injury of the milder degree.(115,117,135)

RESPONSE TO INJURY

Injury to a peripheral nerve triggers an initiation of a response that incorporates a sequence of biochemical and morphologic alterations. Each component of the injured nerve reacts in an individual manner to the injury process. The effects of injury may be categorized into those that involve (1) the spinal cord, particularly the ventral cell body; (2) the proximal nerve stump; and (3) the distal nerve stump and its associated end-organs.(45)

Ventral Cell Body

After injury, sequential histologic evaluation of the ventral cell body shows marked changes in response to injury. The size of the nerve cell body enlarges for 10 to 20 days after injury. This "hypertrophy" is visible for the course of the regenerative process, and "atrophy" back to normal size occurs once healing is complete. It was once accepted that this change in cell body size, along with changes in staining characteristics described below, represented nuclear degeneration of the injured nerve cell. Recent observations with electron microscopy, along with an improved understanding of nerve repair biology, now suggest that the alterations noted represent early induction of metabolic processes required for nerve regeneration. Staining properties of the intracytoplasmic organelles change in response to injury. Intracytoplasmic ribonucleic acids (RNAs) migrate peripherally and fragment into subunits. This process, referred to as chromatolysis, transforms the RNA into a more active molecular complex with increased enzymatic activity and greater biosynthesis.(17,42,45,46,82,104)

The degree of cellular change is dependent upon the level of the lesion in relation to the cell body. If the level of the injury is close to the nerve cell body, proportionally more axoplasm is lost, and greater biosynthesis must occur for regeneration to result. A proximal injury may exceed the biosynthetic capability of the cell, thereby causing failure of regeneration. Distal nerve lesions do not activate the cell body to a high degree of biosynthesis. The nerve cell, therefore, is capable of limited regenerative

potential without initiating severe changes in cellular metabolism.(42,45,46,81,135)

Proximal Nerve Stump

If the nerve trunk has been severed, retraction of the stumps occurs owing to elastic tissue contained within the epineurial sheath. Hemorrhage and clot projection are evident immediately at the severed ends. Intraneural swelling due to tissue edema and exudation of acid mucopolysaccharides may be noted within one hour after injury. Acid mucopolysaccharides have an affinity for water and an indirect affinity for plasma, blood, and serum. The swelling and tissue constituents form a clot that is evident for 7 to l0 days. (3,46,81)

The extent of degeneration in the proximal stump is related to the etiology of injury. Sharp lacerations or surgical wounds produce minimal proximal stump degeneration. Traction or jagged laceration injuries result in extensive degeneration. In either case, within 24 to 72 hours, neurofibrillar degeneration in a clean wound occurs for a minimum of two to three nodes of Ranvier proximal to the point of injury (Fig. 65-8B). Loss of axoplasmic components quickly follows during this time. The myelin sheath begins to lose its defined layered appearance and blends into a homogenous granular tissue that appears as a series of rings surrounding degenerating axoplasm. These contorted lamellar rings, which form hollow luminal structures, are classified as digestion chambers. Macrophage invasion begins to digest and remove degenerated myelin from the damaged nerve tissue. Schwann cells respond vigorously at this time and proliferate to form dense cords along the axis of the now digested axoplasm. These cords possess phagocytic properties and ingest clumps of degenerating axon, myelin fragments, and other cellular debris. Mesenchymal cells proliferate in response to the inflammatory process and initiate collagen deposition at the end of the proximal stump. This, in conjunction with fibrin remnants from the initial hemorrhage, may lead to formation of a neuroma.(12,13,42,46,81,104)

Approximately 2 to 20 days after injury, axoplasmic regeneration may begin. This event is associated with the increased biosynthetic capabilities of the nerve cell body. Synthesis of new axoplasm is transported by migration along the remaining viable axon to the site of injury. The flow rate for this process is approximately 1 mm to 3 mm per day and advances by the intracellular fibrillar network described above. At the site of injury, cellular proliferation of Schwann cells has already commenced. The Schwann cell outgrowth attempts to connect the proximal stump with the Schwann cell elements of the distal nerve stump. The Schwann cell attempts to grow concurrently with the axoplasm, thus providing a framework for axonal growth.(3,46,l35) If surgical realignment or nerve stump approximation does not occur, the migration axoplasm may form a neuroma, a meshwork of organized clot elements, mainly fibrin strands, that provides an errant scaffolding framework for axonal migration. As the Schwann cells migrate distally, their pathway is deviated to align with the random fibrin clot at the nerve stump. The regenerating axons follow the Schwann tubules and continue the random growth pattern. Axoplasm migration in this disorganized tissue produces multifilamentous branching that attempts to seek the distal nerve stump (Fig. 65-8C). (12,46,134) Extraneural connective tissue may also produce ingrowth to the site of injury and can additionally distort and block the path of axon migration. In contrast, surgical repair of peripheral nerve injury permits smooth, unbranched axoplasmic migration into the distal stump. It is hypothesized that axoplasmic branching attempts to compensate for the neuroma roadblock to ensure axonal migration into the distal stump.(7,77,81,148,151)

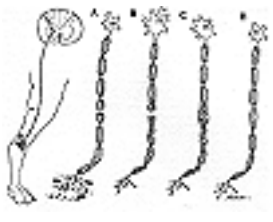

FIG. 65-8 Pictorial description of nerve injury. After transection of axon (A), morphologic hypertrophy of nerve cell body to aid in biosynthetic regeneration is demonstrated. All neural degenerate in the distal stump and terminal portion of the proximal stump (B). Axoplasmic filaments arise from the proximal stump in an attempt to recannulate the distal Schwann cell tube (C) After appropriate recannulation, all axoplasmic migration is directed into the distal fragment for regeneration (D).

Neuromas can be a painful sequela of nerve severance in all species, especially humans and horses. (135)

Any time a neurectomy or limb amputation is performed, the potential for neuroma formation exists. The risk of neuroma formation in the dog and cat appears to be small; however, good surgical technique regarding hemostasis and closure of the proximal nerve stump reduces the incidence of neuroma formation. Many methods to achieve stump closure have been proposed. In the horse, silicone caps, epineurial closure, and electrocoagulation are methods currently used to prevent neuroma formation.(135)

The entire distal stump undergoes a process of degeneration first described by Waller and referred to as wallerian degeneration. Within 24 to 48 hours after injury, axon thickening is evident histologically. An increase in acid phosphatase and nicotinamide adenine dinucleotide (NAD) diaphorase in surrounding myelin reflects increased metabolic activity. Evidence of axoplasmic fragmentation and clumping is noted at this time. Four to five days after injury, all axoplasm is absent, and myelin degeneration and clumping occur by a process similar to that described for proximal stump degeneration (Fig.65-8B). Tissue macrophage invasion is noted during this period. The origin of the macrophage activity is thought to be connective tissue histiocytes and converted monocytes from the peripheral blood. This activity may last from 7 to 32 days after injury. After macrophage and Schwann cell activity diminishes, only Schwann cells and connective tissue remain. These diminish with time, and total atrophy of the distal stump may occur 18 months after injury owing to the increased intertubular deposition of collagen, which reduces the diameter of the lumen of individual neural elements. (12,13,42,81,135)

The proximal end of the distal stump deserves special note. The axons in this region tend to enlarge and isolate from the other portions of the degenerating nerve stump. This unit may survive for as long as 2 weeks prior to degeneration. As connective tissue elements proliferate in the early degenerative phase, endoneural fibroblasts intertwine in this isolated segment. This swelling is referred to as a glioma, schwannoma, or distal neuroma. Its gross appearance is not as marked as the previously described neuroma because it is composed solely of connective tissue elements originating from perineurium, endoneurium, and pleomorphic Schwann cells. With the passage of time, shrinkage of the glioma will occur in conjunction with distal stump atrophy.(13,46,66,135)

