MANAGEMENT OF PERIPHERAL NERVE INJURIES

Basic Principles of Microneurosurgical Repair

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The management of peripheral nerve injuries has become increasingly sophisticated as our understanding of the pathophysiology of neural degeneration and the basis of neural regeneration has improved. The purpose of this article is to focus on the surgical principles related to nerve injury and repair, forming a bridge between the early articles on physiology and pathophysiology, sensory evaluation, and electrical and radiologic diagnosis and the articles to follow which deal with specific problems of individual branches of the trigeminal nerve.

The management of peripheral nerve injuries has been made enormously easier by the classification of these injuries by Seddon and Sunderland. The details of these classifications have been reviewed recently and updated and are covered again in the second article of this issue. Sir Sidney Sunderland has cataloged in encyclopedic fashion most of the knowledge related to nerves, but this work is certainly not "user friendly." A multiauthored text attempting to coordinate the experience of hand surgeons (general, orthopedic, and plastic surgeons) appeared in 1980. Since then, experimental models for chronic nerve compression, neuroma formation, and neural regeneration, as well as advances in sensibility evaluation, have permitted a coordinated approach to the management of peripheral nerve injuries that has proven effective for both the upper and lower extremities. This systematic approach appeared as a monograph by MacKinnon and Dellon in 1988. It is appropriate at this time to extend these concepts to the maxillofacial region, and the trigeminal nerve in particular.

PERIPHERAL VERSUS CENTRAL NERVE

Is the trigeminal nerve a peripheral nerve? And does it matter? Nerves within the CNS are believed, in general, not to regenerate or to regenerate poorly, whereas those of the peripheral nervous system are known to regenerate (although perhaps not as well as we would wish). If the trigeminal nerve, being a cranial nerve and therefore being closely related to the brain, is not a peripheral nerve, perhaps we need not consider how to reconstruct it! If, however, the trigeminal nerve behaves like a peripheral nerve, then we have the potential to restore its function.

Nerves in the upper and lower extremities are considered peripheral nerves, and so are those of the thorax. The nerves within the...
brain and the spinal cord are classically considered part of the CNS. What are cranial nerves? They connect neurologic areas that are intracranial and extracranial, but they are not all the same. In particular, the optic nerve and the olfactory nerve originate from cell bodies that are considered embryologic extensions of the brain. These nerves are surrounded not by supporting connective tissue sheaths that contain Schwann cells, but by glial cells such as oligodendrocytes. Although the oligodendrocyte does produce myelin, it is immunologically distinct from that produced by Schwann cells. The glial supporting cells of the CNS do not appear to produce the neurotrophic factors necessary to support neural regeneration. Thus, the first and second cranial nerves are in reality part of the CNS, and blindness and anosmia, respectively, result from injury to these two nerves. In contrast, the other cranial nerves originate from cells within the brain and extend as axons into tissues external to the CNS. These other cranial nerves are surrounded by connective tissue supporting structures that contain Schwann cells, which are highly supportive of neural regeneration. These observations have been confirmed by the ingenious models from Aguayo's laboratory, where segments of a peripheral nerve, e.g., the rat sciatic, are inserted into the CNS, e.g., the spinal cord, with the result that axons from the spinal nerve regenerate into and along the sciatic nerve. Thus, the injured trigeminal nerve has the capacity for neural regeneration.

NERVE REGENERATION AS A SOURCE OF PAIN

With chronic compression, the response of the nerve is increased fibrosis of its connective tissue support structures, such as the epineurium and the perineurium, and demyelination of individual nerve fibers. Examples of this type of nerve problem in the maxillofacial region are uncommon, in general, with the exception of facial nerve compression within the temporal bone, i.e., Bell's palsy, and are rare for the trigeminal nerve in particular. Conceivably, following facial trauma there may be blunt or crush type damage to the infraorbital nerve or the mental nerve, or following a radical neck dissection scarring or electrocautery injury to the lingual nerve that might constitute this degree of nerve injury. The appropriate treatment surgically would be an external neurolysis of the involved nerve, which involves surgically separating the nerve from its adherent surrounding tissues. Once separated from surrounding scar, the possibility that significant intraneural scarring may be present must be considered. With microsurgical technique, the epineurium should be opened across the region of compression. If the neural tissue within is soft and is characterized by bands of Fontana, no further intraneural dissection is indicated. Because branches of the trigeminal nerve have as many as 20 fascicles, intraneural neurolysis could be done at this point. Because there would not have been axonal loss with this degree of injury, a period of sensory recovery without discomfort would be expected. The recovery might occur almost immediately following the decompression of the nerve or over a period of 3 to 6 months.