Regeneration of axons in the distal stump occurs at a rate of 1 mm to 3 mm per day. This rate is variable depending upon the zone in which regeneration is occurring. Near the site of injury and at the motor endplate region, growth is slower owing to external factors. More rapid regeneration occurs in the body of the distal nerve stump. Extension of Schwann cell and connective tissue elements provides a pathway for migration of axoplasm filaments into the tubules of the distal stump. As regrowth of axoplasm into the distal stump proceeds, myelination of the Schwann cell envelope occurs in regions recently recannulated by axoplasmic elements. Marked enzymatic activity is present to aid in the myelination process. The presence of myelin sheaths is evident 6 to 7 days after regeneration has occurred in any zone.(46,134) Nodes of Ranvier appear after day 14 in the regenerative process. Apposition of myelin occurs for as long as one year following the repair process.(104)

It is important to recognize that even under the best of circumstances, aberrant recannulation of the distal stump may occur. Transposition of sensory and motor components in a mixed-function nerve is a common sequel to injury. As the motor end-plate region is reached by the advancing axoplasm, rapid division of the axoplasm occurs until a myoneural junction is formed. This may stimulate the reemergence of previous motor end-plate structures, or new areas may be formed by a process similar to neural neurotization. A similar sequence of events will occur in the regeneration of sensory components in mixed-function nerves. However, if axonal transposition has taken place, failure of maturation and atrophy of the axon will follow. A nonfunctional axon unit may then be the ultimate result. At 12 to 16 months post injury, a deficit of 25% of nerve function is reported even with ideal surgical repair. (58,77,109,111,112,113,135)

FACTORS INVOLVED IN NERVE HEALING

Numerous reports in the literature attempt to assess various factors that contribute to successful nerve healing. Factors may be described as intrinsic, or those beyond control of the surgeon, and extrinsic, those

in which clinical management may influence return of function.

Intrinsic factors include species, age, state of tissue nutrition, time since injury, type of injury, nerve or nerves involved, and level at which injury occurred. This information can be gathered from history and physical examination and may aid in prognostic evaluation. As has been discussed earlier, the time since injury, level of injury, and type of injury relate to factors concerned with nerve biology. Young patients heal more rapidly and to a more complete recovery, probably related to increased biosynthetic capabilities already present and to a greater capacity for adaptation. Tissue nutrition is important to meet anabolic requirements related to the regenerative process.(80,99)

Extrinsic factors relate to surgical and postoperative management of nerve lesions. Attention to surgical technique and appropriate selection of instrumentation and suture material can contribute to return of function. These areas are covered later in this chapter. As with any surgery, an understanding of biology and physiology, coupled with appropriate surgical repair, results in maximum potential for successful return of clinical function. (3,58,90)

METHODS USED IN ASSESSMENT OF PERIPHERAL NERVE INJURY

Diagnosis of peripheral nerve injury begins at the time of initial examination. A complete history is invaluable for both diagnostic and prognostic data bases. Owner's observations of type and location of dysfunction, time of onset and historical course, and estimation of severity of the present lesion can aid in formulation of a rational diagnostic plan. In addition, owner judgment as to progression or lack of change in the course of the injury, compensatory activity related to the injury, and changes in locomotion may aid in formulation of clinical prognosis and possible courses to pursue for returning function to the area of injury.

Physical examination with special emphasis on neurologic evaluation should be performed. A standardized method familiar to the examiner should be adopted and practiced such that all components of the central and peripheral nervous systems are examined and evaluated in a uniform manner. By adapting this approach, subtle changes are more readily recognized and appropriately noted. Clinical evaluation of peripheral nerves involves examination of both sensory and motor function. Sensory examination of cutaneous zones supplied by individual peripheral nerves involves application and observation of response to a noxious stimulus. Heat, cold, pain, and electrical stimuli can be used for this procedure. Evaluation of response to these stimuli may locate the region of denervation and affected peripheral nerves. In a similar manner, evaluation of motor function by observation of gait, segmental and integrated response to the application of noxious stimuli, and physical examination of asymmetry in muscle mass and tone can provide direction as to the nerve trunk injured and the extent of trunk involvement.(50,59)

ANATOMY OF PERIPHERAL INNERVATION

There are six nerve trunks that supply innervation to the forelimb from the brachial plexus. The suprascapular nerve supplies motor innervation to the supraspinatus and infraspinatus muscles. Injury to this nerve will cause neurogenic atrophy and fibrosis of these muscles. Clinically, a prominent scapular spine and loss of palpable musculature is evident. The motion and gait of the animal are usually unaffected.(64,106)

The axillary nerve supplies motor innervation to the muscles that make up the flexor group of the shoulder. A small region on the lateral surface of the upper arm derives sensory innervation from this nerve. Experimental transection of the axillary nerve produces cutaneous anesthesia over the lateral surface of the upper arm and minimal motor dysfunction. (64,79,106)

The radial nerve is a mixed component nerve that supplies innervation to all extensor muscles of the elbow, carpus, and digits. In addition, sensation in the skin of the dorsal and lateral aspects of the forearm and the dorsal aspect of the paw originates from this nerve. Injury is usually associated with a traumatic

incident. Fractures of the first rib or avulsion of the nerve roots from the spinal cord creates radial nerve paralysis. Signs of total paralysis include a non-weight-bearing condition with the elbow in flexion due to loss of voluntary motor function to the extensors of the elbow. Loss of sensation occurs to the areas described above. (64,79,106)

In lower level injuries to the radial nerve (distal to the triceps muscle), paralysis is less marked. Dorsal knuckling of the paw is seen as a result of extensor muscle denervation, and cutaneous sensation to the region is diminished. This injury may accompany humeral fractures. Neural integrity should be demonstrated prior to orthopaedic correction; however, a complete and accurate appraisal is not always possible. (64,79,106)

The musculocutaneous nerve supplies motor function to the flexor muscles of the elbow. In addition, sensation to the medial side of the forearm is supplied by this nerve. Injury to the nerve is associated with slight straightening of the elbow joint and loss of some elbow flexion. Desensitization of the medial side of the forearm is noted.(64,79,106)

In this discussion the median and ulnar nerves will be considered as one group. They supply motor innervation to flexor muscles of the carpus and digits. Sensation to the caudal aspect of the forearm, palmar surface of the paw, and dorsolateral aspect of the fifth digit is supplied by these nerves. If injured, clinical signs will be overextension of the carpus and loss of sensation to the above-mentioned regions. Loss of carpal flexion will also be evident in the gait.(64,79,106)

The hindlimb has fewer major nerve groups that are susceptible to injury. The femoral nerve is responsible for the motor supply to muscles that extend the stifle. In addition, a branch provides sensation to the medial side of the thigh, stifle, leg, and paw. With damage to the nerve, the leg will collapse owing to inability to extend the stifle. (64,106)

The sciatic nerve supplies a great portion of the innervation to the hindlimb. It may be injured in cases of pelvic fracture, femoral fracture, or injection of agents in its anatomical region. Motor function to the caudal thigh muscles is provided by this nerve. If injured, desensitization to the caudal and lateral side of the lower leg will be noted. (64,106)

Distally, the sciatic nerve divides into the peroneal (fibular) and tibial nerves. The peroneal nerve supplies motor innervation to the digital extensor muscles and provides sensory input from the dorsal aspect of the lower leg, hock, and paw. The tibial nerve supplies motor innervation to digital flexor muscles and the gastrocnemius muscle and supplies the sensory component to the plantar surface of the paw. (64,106)

Signs of sciatic nerve damage will be dictated by the level of injury. In a low-level lesion, signs referable to peroneal or tibial nerve damage may be seen. The peroneal nerve is situated on the lateral aspect of the leg, and its location renders it susceptible to injury. Signs seen clinically are straightening of the hock, knuckling of the digits so that the dorsal surface may touch the floor, and loss of cutaneous sensation over the dorsal surface of the distal leg, hock, and paw. If the tibial nerve is injured, accentuated hock flexion will be noted in the weight-bearing position, and loss of sensation over the plantar surface of the foot will be apparent. (64,106)

In the case of an upper-level sciatic nerve lesion, signs of both peroneal and tibial nerve damage will be apparent, and marked gait abnormalities will be seen. Innervation to the flexors of the stifle will be lost, and extension of the stifle will be exaggerated owing to action of the quadriceps femoris muscle group. The hock will passively rest at a level determined by the position of the stifle. All sensation except that to the medial portion of the leg will be lost.(64,106)

Once an assessment of peripheral nerve injury has been made, ancillary tests may help to confirm the nature of the injury and in addition provide estimation of prognosis. In the last two decades, use of electromyography (EMG) and determination of nerve conduction velocity have proved valuable aids in the assessment of peripheral nerve injury.