With more prolonged compression, or compression of a more severe degree, e.g., higher pressure, axonal loss occurs. In the maxillofacial region this is most often seen associated with facial fractures in which the infraorbital nerve is directly in the fracture site of the zygoma or the inferior alveolar nerve is directly in the fracture site of the mandible. Neural regeneration is the normal response to a nerve injury severe enough to cause axonal loss. When neural regeneration is blocked or impeded, however, as it would be by the compressive forces of bone at a fracture site, normal regeneration does not occur. Abortive neural regeneration results in the formation of a neuroma, which may or may not be painful.

Complete or incomplete division of the nerve, of course, also results in distal degeneration of the nerve, as described by Waller in 1850. If the two ends of the divided nerve lie in close proximity, as they might within the alveolar canal, where the division might have occurred during a sagittal split osteotomy, the normal process of neural regeneration may result in the correct direction of proximal axonal sprouts into the distal portion of the nerve. Almost always, however, a percentage of the sprouts fail to be directed appropriately and develop into a "suture line" or neuroma-in-continuity. As just suggested, this may well be the result even if a
microsurgical repair of the divided nerve is done. This neuroma, again, may or may not be painful. Furthermore, the process of neural regeneration implies the distal progression of axonal sprouts over time. This often is perceived by the patient as a painful experience, even though its duration is finite, on the order of 3 to 6 months. If neural function appears to be recovering, but significant pain persists at the site of injury, neurolysis of the nerve at this site may be indicated. If neural regeneration appears to be poor and the pain is significant, surgical treatment should proceed as discussed below for the painful neuroma.

TREATMENT OF PAINFUL NEUROMAS

Documentation of maxillofacial pain due to neuromas of the trigeminal nerve exists and is usually found in the setting of retained root tips following dental extraction, fractures, or direct surgical (i.e., iatrogenic) injury, which includes placement of plates, screws, and osteointegrative devices.11, 26

The treatment of the painful neuroma has received a great deal of attention, especially in the extremities. An algorithm to approach this problem has been developed based upon the observations that painful neuromas (1) most often appear in areas where neural regeneration is subjected to tension, movement, and the influence of local neurotrophic factors, (2) have axonal regeneration thwarted by some mechanical problem, e.g., technical misalignment of the two ends of the nerve, fracture site compression, or metal plate or screw interposition, and (3) are influenced by the microenvironment into which they regenerate, i.e., medullary cavity of bone, innervated muscle, or distal nerve with intact end-organs.7, 8, 19

If a distal nerve exists, and especially if appropriate distal target end-organs such as the tongue, lower lip, or cheek skin are present, the recommended surgical treatment is excision of the neuroma, whether it be end bulb, lateral, in-continuity, or some other shape or appearance, and reconstruction of the nerve gap. The usual technique for nerve gap reconstruction is the interposition interfascicular nerve graft as described by Millesi; the technical details are considered below. In the absence of appropriate distal tissue to reinnervate, treatment of pain is best achieved by neuroma resection and implantation of the proximal end of the nerve into an innervated muscle or into the medullary cavity of bone.14 In membranous bones having a virtually nonexistent medullary cavity, an alternative is to place the proximal end of the injured nerve into an adjacent sinus, i.e., frontal sinus for the supraorbital nerve, maxillary sinus for the infraorbital nerve.

Recently, Gregg has reported the results of his treatment of painful neuromas of the trigeminal nerve by a microsurgical technique, which appears to have been a combination of neurolysis, neuroma resection, and nerve repair or graft. He reported relief of pain in about 60% of his patients whose pain was characterized by hyperalgesia or hyperpathia.10 If a patient refuses to have autogenous nerve harvested for the nerve graft donor tissue, or in the case of an iatrogenic injury in which any additional damage is minimized, a nerve conduit of an appropriate alloplastic material is a reasonable alternative.6 Crawley and Dellon have reported such a case for a painful neuroma of the inferior alveolar nerve.4 The use of alloplastic materials in the maxillofacial region is discussed in detail in another article.

NERVE REPAIR AND NERVE GRAFTING

Nerve repair should not be mysterious. The history of nerve reconstruction is fascinating, and several accounts are worth reading.17, 24, 29 The early physicians, such as Hippocrates, did not distinguish nerves from tendons. This distinction was made by Galen in the second century A.D. Nerve repair was at first not attempted because nerve regeneration was not considered a possibility. Partial nerve injury was believed to cause convulsions, and completing the nerve division was the recommended course of action. When attempts to suture a nerve were begun, all types of suture material were utilized, including thread prepared by boiling the tendon from a turtle’s leg and then peeling off strands for suturing. Once it became accepted, in the nineteenth century, that nerve repair was possible, the controversy centered on the source of neural regeneration: Did neural regeneration come from the
Figure 1. The term *trunk graft* referred to the use of a large diameter donor nerve to reconstruct a nerve gap. Because of the large diameter, the revascularization of the center of the graft was poor, leading to collagenization and impeded neural regeneration.