ELECTROMYOGRAPHY

EMG is a method in which electrical activity within a striated muscle belly is detected and recorded. The electrical signal that arises from muscle tissue is detected by an electrode pickup, magnified by a high-gain amplifier, and monitored by oscilloscope or speaker or recorded on magnetic tape for future use. Alterations in this signal are seen in various neuromuscular diseases. Serial testing using EMG may provide a clinical aid to assess response to therapy, and monitoring of EMG aids in accurate prognosis for return of function. (16,33)

The signal detected by EMG reflects actions of motor units. These units are comprised of a motor neuron branch and the muscles fibers innervated by that nerve. The ratio of muscle fiber numbers to peripheral nerve branch varies with function related to that particular unit. As discussed above, fine-control areas such as extraocular muscles have a high ratio of motor neurons to muscle fibers. Conversely, coarse-control areas, represented by skeletal muscles, have a low ratio. The EMG can demonstrate quantitative or qualitative changes in electrical activity of the muscle motor units in the resting state, following direct or indirect electrical stimulation, or during voluntary or reflex motor unit activation. In addition, the EMG can be used to evaluate nerve conduction velocity and nerve terminal conduction time. (16,33)

The techniques used for testing and recording of EMGs are relatively easy. In one common form, three small needle electrodes are placed percutaneously in the area to be studied. One electrode serves as an electrical ground, and the second serves as a reference. They are placed in a region of bioelectrical quiescence (over a tendon or bone) (Fig. 65-9). Since only relative changes in electrical activity are recorded by the EMG, the recording electrode is read against the reference to assess changes in electrical activity. The recording electrode is placed into a striated muscle belly and used to pick up electrical signals that originate from the tested muscle. The type of needle electrode used in this arrangement is termed monopolar in that each needle represents only one electrical polarity. Another commonly used design of needle electrode is the concentric or coaxial electrode. In this arrangement, two separate polarity electrodes are housed in a common needle. This arrangement has the advantage of sampling a smaller volume of tissue than the monopolar design. In addition, 60 Hz interference is less of a problem owing to the close proximity of both polarity probes.(16,33,105)

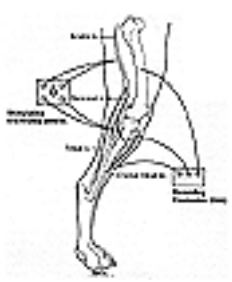

FIG. 65-9 Example of electrodiagnostic evaluation of a region of the hind-limb. Needle electrodes are placed within muscle tissue and electrical activity for that area is recorded (EMG). Additional data may be gained by producing an electrical stimulus that is applied to a nerve. The time needed for the impulse to transverse the nerve trunk and produce a response of the muscle is recorded and reported as a nerve conduction velocity. (Raffe MR: Peripheral nerve injuries in the dog, Part II. Compendium on Continuing Education for the Small Animal Practitioner 1:269-276, 1979)

After the electrical signal is generated and detected by the electrodes, it is amplified by a high-gain preamplifier and amplifier unit. The signal is then screened through band-pass filters and presented to the examiner. Common forms of signal display include audio and oscilloscopic display in real time. Preservation for future evaluation may be performed by magnetic tape, photographic, or paper recordings. (16,33)

In the neurally intact animal, a brief burst of electrical activity upon electrode insertion is considered normal. This activity is a result of sarcolemmal depolarization by electrode placement. After this activity, quiescence should return and remain except for voluntary muscle contraction or passive limb movement. (16,33)

In cases of neural, neuromuscular, or muscular disease, aberrant patterns may result. Changes in frequency, amplitude, and character of these electrical signals will occur, and bursts of spontaneous electrical activity without appropriate initiation may be noted. These changes are usually related to

specific disease processes. (16,33)

With peripheral nerve injury, denervation to a group or region of muscles will occur. Spontaneous electrical activity due to the loss of neural influence begins in the muscle 5 to 7 days after injury. This activity may continue for a variable time until either nerve regeneration or muscle fibrosis ultimately occurs. At this point, reversion to a near normal pattern of activity following nerve repair or complete absence of electrical activity due to muscle fibrosis will predominate.(15,16,33,105)

Fibrillation and fasciculation waves are commonly seen in neuromuscular injury. Both wave forms may be seen in conjunction with electrical alterations described above. They may also appear singularly in denervated muscle. Fibrillation potentials that are monophasic and have an initial positive deflection are classified as positive sharp waves. Positive sharp waves are frequently associated with denervation of tested muscles. They are identified by their characteristic appearance plus an irregular rate and rhythm. Positive sharp waves represent a lack of the inhibitory "feedback" that nerves exert on muscle fibers to maintain quiescence during the resting phase. They are initiated by insertion of a needle electrode into a muscle belly. Continued electrical activity in excess of that associated with electrode insertion is noted. (16,33)

Fibrillation potentials are closely associated with the end-plate region of the muscle. An instability of the membrane potential initiates fibrillation. The wave form has an initial negative deflection in the end-plate region, while in other areas of the muscle an initial positive deflection is noted. Fibrillation potentials are mainly monophasic or biphasic in configuration. The time of appearance after injury is species dependent. The dog usually exhibits fibrillation 5 to 7 days post injury. As long as viable denervated muscle fibers are present, fibrillation will occur. In the reinnervation phase, a marked decrease in fibrillation occurs 2 weeks prior to reappearance of motor unit action potentials. Polyphasic waves may be noted in conjunction with this event.(16)

Nerve Conduction Velocity

Additional information may be gathered by testing sensory or motor nerve for conduction velocity. In veterinary medicine, motor nerve conduction velocity is more commonly measured, although recently a technique for sensory nerve conduction velocity for certain nerves in the forelimb has been presented. (16,64)

The technique requires placement of two sets of stimulating electrodes along the nerve trunk to be tested. A recording electrode similar to that described above for EMG is placed in a muscle belly that is known to be innervated by the nerve to be tested. A stimulus is applied at one point along the nerve, and an evoked muscle depolarization is noted. By stimulating the nerve trunk at two points and recording the evoked response, the time difference between stimulation at the two points can be determined (Fig. 65-9). With measurement of the distance between the two electrodes and determination of the time difference involved, the velocity of stimulus conduction along the nerve trunk can be determined. Standard values have been reported in the dog. Alterations in nerve conduction velocity may be seen in several disease states.(16,47,57,136)

Injury to the axon may be of a complete or incomplete nature. Incomplete injury may only slightly alter the results of EMG and nerve conduction velocity testing. Reduced amplitude in evoked potentials may be seen. In addition, prolongation of the potential evoked from a point distal to the injury site may be noted. This is considered to be a reflection of delayed conduction in the injured fascicle. Following total transection, normal conduction in the distal stump will be noted for 4 to 6 days post injury. After this time, no conduction velocity or evoked potentials will be noted. Stimulation at the proximal area of a complete injury will elicit no evoked potential owing to failure of impulse transmission. As with EMG, further information on specific techniques and normal values may be found in standard veterinary neurology texts.(16,47,57,119,147)

Surgical Repair of Peripheral Nerves

GENERAL PRINCIPLES

Successful results in peripheral nerve surgery come from familiarity with technical surgical concepts, an understanding of tissue biology, appropriate surgical instruments, practice, and patience. Attention to detail and the desire to spend a few extra moments to obtain technical perfection are rewarded by a higher rate of success and less time lost in repeat exploratory procedures.