Figure 2. The term *autograft* refers to the donor nerve coming from the same host, and is in contrast to *homograft*, in which the donor is another member of the same species, and *xenograft*, in which the donor is a member of another species. These terms do not refer to the size of the graft or to the technique of placing the graft.
neuron in the spinal cord or dorsal ganglion or did regeneration occur from individual cells, parts of the distal nerve in the periphery? The first nerve graft, done in 1869 by Philipeaux and Vulpian, was done in the maxillofacial region and involved the trigeminal nerve. Their operation was the transfer of a segment of a dog’s lingual nerve into that dog’s hypoglossal nerve. Their intent was to determine if the piece of sensory nerve would reinnervate the tongue muscle, not by serving as a conduit or passive bridging material but by having the cells within it connect to the proximal and distal segments of the motor nerve. Thus Vulpian, who was a preeminent pathologist in Paris, was a reticularist and did not embrace the neuron concept.

The evolution of our current concepts of nerve repair and regeneration has been reviewed recently and strongly supports the approach to tension-free nerve repair, as pioneered by Hano Millesi. Millesi’s own review of his efforts to demonstrate that tension at the nerve suture line produces inferior results by inducing increased collagen formation from the epineurial and perineurial fibroblasts and his courageous introduction of interposition interfascicular grafting into clinical practice are worth reading.

The nomenclature that is most appropriate must be emphasized at this point and represents the recommendations of the International Microsurgery Society (see Glossary). Vessels are anastomosed; nerves are repaired or reconstructed. In parts of the body in which the nerves are larger than they are in the head and neck region, there are appropriate concerns with the number of fascicles present. If a peripheral nerve has several large, identifiable fascicles, these are each surrounded by perineurium and separated from each other with interfascicular or internal epineurium. External or extrafascicular epineurium surrounds the entire group of fascicles. Even though multiple small fascicles can be identified in, for example, the inferior alveolar nerve, all are sensory and only an epineural repair is required.

A nerve graft requires a nerve repair at each end of the graft. The poor prognosis of nerve grafting following World War II came from the use of trunk grafts (Fig. 1). Unfortunately, the nomenclature for grafts has become confused. Grafts taken from an individual and placed into that same individual are autografts (Fig. 2), regardless of how these grafts are arranged or what size they are. In the early nerve grafting experience, grafts were often taken from other individuals (homografts is the appropriate term for these), again regardless of how they were used or in what size, with the term denoting only the biologic source of the graft. A xenograft is a graft from a different species placed into a human. Clearly immunologic rejection accounted for these nerve graft failures. The
trunk grafts were nerve grafts of a large cross-sectional area, such as an ulnar nerve being used to graft a median nerve defect. It is now clear that these grafts failed owing to insufficient blood supply to the inside portions of the donor nerves; neural regeneration failed because it could not proceed through the ischemic, collagenized centers of these large trunk grafts. Some donor nerves were obtained from thinner cutaneous nerves, such as the sural, but these were woven or wrapped around each other to form a “cable” (Fig. 3). Cable grafting was not successful for reasons quite similar to those just discussed; the graft segments in the center of the cable were not easily revascularized from the recipient bed.

Because the early to mid-twentieth century nerve grafting experience was not good, nerve reconstructions were accomplished by widely dissecting the two ends of the damaged nerve, flexing joints, even shortening bone length if necessary, toward the goal of bringing the two ends of the nerve together. Gradually, in the postoperative period, the extremity was mobilized, with scar ultimately being introduced as tension was created at the suture line. Controversy centered on whether to do a primary or a secondary nerve repair. To Millesi goes the credit for proving that placing thin cutaneous nerve segments, and multiple ones if necessary, across a defect in the nerve not only relieves tension at the repair site but also ensures good vascularization of the grafts if they are not bundled together. Thus the present preferred term is an interposition interfascicular nerve graft, in which multiple strands are usually used (Fig. 4). The principles of nerve reconstruction are illustrated with two upper extremity examples (Figs. 5, 6, and 7).