The decision most important to the surgeon and the patient is whether or not surgery should be performed and, if so, when. Exploratory surgery is justified in five instances: to establish an accurate diagnosis in cases in which ancillary clinical diagnostic methods have been inconclusive or contradictory and to visualize the extent and severity of the lesion; in cases in which incomplete loss of function has occurred, but no clinical improvement is evident; in animals in whom injury has occurred more than 3 weeks prior to surgery and no function has returned; to improve by surgical means the function of the nerve in question; and to establish a prognosis. (115,126,135)

Judgment as to probable etiology of the lesion will aid in the decision of whether surgery is a justified course of action. Penetrating external wounds that transect nerve trunks in a focal area or fractures that lacerate nerve tissue are examples of cases amenable to surgical intervention. Animals sustaining injuries to extensive areas of nerve by traction to a nerve trunk or blunt injury to a large zone of soft tissue may not be candidates for surgical exploration. (135)

The timing of surgical repair depends upon the type of injury encountered and the facilities available at the time of initial presentation. Two basic types of surgical repair have been advocated in the literature: immediate (primary) repair in which definitive surgery is performed 8 to 12 hours after injury; and early delayed (secondary) repair, which is performed 2 to 6 weeks after initial injury. Immediate repair is indicated in cases of transection of a nerve trunk related to a clean sharp wound such as a glass cut. If partial transection of a nerve trunk has occurred, immediate repair of the injured tissue is also indicated. (117,134,135) Advantages of immediate suture repair include earlier return to function, better funicular visualization for more accurate realignment of nerve tissue, and decreased tension upon the suture line at the site of repair as a result of stump contraction. Disadvantages to primary repair include the following: only specific types of injury are amenable to immediate surgical correction; primary repair has no advantage in ultimate functional recovery over early secondary repair; there is a potential for suture line dehiscence due to delayed necrosis; and primary repair is performed on a more friable epineurium. If primary repair is not performed but nerves are visualized at initial surgery, placement of metallic sutures of fine size (6-0) in the epineurium will allow for radiographic evaluation of stump retraction until definitive repair is performed.(75,104,125,135,145)

Delayed (secondary) repair is preferred in cases in which major trauma and contamination are associated with nerve damage. Abolishment of wound contamination and inflammatory response results in a better environment for nerve regeneration. This delay is also biologically compatible with changes in peripheral nerve metabolism and nerve cell body changes described above. Phagocytosis of neurotubular debris and hypertrophy of connective tissue elements allow for immediate initiation of proximal stump regrowth peripherally. Advantages of delaying definitive repair for 2 to 6 weeks after injury include hypertrophy of the epineurium for easier suturing and greater tensile strength, demarcation of injured nerve elements at the site of injury for easier resection of neuroma, and the above-mentioned changes in cell physiology for initiation of regrowth. Disadvantages of secondary repair are stump retraction and neuroma debridement, both of which contribute to increased tension at the site of the suture line, increased tissue fibrosis and hemorrhage in the surgical field, and later return of function. Delaying definitive repair beyond 6 to 8 weeks can contribute to poor clinical results. Progressive stromal fibrosis and narrowing of Schwann cells in the distal stump decrease chances for successful axoplasmic recannulation. Atrophy and fibrosis of denervated skeletal muscle impair the degree of ultimate clinical recovery. Surgical identification of

anatomical structures is impeded. Finally, stump retraction and healing may produce large nerve gaps. (54,81,86,117,125,135,139)

Instrumentation for peripheral nerve surgery can be procured Tom several manufacturers of ophthalmic and microsurgical instruments. Generally, ophthalmic instruments are adequate for all but sophisticated repair procedures and are usually less expensive. General surgical instruments are appropriate for initial surgical approach. Suggested instrumentation for peripheral nerve surgery includes a small ophthalmic needle holder, two pair of jeweler's forceps, 4" strabismus scissors, 4" iris scissors, a mouse-tooth Adson forceps, and a razor blade holder. Disposable supplies include lint-free sponges such as Gelfoam (Gelfoam, Upjohn Co., Kalamazoo, MI.) or Weck-Cel, (Weck-Cel, Edward Week Co., New York, NY) wooden tongue depressors, double-edge razor blades or scalpel blade, silicone nerve cuffs, and suture material. The type of suture material is optional; however, a suture material that is monofilament and has low tissue function is preferred. Polypropylene or nylon in 5-0 to 7-0 with a swaged taper-point needle is adequate for most surgical techniques. Funicular repair may dictate 8-0 to 10-0 suture of the same composition and needle design.

Preparation of surgical instruments is Critical to ensure success. Cleansing in a detergent-free soap solution is recommended. Ultrasonic bathing may be used as a final cleansing process. Good instrument cleaning is essential to remove tissue debris, blood, dust, lint, and grease from fingers. Any or all of these factors could contribute to excessive fibroplasia at the suture line with blockage of axonal migration. Instruments should be placed on a tray lined with a lint-free towel material. Disposable dental napkins may be used for this purpose. Sterilization should be accomplished by dry heat or ethylene oxide processes. Repeated use of moist heat may corrode instruments and dull working edges of delicate instruments. Sharp edges of razor or scalpel blades may also be dulled after the application of moist heat. (135)

Preparation of the patient for surgery is important for successful results. Standard clipping and preparation for aseptic surgery must be followed rigidly, and the use of skin drapes, or incorporating the limb in a stockinette is helpful. The stockinette may be affixed to the subcutis with suture material or wound clips to aid in exclusion of surface debris and tissue fragments. (105,107)

Tissue dissection should occur along anatomical lines of separation. If exposure requires separation of muscle tissue, the muscle is split in the direction of its fibers. If this is not possible, transection of a muscle at its ligamentous attachment is recommended. Reattachment is made at the conclusion of the surgical procedure. Major goals are hemostasis and minimal tissue damage, since bleeding and tissue debris promote excessive scarring, which will attenuate the results of the surgical procedure. Lavage of the surgical site to remove tissue debris is helpful if not done excessively. Hemostasis can be expedited by the use of low-voltage electrocoagulation on transected vascular beds. (134,135)

After the nerve is exposed, it is mobilized from the surrounding tissues. Each nerve is surrounded by an adventitious tissue (mesoneurium) that contains collateral vessels. Some of this tissue must be incised and stripped from the nerve trunk. While the amount of tissue that can safely be removed is controversial, it appears that 6 cm to 8 cm can be stripped without adverse effects. This is usually sufficient to accomplish adequate mobilization of the nerve trunk.(101,123)

Manipulation of the nerve trunk should be done with great care. Nerve tissue can be safely handled by one or a combination of three methods. Gentle handling of the epineurium with jeweler's forceps is one method; however, care must be exercised to avoid incorporating funiculi with the forceps, thus creating additional tissue injury. Manipulation using the incised mesoneurium is another technique. More commonly, traction sutures are placed through the epineurium, and the sutures are then manipulated. These sutures provide, in addition to traction, landmarks for alignment if resection and anastomosis of the nerve trunk is required.(101,105,135)

At this point, examination of the nerve and assessment of damage is important to plan for corrective techniques. If continuity of the nerve trunk is present, electrical stimulation with microelectrodes and

observation of reactions may provide information as to level of the lesion. One may also note the presence of a swollen, indurated area within the substance of the nerve trunk. This area would be classified as a neuroma and would require surgical judgment as to disposition prior to surgical repair.(57,67,68,78,135)

The presence of neuroma formation indicates axonotmesis or neurotmesis. The shape and location of the neuroma may give an estimation of the prognosis. A fusiform neuroma indicates integrity of some fascicles in the area of injury (Fig. 65-10A). if the neuroma is firm, fibrosis has occurred at the point of injury and there will be little chance of spontaneous recannulation of neurotubules by regenerating axoplasm. If a softer consistency is evident, there is a greater chance for spontaneous healing.(107,117, 134)