RECOMMENDATIONS FOR TRIGEMINAL NERVE RECONSTRUCTION (APPENDIX)

Primary repair of a nerve injury should be done whenever possible. If the ends of the nerve have been sharply divided and there is no loss of neural tissue, a direct repair is indicated. Because the trigeminal nerve branches are usually polyfascicular and purely sensory, a microsurgical epineurial suture technique is best. Even if there are multiple fascicles, the dissection required to separate these may well cause more scarring than it is worth. Usually two 8-0 or 9-0 nylon sutures are used, or a few more if it is necessary to maintain orientation.
Figure 5. A. Left hand of a 35-year-old woman who 7 years before, sustained a division of the ulnar digital nerve to the thumb when cut in the palm with an oyster knife. She was repaired 3 weeks after the injury, and the surgeon resected the ends of the nerve and believed he could approximate them without "undue" tension. B. Seven years later, she has pain at the repair site that radiates into her thumb, and has no functional sensory recovery at the ulnar tip of her thumb. C, Exploration reveals a neuroma-in-continuity. D, Proximal and distal resection is required until scar-free nerve is encountered, here leaving a gap of 2.5 cm to be reconstructed when the thumb is extended. E, The anterior branch of the medial antebrachial cutaneous nerve is chosen as the nerve graft donor. The posterior branch, which supplies sensation to the elbow, is not taken. F, A close-up view of the nerve graft in place using two 8-0 nylon sutures at each nerve juncture.

If the wound is grossly contaminated or if the mechanism of injury is such that scarring of the proximal and distal ends over the next few weeks is anticipated, then the ends of the nerve should be tagged or approximated to each other with 3-0 nylon. One should plan to return for a delayed nerve repair, or preferably a nerve graft, when soft tissue stabilization has occurred. Blunt, contusive, or avulsive injuries, such as gunshots or motor vehicle accidents, may create this extended nerve injury. If it is unclear whether the nerve is just bruised or will undergo progressive collagenization, a nerve repair may be done primarily, but the patient and family must be informed that if signs of...
Figure 6. A 26-year-old woman had her distal right forearm explored because of pain, thought to be ulnar nerve compression. She had had a childhood injury in that area, thought to have been of no consequence. The first exploration revealed what the surgeon took to be a neural tumor within the ulnar nerve. A, The distal forearm incision is visible, and the sensibility evaluation demonstrated no functional sensation in her ulnar nerve distribution. B, There was wasting of her ulnar innervated intrinsic muscles, and here the clawing is noted. C, Exploration demonstrated the large neuroma-in-continuity related to the childhood injury to her ulnar nerve. Distally, the ulnar artery and the motor and sensory fascicles of the ulnar nerve have been identified. Proximally, the dorsal cutaneous branch of the ulnar nerve has been identified, and it is intact. The proximal ulnar motor and sensory fascicles have been identified topographically to permit the correct positioning of the interposition nerve grafts. D, Harvesting a long length of the medial antebrachial cutaneous nerve with its multiple anterior branches. E, The resected neuroma leaves a gap of 6 cm in the nerve to be reconstructed by the nerve graft on the gauze. F, The multiple interfascicular interposition nerve grafts in place.
neural regeneration do not occur, a secondary nerve reconstruction with a graft will be necessary to restore function.

In the setting of nerve injury that is not acute, such as following dental extraction or fracture plating, the surgical planning must be to replace the damaged segment of nerve with a graft. Too often failure to provide a tension-free reconstruction by means of a graft is the reason for failure to recover function; it is not the fault of the nerve repair, but rather the choice of an inappropriate technique for the reconstruction.

The most appropriate source of donor nerves for the maxillofacial region may not be the head and neck! Traditionally, branches of the cervical plexus have been used, and these, such as the greater auricular nerve, are appropriate in length and in diameter. The disadvantage of the cervical plexus is a scar in what may be thought by the patient to be a cosmetically unacceptable site. Furthermore, an anesthetic ear lobe may be disturbing to someone wearing earings. As noted in Figures 5, 6, and 7, the forearm, and especially the anterior branch of the
medial antebraehial cutaneous nerve, can leave an acceptable donor site scar and often leaves very little donor site sensory disability. Although the sural nerve is probably the most commonly used donor nerve source worldwide, it has the disadvantage of leaving a disfiguring scar and the potential for a painful neuroma near a shoe top region. The sural nerve is certainly a justifiable donor site if a great deal of nerve is required in the maxillofacial region, such as for a cross-facial nerve graft for facial palsy.

SUMMARY

This article presents a brief overview of the principles of management of peripheral nerve injuries. The connective tissue and axonal response to chronic compression may result in abnormal and painful sensory recovery. In more severe nerve compression or in complete or incomplete nerve division, neural degeneration and regeneration may occur. Misdirected axonal sprouts may develop into neuromas, which may or may not be painful. Painful compression injuries without neuroma formation can be managed generally with extraneural and intraneural dissection as dictated by the severity of connective tissue scarring. Painful neuromas are treated by excision with either reconstruction of the nerve gap or implantation of the proximal end of the nerve into an innervated muscle, medullary cavity of bone, or sinus. Finally, nerve repairs must be tension free. If necessary, an interpositional interfascicular graft should be used to achieve a tension-free repair.

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