Location of the neuroma within the nerve trunk may also aid in determining lesion severity. Lateral neuromas indicate partial neurotmesis with functional tissue remaining (Fig. 65-10C). if the injury does not exceed 50% of the width of the nerve trunk, spontaneous recovery may occur without surgical intervention. However, if greater than 50% involvement is present, resection and neurorrhaphy is indicated. Bulbous and dumbbell-shaped neuromas suggest widespread neurotmesis with poor prognosis for spontaneous recovery (Fig. 65-10B, D). Excision of the neuroma and neurorrhaphy is indicated in these cases (32,78,117,134)

If a neuroma is encountered at the time of exploration, it should be classified as described above and a decision made for or against surgical resection. If uncertainty exists, trial section of the neuroma may be done. Trial section for examination may be accomplished by one of two methods. Internal neurolysis may be performed by longitudinal incision through the epineurium only. Careful dissection and separation of individual nerve fascicles with removal of excess fibrous tissue can be performed. If disruption of greater than one half to three fourths of the anatomy is present, resection and anastomosis is then performed. Alternately, trial section of a neuroma may be performed by a transverse method. Two techniques have been used to accomplish transverse trial section. In one procedure the neuroma is supported by a wooden tongue depressor acting as an anvil. A transverse incision is made at the point of greatest induration and deepened 0.5 mm at a time until normal nerve tissue is visualized. If over one half to three fourths of the diameter of the nerve trunk is involved, resection of the neuroma and anastomosis of the nerve is indicated (Fig. 65-11). In an alternate method, a collar of polyethylene surgical drape is placed around the nerve trunk and affixed with right-angle forceps. Trial incision is then performed using a razor edge in a fashion similar to that described above.(20,32,78,110,134)

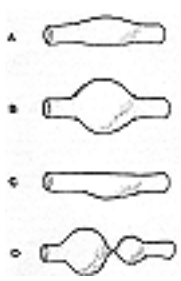

FIG. 65-10 Examples of neuromas that may be visualized at time of surgery: (A) fusiform, (B.) bulbous, (C) lateral, (D) dumbbell. (Raffe MR: Peripheral nerve injuries in the dog, Part II. Compendium on Continuing Education for the Small Animal Practitioner 1: 269-276, 1979)

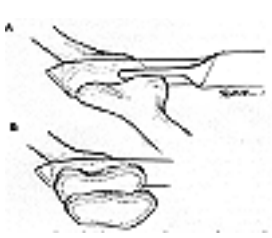

FIG. 65-11 Examples of trial incision of a neuroma. Incremental incision depth through the neuroma is indicated in A. If trail section reveals complete involvement, sequential resection to normal-appearing tissue is performed (B). (Raffe MR: Peripheral nerve injuries in the dog, Part II. Compendium on Continuing Education for the Small Animal Practitioner 1:269-276, 1979)

The neuroma is transected back to normal nerve tissue. Serial transverse sections of 1 mm are removed from the incised edge of the neuroma until normal tissue is seen. This procedure is done on both the proximal and distal stumps. Constant inspection of the excised tissue and maintenance of adequate length without undue tension are necessary. Wide and extensive tissue excision must be avoided so that anastomosis can be accomplished without undue tension.(32,78,134)

Hemostasis is imperative following resection because excessive fibrosis and distortion of nerve architecture may occur if it is inadequate. Only lint-free ophthalmic sponges or absorbable gelatin sponges should be used. The amount of intraneural vasculature is surprising, and if excessive hemorrhage is encountered, the sponges may be dipped in a 1:100,000 epinephrine solution.(106)

Suture placement is critical to the success of surgery. Suture material should be passed through the epineurium only. Incorporation of neural elements by suture material results in scar tissue formation proportional to the amount of fibrous invasion from the suture. All sutures should be tied with equal tension. The tension applied should be just enough for alignment and contact of the neural bundles. Excessive tension may result in crushing and malalignment of the nerve bundles. This predisposes to poor recannulation of distal nerve tubules and neuroma formation at the surgical sited.(9,101)

Optical magnification and supplemental lighting are beneficial to the attainment of optimum results. A binocular magnifying loupe similar to one used in ophthalmic surgery is helpful. Interchangeable eye pieces allow magnification up to two and a half to five times the surgical field. Supplemental lighting may be provided from spot-type surgical lamps, fiberoptic headlamp sources, or flexible neck light sources. As techniques of surgical repair and tissue transplantation have improved, the use of the operating dissecting microscope has increased. The operating scope should have a magnification range of 10 to 25 power and usually has an auxiliary light source built into the unit. This unit is helpful in identification and dissection of nerve elements from a neuroma and in visualization of normal or distorted nerve architecture. It is also useful in repair techniques that suture subunits of the nerve trunk, and it can increase accuracy in suture placement and rotational alignment of the nerve stumps. Equal application of tension at the suture line can also be visualized.(2,72,134,135)

SURGICAL TECHNIQUES

The simplest class of surgical repair from a technical standpoint is the end-to-end repair. In this surgical procedure, the entire nerve trunk is sutured as a unit by application of sutures placed in the epineurium or by placement of a single suture through the axial center of the injured nerve trunk. (134, 135) The most common technique of nerve repair (neurorrhaphy) involves placement of a series of simple interrupted sutures through the epineurium. Low-power magnification from a five-power binocular loupe, as described above, may be helpful in distinguishing structures and ensuring suture passage through only the epineurium. The epineurium is grasped and tensed with the jeweler's forceps. Since the tissue has elastic fibers, the epineurium may be slightly stretched to facilitate suture placement. Prior to suture placement, the surgeon should be confident that correct realignment of peripheral nerve stumps has been accomplished. (104,105,106,134,135)

Placement should be approximately 0.5 mm to 1.0 mm from the incised edge. The suture material is placed from the surface of the nerve and emerges just subepineurially. It is brought out to the free edge and the process continued in the opposing nerve stump. The second passage begins subepineurially and emerges on the surface. This completes one simple interrupted suture (Fig. 65-12A, B). The number of sutures required for adequate alignment of the stumps varies depending upon the diameter of the nerve. The smallest number of sutures possible is desirable so that inflammatory reaction to the suture material is minimized. However, adequate alignment is paramount for the success of the surgical procedure. Swaim states that four equidistant sutures will generally provide sufficient alignment for healing. Depending upon the size of the nerve, more may be required to ensure adequate alignment.(24,28,104,105,134,135)

It is advisable to preplace sutures and then tie them all at the same time. This will minimize the chance of excess traction being applied at one point and the suture tearing through tissue. To begin, two sutures are placed ill the nerve trunk 180 degrees apart. These sutures maintain alignment of the nerve stumps. An additional suture or sutures are then placed in the upper portion of the nerve. Several or all of these sutures may be tied to obtain adequate alignment. The suture ends may then be carefully grasped and the nerve trunk rotated to expose the underside of the nerve. An additional suture or sutures are then placed and tied to complete apposition of the nerve trunk. All knots are inspected to ensure that equal tension is

present (Fig. 65-12C).(24,28,104,105,134,135)

An alternate suture technique for end-to-end anastomosis involves placement of a single suture aligned with the longitudinal axis of the nerve trunk; the two ends of the suture are secured by means of small buttons on the outside of the nerve trunk. This may be accomplished in one of two ways. In the first method, the suture is begun 7 mm to 8 mm from the transection site and directed perpendicular to the longitudinal axis into the center of the nerve trunk. The suture is then redirected to follow the central axis of the nerve trunk and emerge at the center of the transection site. It is then carried to the opposing stump. This stump is visualized and the needle is inserted in the central axis. It is advanced for 7 mm to 8 mm and then redirected to emerge 180° opposite the site of initial suture placement. The end result has the appearance of the letter Z.(54,134,135,137)

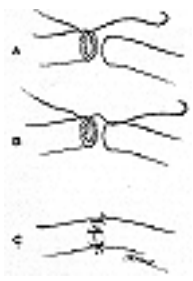

FIG. 65-12 Placement of epineural sutures for neurorrhaphy. As described in the text, caution should be exercised to ensure placement only through epineurium as represented in A and B. Preplacement of all sutures prior to tying will ensure even suture line tension (C). (Raffe MR: Peripheral nerve injuries in the dog, Part II. Compendium on Continuing Education for the Small Animal Practitioner 1 269 276, 1979)

The second method involves use of a double-armed suture material. Each needle is centrally inserted into one of the two nerve stumps. They are directed down the longitudinal axis and redirected so that each emerges 180° from its counterpart. This modification increases the likelihood of central suture placement, which is critical for proper alignment (Fig. 65-13A).(105,106)

Fascial or silicone buttons approximately 3 mm square are prepared. Each end of the suture is attached to a button, which acts as an anchor. One end is secured by placement of a square knot on top of the button. The other button is affixed by use of a slip knot, which acts to apply tension for alignment and apposition of the nerve trunks. The slip knot involves a triple suture passage and use of a loop and suture strand to tie a square knot. This has been used to provide good alignment and knot security (Fig, 65-13B, C). (54,105,137)

The main advantage of the one-suture technique for anastomosis is that less postsurgical neuroma formation and ingrowth of scar tissue are seen. However, the technique is technically more difficult, and there is the potential for severe complications. The most common complication is stump rotation and instability unless the suture is carefully centered in the nerve trunk.(54,105,137)

FIG. 65-13 Example of an interneural neurorrhaphy. Note importance of suture placement in the axial center of the nerve trunk (A). Attachment of the suture to fascial or silicone buttons is noted in B, along with triple suture passage for tying suture. A simple knot is then tied (c) (Raffe MR Peripheral nerve injuries in the dog, Part II. Compendium on Continuing Education for the Small Animal Practitioner 1:269-276, 1979)

As expertise and technical development in the field of microsurgery have progressed, suture repair of peripheral nerve subunits has increased in popularity. Placement of one or two sutures of 10-0 suture material in the perineurium to anastomose individual funiculi has found favor in the past 10 years (Fig. 65-14). This type of surgical repair allows definitive anastomosis of funiculi and eliminates the potential for aberrant centrifugal regrowth possible with epineurial sutures. An additional refinement of this technique uses electrical stimulation of individual funiculi in cases of acute injury to match, by positive identification, both stumps of a transected funiculus. Clinical results show no superiority of electrical stimulation over anatomical repair of nerve stumps. Funicular repair may be combined with epineurial suture to aid in strength of the suture line at the site of repair. Controversy still remains as to which method is superior to obtain return of clinical function. Expertise of the surgeon and species variability in

experimental studies have contributed to lack of resolution to this question. An interesting technique incorporating principles of both epineurial and funicular repair has been reported by Tsuge and co-workers and has been termed the anchor funicular suture. This technique utilizes placement of horizontal mattress sutures to incorporate both the epineurium and perineurium, thereby aligning major funiculi and incorporating the holding strength of the epineurium. The major disadvantage of this technique is the lack of approximation gained in all funiculi.(2,14,18,40,56,71,102,133,143,144,155)

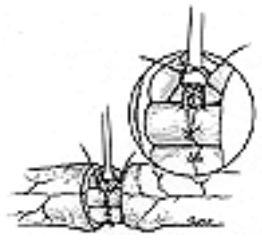

FIG. 65-14 Example of funicular repair. Individual funiculi are sutured within the nerve trunk. Adjunct epineural sutures may or may not be added.

Ideally, a tissue repair technique that uses methods other than sutures would be preferred. All suture material evokes an inflammatory reaction, which can result in production of excess granulation tissue. Recognizing the advantage of sutureless repair, several researchers have evaluated various techniques of repair in the last 4 decades. Several groups reported on the use of plasma clot techniques in repair of transected nerve stumps. The major disadvantages to this technique were technical difficulty and lack of tensile strength in a position of traction to the nerve. Later groups investigated the use of hydrocarbon chain cyanoacrylate cements for tissue repair and found excessive tissue reaction and actual neural element damage that precluded clinical use. The most promising implanted synthetic material was a micropore adhesive tape composed of rayon fabric with a polymer adhesive, which was used as a coaptation splint at the site of surgical repair. Favorable healing with minimal tissue reaction has been reported with this technique. The material is nearly resorbed with little tissue response 28 days after implantation. The major drawback, like that of plasma clot techniques, is the potential for tissue dehiscence under low tension. This factor has prevented widespread clinical use of this repair technique.(19,51-53,76,82,93,139,140,158)

NERVE CUFFS

Two of the major difficulties in achieving optimum surgical results are ingrowth of connective tissue from neighboring regions and prevention of misguided axon migration. Many biologic and synthetic materials have been employed as an ensheathing cuff to shield the surgical site, including tantalum, plasma clots, gold, autografted and homografted blood vessels, muscle, Surgicel, surgical tape, liquid plasticizers, collagen, Millipore and Silastic sheets, and tubes. The most acceptable materials for use have been plasma clot, Millipore, and Silastic.(76,117,135)

Millipore showed promise as a sheath material. With a pore size of 0.45 gun, normal flow of extracellular tissue fluid without tissue migration could be obtained. This aided in meeting nutritional requirements for regenerating epineurial tissue. The prevention of early ingrowth of connective tissue allows for early epineurial continuity to be reformed and a subsequent linear pattern of regeneration by means of the "contract guidance" phenomenon. The disadvantage of Millipore is subsequent dystrophic calcification and fragmentation about 8 weeks after implantation. Micropore tape similar to that used to create sutureless repair was also evaluated as a nerve cuff material. Disruption of the adhesive surfaces has lead to impaired healing and neuroma formation.(29,51-53,86,134)

Currently, silicone rubber compounds (Silastic) are used in clinical settings as a shielding implant. Silicone rubber is relatively inert biologically, flexible, thin-walled, and uniform in diameter. Assorted diameters and lengths are available commercially to be used in a variety of surgical repairs. Silicone rubber is in sterile glass vials and is ready for use.(44,96,97)

Certain guidelines must be followed if a nerve cuff is to be used. The cross-sectional area of the cuff should be two to three times that of the nerve trunk. A cuff smaller than this may create constriction at the anastomotic site as nerve swelling occurs and may predispose to neuroma formation. A larger cuff may

invaginate and Constrict the nerve trunk. Also, ingrowth of connective tissue may predispose to neuroma formation. The length of the cuff should not exceed 8 mm to 10 mm. Greater length may inhibit collateral circulation to the nerve trunk; inadequate length may not provide sufficient shielding at the surgical site. A neuroma may form at the edge of the cuff; however, the surgical site should remain protected (Fig. 65-15) (42-46,151)

Placement of the cuff onto a nerve stump prior to anastomosis is required. The cuff is placed onto a jeweler's forceps or small hemostat. The epineurium is grasped gently and the cuff slipped onto the nerve stump. After the end-to-end anastomosis has been completed, the cuff is centered over the anastomotic site and affixed in position with sutures into the epineurium. One suture at each end of the cuff will provide sufficient anchorage and prevent cuff distortion (Fig. 65-15).(97,134,135)

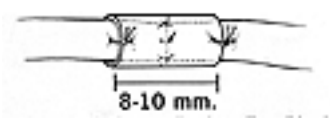

FIG. 65-15 Completed nerve cuff is shown. The cuff length should not exceed 8 mm to 10 mm for optimum results. (Raffe MR Peripheral nerve injuries in the dog, Part II. Compendium on Continuing Education for the Small Animal Practitioner 1:269-276, 1979)

Complications of cuff use result from improper adherence to guidelines concerning sizing of the cuff. A recent report in humans suggests that reevaluation of these guidelines may be required.(22)

NERVE GRAFTS

In extensive injuries, loss of nerve tissue may result in a nerve gap. This gap may be surgically irreducible, and alternative management techniques are required to attain the best potential for return of function. In the past decades, numerous techniques have been used to obtain reapposition of severed nerve ends. These include stretching of the nerve stumps by mobilizing the mesoneurium and surrounding tissues, joint Sexton to shorten the nerve course, transposition of the nerve route, osseous resection and limb shortening, nerve pedicle flaps, gap tubulation with a variety of materials, direct neurotization of muscle, and nerve grafting. All of the above methods have been applied on a clinical basis, with reported success rates dependent upon the species of the patient and expertise of the reporting authors.

Nerve stumps may be stretched to a limited extent to attain apposition, with surgical factors being course of the nerve, vascular supply, and species. Any degree of stretching may decrease the possibility of healing of the nerve. Generally, enough length is present to overcome a gap of 2 cm to 3 cm. Stretching or mobilization in excess of this length endangers the extrinsic vascular supply to the nerve and predisposes to failure of the repair by increased suture line tension. In experimental studies, the rate of regeneration through a suture line under tension was no greater than a properly performed nerve graft. (10,28,38,60,61,63,74,98,100,154)

Tubulation of nerve gaps to promote healing has been proposed by several authors. Use of various biologic and synthetic materials has been reported; however, the success rate varies with author and species. Successful clinical use of this technique has been reported in primates. Alternate procedures to obtain apposition of nerve ends without grafting have met with variable success, dependent upon individual investigators. Further information may be obtained from their reports. (7,11,94,134,149,150)

Any tissue grafting procedure is classified by a donor-recipient nomenclature. An autograft is a graft in which the donor and recipient are the same biologic organism. This graft circumvents the potential for immune stimulation and destruction of the graft, which result in graft rejection. An allograft is a graft in which an immunologically dissimilar donor and recipient of the same species are involved in the graft procedure. Heterografts involve dissimilar species as donor and recipient. The latter two categories predispose the recipient to adverse immune reaction unless cell-mediated immune components are either destroyed during graft processing or suppressed in the recipient host.(8,89)

Much research effort has been expended to develop techniques for suppression of the immune reaction. Currently, freezing, irradiation, and immunosuppressive drugs appear to overcome detrimental effects of homograft and heterograft procedures.

Preparation of a nerve trunk for use later as an allograft or heterograft involves a combination of freezing and irradiation of the donor tissue. The graft is harvested, stripped of excessive tissue, and sealed in a polyethylene bag. This unit is then frozen and stored at -40°C. An electron irradiation source is used to decrease antigenicity and effect tissue sterilization. The graft may then be stored up to 6 months; however, earlier use is encouraged. The literature contains several reports of functional recovery in several species after experimental transection and graft implantation. The major disadvantage to this type of graft preparation is the lack of clinical success in human patients that correlates with animal experimentation. (87-91,152)

Additional suppression of immune reaction noted with the above preparation technique involved the adjunctive use of an immunosuppressive drug, azathioprine (Imuran) [6-(1-methyl-4-nitro-5-imidayolyl) thiopurine] at a dosage of 2 mg/kg/day starting 1 week prior to surgery. The use of this drug in combination with irradiation of heterografts in dog experiments aided in successful return of function in 60% of the subjects at 8 weeks following surgery, with an overall recovery of 100% at 16 weeks. Poorer results were obtained using irradiated grafts without Imuran. Only 40% recovery was noted at 8 weeks, with an overall success rate of 60% at 16 weeks. Unfortunately, experience in humans has not been as rewarding.(85,90,92)

As one may conclude from the above discussion, the technique most widely available for grafting in clinical veterinary medicine probably remains use of an autograft. The question of fresh grafts versus preserved grafts versus predegenerated grafts remains unsolved. From practical viewpoint, fresh grafts are probably the most frequently used in veterinary medicine. Free graft donor sites in the dog are the lateral cutaneous nerve of the thigh and the median nerve of the forearm. In addition, nerve transposition to restore function by anastomosis of a viable proximal stump to the distal stump of another nerve has been documented. The decision to use a nerve graft is based on the diagnosis of irreducible nerve gap at the time of surgery. From the previous discussion and anatomical mapping experiments, it should be realized that funiculi are not distinct subunits but undergo a continuous process of division and integration with neighboring fascicles. The pattern of funiculi changes every 0.5 cm along the course of a peripheral nerve; therefore, unless grafts are united to individual funiculi by microsurgical techniques (cable grafting), interposition of a nerve graft segment does not guarantee perfect axonal migration and cannulation of the distal stump.(9,99,112,131,132,146,159)

To maximize the potential for successful grafting procedures, guidelines have been formulated. The diameter of the graft should closely approximate that of the nerve trunk to be grafted. Inadequate graft diameter may predispose to incomplete axonal regrowth owing to an insufficient number of Schwann tubes provided by the graft. The length of the graft should be 15% to 25% greater than the gap to be spanned. This is to allow for graft shrinkage and to release tension on suture lines at anastomotic sites. (9,63,116,134)

Autograft failures are of several types. Inadequate training and instrumentation can lead to poor results. Failure to match graft diameter and length to the injured nerve may lead to poor functional return. Improper matching of donor and host funiculi at the time of surgery may lead to clinical failure. Tension at either suture line may result in dehiscence and failure. Finally, recognition of biologic aspects of nerve grafting is important. Nerve grafts are similar to other devascularized tissue implants. Regeneration of blood supply must be provided by surrounding tissues to provide nutrition for neurilemmal elements. The pattern of revascularization has been studied and found to proceed axially from surgical sites of the graft and abaxially from the epineurial surface in a centripetal direction. The danger of ischemic necrosis of the central graft core is increased, particularly in a poorly vascularized tissue bed, and could result in destruction of Schwann tubules and failure of axonal regeneration through the graft. This danger is compounded in allografts and heterografts in that patency of Schwann tubes is threatened not only by

vascular supply but the tissue-mediated immune inflammatory response. It is important to recognize that a race between regeneration of axons across a free graft and destruction of patent Schwann tubes is always present.(6,34,36,89,93,108,118,126,132,141)

Recent advances hold promise in the area of nerve grafting. Microsurgical techniques have been used to allow for reconstruction of microvasculature with a free nerve graft. This will allow for live graft tissue and prevent degeneration of the graft due to lack of vascularity. Further work in the area of microsurgery has demonstrated that reversing the polarity of free grafts has no effect. Cable grafting of funiculi may provide faster return of function when predegenerated funicular grafts are used. The use of nerve cuffs at anastomotic sites of nerve grafts remains controversial. Proponents recognize decreased tissue reaction at surgical sites in the early postoperative period. Opponents point to the dangers of shielding vascular ingrowth with degeneration of the graft. Use of cuffs 8 mm to 9 mm in length at the anastomotic sites may yield good results (Fig. 65-16).(29,39,44,62,71,95,97,127,142)

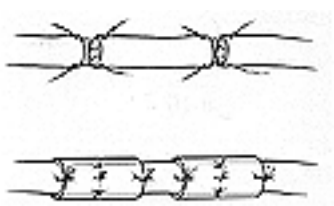

FIG. 65-16 Example of incorporation of nerve graft and cuffs. Care should be exercised to attempt as much funicular alignment as is possible. Technical aspects of graft incorporation do not differ from simple neurorrhaphy.

NERVE GAPS

On occasion, a short irreducible gap may be encountered without immediate provision for graft repair as described above. In these cases, an alternative approach may be to bring the nerve stumps as close as possible in a dry tissue bed and tack the stumps to the tissue bed with two epineurial sutures in each stump. This will create a nerve gap without continuity. This technique may be used for defects not exceeding 1 cm to 2 cm in length. Successful regeneration across nerve gaps has been reported in the dog and in children. However, factors discussed previously must be overcome to obtain success. In addition, increased regeneration time should be expected. (83)

FACTORS INFLUENCING SUCCESS OF SURGICAL REPAIR

It is important to recognize that application of surgical techniques for repair of peripheral nerve injuries only mechanically sets the stage for orderly progression of healing. Ultimate repair and regeneration follow the biologic considerations presented in the first section of this chapter. Unfortunately, it is not uncommon that complications arise and failure occurs in operative repair. Most failures can be attributed to technical errors during surgical repair or to errors in postoperative management. However, certain observations related to biologic considerations in reparative procedures have been documented to influence the course of functional return.

The type of nerve involved can determine the course of healing. Severance of a pure motor or pure sensory nerve is usually accompanied by a less complicated course of recovery. Mixed-function nerves have the potential for transposition of axons during regeneration and therefore the potential for improper end-organ reinnervation, which can result in patient disorientation and a lower level of ultimate functional recovery. The likelihood of this occurring can be minimized at surgery by the careful matching, and in some cases suturing, of the funicular bundles.(21,69,80)

The age of the patient may determine return of function. Younger patients recover more completely and in a shorter time period. This can be attributed to several factors. The length covered in the course of regeneration is shorter owing to shorter limb length. There appears also to be a faster rate of degeneration in distal nerve stumps, which can contribute to a quicker and more satisfactory regrowth of axons. Metabolic processes are already present in a biosynthetic mode, thereby decreasing the lag phase for preosteosynthesis. Finally, adaptability and compensatory sensory and motor reeducation appear to be greater in younger patients.(21,69,80,83)

As discussed above, the level of injury is an important consideration in functional return. Proximal injuries require greater metabolic biosynthesis for functional return. This may exceed the capabilities of the nerve cell body and result in cell death. If cell death occurs in the nerve on a widespread basis, failure of regeneration will result.(21,42,69)

The extent of the injury is also important. Lesions in continuity or those with focal neuroma formation or small gaps will respond better than injuries with irreducible gaps or long length of defect owing to segmental vascular supply, suture line tension, and biologic considerations in nerve grafting. In addition, large deflects interrupt funicular architecture and increase the potential for cross-functional innervation in mixed-function nerves. Appearance of surrounding soft tissue is also important. Clean, vascular beds for regeneration will decrease the potential for neuroma formation and suture line failure related to motion of tendons, joints, and regional bones. Rerouting of the nerve may be required to achieve the best site for regeneration. Application of tension at the suture site in attempting to gain length of the trunk may result in failure of regeneration. Minimum tension will increase the potential for nerve healing. (10,21,103,134)

Associated injury may superimpose additional burdens on nerve regeneration. Polysystemic trauma or massive deep wounds may compromise the vascular supply to superficial and deep soft tissues. Orthopaedic disease may superimpose management complications. Sepsis, scar formation, and contraction wound healing, as well as all the above factors, interfere with physical, medical, and surgical management of the patient. Formulating a rational plan for reconstruction will detail priorities in patient and surgical management for all tissues involved. Recognition of the wound biology for individual tissue types will also aid in formulation of a management plan.(21,55)

Timing of surgical intervention is important in successful management. The merits and indications for immediate versus early secondary repair are familiar to the reader. However, as the interval between the time of injury and surgical intervention increases, irreversible changes occur in the nerve trunk, particularly the distal segment. In addition, neurogenic atrophy and fibrosis of denervated muscle segments complicate the potential for functional recovery. Therefore, early repair of nerve injury is advocated, with the time of repair dependent upon other surgical factors.(21,66,69,117,125,156)

POSTOPERATIVE CARE

Routine closure is performed after nerve repair. If tension at the suture line is evident at the time of surgery, the limb should be splinted or cast in a relaxed position for no less than 2 weeks. After this time, passive motion of the limb may be begun slowly; the goal is to obtain full range of motion by the sixth postoperative weeks (5,105,134 ,135)

The denervated limb must be protected from mutilation until evidence of reinnervation is apparent. Such protection may be provided by padded bandages, splints, or moldable cast material. In some cases, self-mutilation of the denervated portion may be attempted and may be correlated with early stages of axon growth and reinnervation of sensory-deprived areas. Conservative management, accomplished by a protective bandage, side brace, bucket collar, or muzzling, is usually sufficient to prevent further damage.

Serial clinical examination and electrodiagnostic evaluation will provide evidence of the degree of progress. Although 100% function will not be regained, the goal is for restoration of sufficient function to allow for adequate daily locomotion and activity.

ASSESSMENT OF NERVE REPAIR

Ideally the postoperative course of healing proceeds at a rate of 1 mm to 3 mm per day. Given the initial tissue reaction to the surgical procedure, the inflammatory reaction and tissue resorption of the initial injury, and the biochemical changes in the ventral cell body, a delay of several weeks may occur until axoplasmic migration invades the distal stump and maximum rate of regrowth occurs. The level of injury will also determine the ultimate time of recovery, as will other factors described above.(46,69)

In humans, accurate records of regional reinnervation may be elicited from patient observations and physical examination. Migration of an uncomfortable pins and needles sensation (referred to as Tinel's sign) down the affected nerve trunk is a measure of postoperative progress. Unfortunately, veterinary medicine does not have the luxury of patient communication; therefore alternate methods must be used. Classically, qualitative return of sensory function has been measured by dermatome examination and recorded for assessment of functional recovery. Recently, work in the application of electrodiagnostics, namely, evoked nerve potentials (motor nerve conduction velocity), has been used as an early indicator of functional recovery.(89)

Evaluation of nerve conduction velocity has been used to assess axon-end-organ reinnervation. As discussed above, approximately 4 to 6 days after transection, conduction through the distal stump will cease owing to myelin degeneration. The latency time differential will show a value of zero and will continue to do so until reinnervation of the end-organ elements (myoneural junction) occurs in the successfully operated upon patient. (16,119) The time of functional recovery varies, ranging usually from 3 to 6 months, depending upon the level of the lesion and factors in regeneration.(105) The return of compound motor-action potentials may precede return of clinical function and therefore can act as a useful prognostic test.(105) Even with return of clinical function, evaluation of motor unit action potentials in experimental animals before and after transection shows differences in amplitude and composition of the wave signal. These differences probably are due to changes in motor endplate innervation related to nerve regenerations (23,27,37,102,105) Motor nerve conduction velocity can be used as a means of evaluation in nerve graft patients also. Experimental studies indicate a longer time from surgery to initial return of nerve conduction velocity but no difference in ultimate values obtained versus those obtained by direct neurorrhaphy techniques. Intrafunicular grafts appear to promise the best chance for recovery.(18,40,138) Analysis of compressive lesions without severance in humans showed complete functional recovery by 12 to 16 weeks post injury. It is hypothesized that compressive lesions undergo reversible biochemical changes without axon degeneration, which account for earlier return function.(23,37,103) Similarly, incomplete transection of a nerve trunk may reveal the presence of evoked potentials with decreased amplitude of the conduction wave form. By comparing the amplitude of the wave form in the immediate postinjury period with that 10 days later, an estimate of the percentage of surviving motor fibers can be determined.(57) Interpretation of changes in wave form should be tempered by recognizing the factors involved in motor nerve conduction velocity testing. Age, regional temperature, electrode placement, and nutrition may all affect performance during the testing procedure. (16) Sensory nerve conduction velocities may also be used. The principles involved and normal values are presented elsewhere.(3,65)

A new technique for evaluation of nerve regeneration involves somatosensory-evoked cortical potentials. Peripheral nerve stimulation with evidence of cortical recognition of the applied stimulus is used. This technique may serve as the sole or adjunctive diagnostic assessment of the reinnervation process.(4)

It should be recognized that successful peripheral nerve surgery requires an interdisciplinary approach. A working knowledge of anatomy, physiology, pathology, wound biology, and surgery is necessary to obtain the best possible results. Failure to adhere to the principles presented above will increase the likelihood that the surgical procedure will fail and the incidence of detrimental sequelae to the patient will be increased.

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